UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 11,806,526 B2
APPLICATION NO. : 17/012481
DATED : November 7, 2023
INVENTOR(S) : Darrell Wagner et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims

At Claim 1 in Column 42, Line 12, cancel the text beginning with “wherein, the non-car-” and ending with “the implantable electrode” in Column 42, Line 15

At Claim 1 in Column 42, Line 23, after the term “parameter”, insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 14 in Column 43, Line 11, between the text “stimulation” and “protocol”, insert the following text:
--therapy--

At Claim 14 in Column 43, Line 11, after the text “protocol”, insert the following text:
--via the non-cardiac stimulation means for stimulating--

At Claim 16 in Column 43, Line 17, cancel the text beginning with “wherein, the non-cardiac stimulation” and ending with “the implantable electrode” in Column 43, Line 20

At Claim 16 in Column 43, Line 29, after the term “cycle”, insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 22 in Column 44, Line 19, cancel the text beginning with “wherein, the non-cardiac stimulation” and ending with “the implantable electrode,” in Column 44, Line 22

At Claim 22 in Column 44, Line 31, after the term “cycle”, insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

Signed and Sealed this
Twenty-fifth Day of March, 2025

Coke Morgan Stewart
Acting Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE

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PATENT NO. : 11,806,526 B2
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In the Claims

At Claim 1 in Column 42, Line 12, cancel the text beginning with "wherein, the non-car-" and ending with "the implantable electrode" in Column 42, Line 15

At Claim 1 in Column 42, Line 23, after the term "parameter", insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 14 in Column 43, Line 11, between the text "stimulation" and "protocol", insert the following text:
--therapy--

At Claim 14 in Column 43, Line 11, after the text "protocol", insert the following text:
--via the non-cardiac stimulation means for stimulating--

At Claim 16 in Column 43, Line 17, cancel the text beginning with "wherein, the non-cardiac stimulation" and ending with "the implantable electrode" in Column 43, Line 20

At Claim 16 in Column 43, Line 29, after the term "cycle", insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 22 in Column 44, Line 19, cancel the text beginning with "wherein, the non-cardiac stimulation" and ending with "the implantable electrode," in Column 44, Line 22

At Claim 22 in Column 44, Line 31, after the term "cycle", insert the following text:
--, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

Signed and Sealed this
Twenty-fifth Day of March, 2025

Coke Morgan Stewart

Coke Morgan Stewart
Acting Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 03/25/2025

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	

ART UNIT	PAPER NUMBER
3792	

NOTIFICATION DATE	DELIVERY MODE
03/25/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DBCLAW-Docket@dbclaw.com
USPTO.PATENTS@dbclaw.com

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00003

APPLICATION NO.	ISSUE DATE	PATENT NO.
17/012,481	25-Mar-2025	11806526

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
MINNEAPOLIS, MN 55402

ELECTRONIC CERTIFICATE OF CORRECTION NOTIFICATION

Your electronic certificate of correction is now available, and can be accessed via Patent Center at https://patentcenter.uspto.gov.

The electronic certificate of correction is the official certificate of correction under 35 U.S.C. 254 or 255. For more information, please visit https://www.uspto.gov/electronicgrants.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00004

UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
17/012,481	**02/24/2025 05:25:58 PM Z ET**	**I618.118.104**

Title of Invention

STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	11806526
CONFIRMATION #	3270	FILED BY	Paul Grunzweig
PATENT CENTER #	69314274	FILING DATE	09/04/2020
CUSTOMER #	25281	FIRST NAMED INVENTOR	Darrell Wagner
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 4

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
2023-07-06 First Notice of Allowance 17012481.pdf	9	Request for Certificate of Correction	1124 KB
2023-07-21 Second Notice of Allowance 17012481.pdf	6	Request for Certificate of Correction	542 KB
2025-02-24Request_Expedited_Issuance_Cert_Correction.pdf	2	Request for Certificate of Correction	22 KB
2025-02-24SB0044.pdf	2	Request for Certificate of Correction	182 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
2023-07-06 First Notice of Allowance 17012481.pdf	C7378CB1D0AB970B497CF7F6F4A3AAA405D1C254FC4C858C12487D0EE3E7D302BCC09C2EE416BC5DFA590F0035057C116001C5DD3F21A22F4F38E42297B3B798
2023-07-21 Second Notice of Allowance 17012481.pdf	575B4C6F2EC976D3B71B08492D393F24739189C051116D01EE04D22DDFA9F3CFBD073F5B4165AB38703F7E34759521742AE429E87850063697130BF5D7CDD895
2025-02-24Request_Expedited_Issuance_Cert_Correction.pdf	DC02078FB7C8BF0E371F56A20BE7A21EF8E40F7B9A181BCD4B253852EB4F1A0A25F0C57EC2C445F5B3F3A952C38649B62B41646C7BC6FCA47236E7FFE6CAA9FB
2025-02-24SB0044.pdf	D10C9EC9E930FBF92540DCEAE83A9228B9B7B948EEC15554A0CD9E8168CD3DFD468265770B85599E4A8C004E5CC51094B1AD8B3FDB487E5490E7874DFD4D8CE0

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

1st Named Inventor:	Darrell Wagner	Docket No.: I618.118.104
Patent No.:	U.S. 11,806,526	Issued: November 7, 2023
Title:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

REQUEST FOR EXPEDITED ISSUANCE OF CERTIFICATE OF CORRECTION – ERROR ATTRIBUTABLE TO OFFICE

Commissioner for Patents
Office of Data Management Attention: Certificates of Correction Branch
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Per MPEP 1480.01, Applicant hereby request an Expedited Issuance of Certificate of Correction (Error Attributable to Office) with respect to the above-identified Patent.

1) Applicant has filed concurrently with this paper a completed form PTO/SB/44.

2) Attached Supporting Documentation:

a. **Second Notice of Allowance mailed July 21, 2023** (including Corrected Notice of Allowability) including a Corrected Examiner's Amendment at Pages 2-4, which was authorized on 7/14/2023 by the undersigned.

b. **First Notice of Allowance mailed July 6, 2023** (including first/original Notice of Allowability) including an Original Examiner's Amendment at Pages 2-3.

3) Justification:

a. The Corrected Examiner's Amendment in the second Notice of Allowance of July 21, 2023 superseded the Original Examiner's Amendment in the first Notice of Allowance/Allowability mailed July 6, 2023. The Corrected Examiner's Amendment does not include any of the changes made in the Original Examiner's Amendment and therefore the Corrected Examiner's Amendment was intended to completely replace the Original Examiner's Amendment.

(1) Applicant further notes that the Form PTO/SB/44 refers to dependent claim 14 of US 11,806,526 whereas the Corrected Examiner's Amendment (mailed July 21, 2023) includes an amendment to dependent claim 16, which later was re-numbered as claim 14 (as it appeared in US 11,806,526) upon the Office accounting for the cancellation of claims 10 and 15.

b. The Error of the Office in printing U.S. 11,806,526 occurred in failing to implement the most recent Corrected Examiner's Amendment on July 21, 2023 and instead incorrectly printing U.S. 11,806,526 using the Original Examiner's Amendment on July 6, 2023.

c. To the best of Applicant's knowledge, the requested corrected text on Form PTO/SB/44 implements the most recent Corrected Examiner's Amendment while accounting for the changes to the claims made by the Office in its implementation of the original Examiner's Amendment when issuing US 11,806,526, and thereby correcting the Error of the Office.

The error(s) listed on the enclosed Certificate of Correction were made by the U.S. Patent and Trademark Office, and therefore, a fee is not necessary, however, if such fees are required, the Patent Office is hereby authorized to charge Deposit Account No. 500471.

Applicant would appreciate the error(s) to be corrected and an Official Certificate of Correction be issued on an Expedited basis per MPEP 1480.01 and sent to Applicant's representatives.

Respectfully submitted,

DICKE, BILLIG & CZAJA, PLLC

Date: February 24, 2025

PSG:bms

/Paul S. Grunzweig/

Paul S. Grunzweig, Reg. No. 37,143

Direct telephone (612) 767-2504

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

25281 7590 07/06/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	
ART UNIT	**PAPER NUMBER**
3792	

DATE MAILED: 07/06/2023

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

TITLE OF INVENTION: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	10/06/2023

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00009

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25281 7590 07/06/2023
DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

TITLE OF INVENTION: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	10/06/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
LAU, MICHAEL J	3792	607-042000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

☐ Electronic Payment via Patent Center or EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☐ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00010

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 07/06/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	
ART UNIT	PAPER NUMBER
3792	

DATE MAILED: 07/06/2023

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00011

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 17/012,481	Applicant(s) Wagner et al.	
	Examiner MICHAEL J LAU	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 3/2/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-9,11-14 and 16-25 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☑ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☑ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MICHAEL J LAU/ Examiner, Art Unit 3792	/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00013

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Response to Arguments

2. Applicant's arguments, see Pages 7-18, filed 3/2/2023, with respect to claims 1-24 have been fully considered and are persuasive. The rejection of claims 1-24 has been withdrawn.

EXAMINER'S AMENDMENT

3. Authorization for this examiner's amendment was given in an interview with Paul Grunzweig on 6/26/2023.

4. Para. 1 of the Specification is amended as follows:

5. [0001] This application is a continuation of utility application Serial Number 15/562,714, filed September 28, 2017, now US Patent 10,898,709, which is a 371 National Phase Application of PCT Patent Application No. PCT/US20 16/022611, filed March 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed March 19, 2015, all of which are herein incorporated by reference.

6. Claim 1 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac stimulation ~~element to stimulate~~ means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode according to a first stimulation therapy protocol including alternating stimulation periods and non- stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-

stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter.

7. Claim 17 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non- stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.

8. Claim 23 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle.

9. Claim 15 is cancelled.

Allowable Subject Matter

10. Claims 1-9,11-14 and 16-25 are allowed.

Reasons for Allowance

11. The following is an examiner's statement of reasons for allowance: Claims 1-9,11-14 and 16-25 are allowed over the prior art because the Examiner found that none of the cited prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing.

12. Examiner found closest prior art would be Bolea, cited previously, that the asynchronous is used for familiarization (eg. Para. 514-515), but does not use it as a therapy for sleep apnea.

13. Another close prior art found was US 2011/0093032 A1 that discloses asynchronous stimulation with pulse trains (eg. Para. 39, 42, 162, and 171) but does not disclose the duration of each respective stimulation period is based on a reference respiratory-related parameter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J LAU whose telephone number is (571)272-2317. The examiner can normally be reached 8-5:30 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on (571) 272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL J LAU/
Examiner, Art Unit 3792

/CARL H LAYNO/
Supervisory Patent Examiner, Art Unit 3792

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
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www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 07/21/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	

ART UNIT	PAPER NUMBER
3792	

NOTIFICATION DATE	DELIVERY MODE
07/21/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DBCLAW-Docket@dbclaw.com
USPTO.PATENTS@dbclaw.com

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00018

Corrected *Notice of Allowability*	**Application No.** 17/012,481	**Applicant(s)** Wagner et al.	
	Examiner MICHAEL J LAU	**Art Unit** 3792	**AIA (FITF) Status** Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

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/MICHAEL J LAU/ Examiner, Art Unit 3792	/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00019

DETAILED ACTION

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Response to Arguments

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4. Para. 1 of the Specification is amended as follows:

5. [0001] This application is a continuation of utility application Serial Number 15/562,714, filed September 28, 2017, now US Patent 10,898,709, which is a 371 National Phase Application of PCT Patent Application No. PCT/US20 16/022611, filed March 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed March 19, 2015, all of which are herein incorporated by reference.

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stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.

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9. Claim 15 is cancelled.

10. Claim 16 is amended as follows: The device of claim 1, comprising: a processor; and a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation therapy protocol via the non-cardiac stimulation means for stimulating.

Allowable Subject Matter

11. Claims 1-9,11-14 and 16-25 are allowed.

Reasons for Allowance

12. The following is an examiner's statement of reasons for allowance: Claims 1-9,11-14 and 16-25 are allowed over the prior art because the Examiner found that none of the cited prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing.

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/MICHAEL J LAU/

Examiner, Art Unit 3792

/CARL H LAYNO/
Supervisory Patent Examiner, Art Unit 3792

PTO/SB/44 (09-07)
Approved for use through 03/31/2026. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.
(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 11,806,526

APPLICATION NO.: 17/012,481

ISSUE DATE : November 7, 2023

INVENTOR(S) : Darrell Wagner, Quan Ni, John Rondoni, Dave Dieken

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

At Claim 1 in Column 42, line 12, cancel the text beginning with "wherein, the non-car-" and ending with "the implantable electrode" in Column 42, line 15;

At Claim 1 in Column 42, line 23, after the term "parameter", insert the following text:
-- ,wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 14 in Column 43, line 11, between the text "stimulation" and "protocol", insert the following text:
--therapy--

At Claim 14 in Column 43, line 11, after the text "protocol", insert the following text:
--via the non-cardiac stimulation means for stimulating--

At Claim 16 in Column 43, line 17, cancel the text beginning with "wherein, the non-cardiac stimulation" and ending with "the implantable electrode" in Column 43, line 20

At Claim 16 in Column 43, line 29, after the term "cycle", insert the following text:
-- ,wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

At Claim 22 in Column 44, line 19, cancel the text beginning with "wherein, the non-cardiac stimulation" and ending with "the implantable electrode," in Column 44, line 22;

At Claim 22 in Column 44, line 31, after the term "cycle", insert the following text:
-- ,wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode--

MAILING ADDRESS OF SENDER (Please do not use Customer Number below):

DICKE, BILLIG & CZAJA, PLLC | Paul Grunzweig
100 South Fifth Street, Suite 2250
Minneapolis, MN 55402

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0033. Public burden for this form is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. If filing this completed form by mail, send to: **Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013). https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf

Routine uses of the information in this record may include disclosure to: 1) law enforcement, in the event that the system of records indicates a violation or potential violation of law; 2) a Federal, state, local, or international agency, in response to its request; 3) a contractor of the USPTO having need for the information in order to perform a contract; 4) the Department of Justice for determination of whether the Freedom of Information Act (FOIA) requires disclosure of the record; 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record; 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations; 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals; 8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)); 9) the Office of Personnel Management (OPM) for personnel research purposes; and 9) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Additional Uses

Additional USPTO uses of the information in this record may include disclosure to: 1) the International Bureau of the World Intellectual Property Organization, if the record is related to an international application filed under the Patent Cooperation Treaty; 2) the public i) after publication of the application pursuant to 35 U.S.C. 122(b), ii) after issuance of a patent pursuant to 35 U.S.C. 151, iii) if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections, or an issued patent, or iv) without publication of the application or patent under the specific circumstances provided for by 37 CFR 1.14(a)(1)(v)-(vii); and/or 3) the National Archives and Records Administration, for inspection of records.

To Promote the Progress *of Science and Useful Arts*

The Director

of the United States Patent and Trademark Office has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this United States

Patent

grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Katherine Kelly Vidal

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

Maintenance Fee Notice

If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number and timing of the maintenance fees required may be changed by law or regulation. Unless payment of the applicable maintenance fee is received in the United States Patent and Trademark Office on or before the date the fee is due or within a grace period of six months thereafter, the patent will expire as of the end of such grace period.

Patent Term Notice

If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, 365(c), or 386(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00027

US011806526B2

(12) **United States Patent**
Wagner et al.

(10) **Patent No.: US 11,806,526 B2**
(45) **Date of Patent: Nov. 7, 2023**

(54) **STIMULATION FOR TREATING SLEEP DISORDERED BREATHING**

(71) Applicant: **INSPIRE MEDICAL SYSTEMS, INC.**, Golden Valley, MN (US)

(72) Inventors: **Darrell Wagner**, Ham Lake, MN (US); **Quan Ni**, Shoreview, MN (US); **John Rondoni**, Plymouth, MN (US); **Dave Dieken**, Minneapolis, MN (US)

(73) Assignee: **INSPIRE MEDICAL SYSTEMS, INC.**, Golden Valley, MN (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 403 days.

(21) Appl. No.: **17/012,481**

(22) Filed: **Sep. 4, 2020**

(65) **Prior Publication Data**

US 2020/0398051 A1 Dec. 24, 2020

Related U.S. Application Data

(63) Continuation of application No. 15/562,714, filed as application No. PCT/US2016/022611 on Mar. 16, 2016, now Pat. No. 10,898,709.

(60) Provisional application No. 62/135,305, filed on Mar. 19, 2015.

(51) **Int. Cl.**

A61N 1/36	(2006.01)
A61B 5/08	(2006.01)
A61B 5/00	(2006.01)
G16H 20/40	(2018.01)

(Continued)

(52) **U.S. Cl.**

CPC ***A61N 1/3601*** (2013.01); ***A61B 5/0816*** (2013.01); ***A61B 5/0826*** (2013.01); ***A61B 5/113*** (2013.01); ***A61B 5/4818*** (2013.01); ***A61B 5/4848*** (2013.01); ***A61B 5/686*** (2013.01); ***A61N 1/3611*** (2013.01); ***G16H 20/40*** (2018.01);

(Continued)

(58) **Field of Classification Search**

CPC A61N 1/3601; A61N 1/36146; A61N 1/3611; A61N 1/36171; A61B 5/0826; A61B 5/0816; A61B 5/113; A61B 5/4818; A61B 5/4848; A61B 5/686; A61B 5/0205; G16H 20/40

USPC 607/42

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,379,462 A	4/1983	Borkan et al.
4,567,892 A	2/1986	Plicchi et al.
4,630,614 A	12/1986	Atlas

(Continued)

FOREIGN PATENT DOCUMENTS

CN	102548610	7/2012
JP	H0323870 A	1/1991

(Continued)

OTHER PUBLICATIONS

Naples Article—Gregory G. Naples et al., "A Spiral Nerve Cuff Electrode for Peripheral Nerve Stimulation," 8088 IEEE Transactions on Biomedical Engineering, 35. Nov. 1988, No. 11, New York, NY, pp. 905-915.

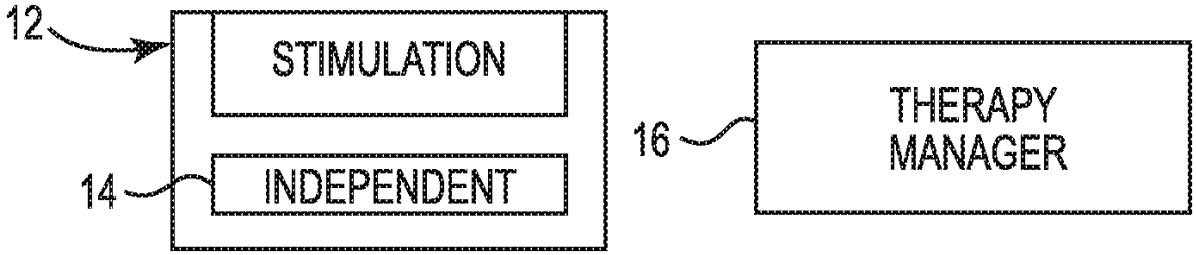
(Continued)

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(57) **ABSTRACT**

A device for treating sleep disordered breathing includes a stimulation element to stimulate an airway-patency-related nerve.

23 Claims, 13 Drawing Sheets



(51) **Int. Cl.**
A61B 5/113 (2006.01)
A61B 5/0205 (2006.01)

(52) **U.S. Cl.**
CPC *A61B 5/0205* (2013.01); *A61N 1/3614* (2017.08); *A61N 1/36146* (2013.01); *A61N 1/36171* (2013.01)

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,813,431	A		3/1989	Brown
4,830,008	A		5/1989	Meer
5,123,425	A		6/1992	Shannon, Jr. et al.
5,133,354	A		7/1992	Kallok
5,134,995	A		8/1992	Gruenke et al.
5,146,918	A	*	9/1992	Kallok A61N 1/3601 607/42
5,148,802	A		9/1992	Sanders et al.
5,158,080	A		10/1992	Kallok
5,167,229	A		12/1992	Peckham et al.
5,174,287	A		12/1992	Kallok et al.
5,178,156	A		1/1993	Takishima et al.
5,190,053	A		3/1993	Meer
5,203,343	A		4/1993	Axe et al.
5,211,173	A		5/1993	Kallok et al.
5,215,082	A		6/1993	Kallok et al.
5,233,983	A		8/1993	Markowitz
5,239,995	A		8/1993	Estes et al.
5,245,995	A		9/1993	Sullivan et al.
5,265,624	A		11/1993	Bowman
5,277,193	A		1/1994	Takishima et al.
5,281,219	A		1/1994	Kallok
5,300,094	A		4/1994	Kallok et al.
5,335,657	A		8/1994	Terry, Jr. et al.
5,344,438	A		9/1994	Testerman et al.
5,351,394	A		10/1994	Weinberg
5,385,144	A		1/1995	Yamanishi et al.
5,388,578	A		2/1995	Yomtov et al.
5,398,682	A		3/1995	Lynn
5,458,137	A		10/1995	Axe et al.
5,483,969	A		1/1996	Testerman et al.
5,485,851	A		1/1996	Erickson
5,522,862	A		6/1996	Testerman et al.
5,524,632	A		6/1996	Stein et al.
5,540,731	A		7/1996	Testerman
5,540,732	A		7/1996	Testerman
5,540,733	A		7/1996	Testerman et al.
5,540,734	A		7/1996	Zabara
5,546,952	A		8/1996	Erickson
5,549,655	A		8/1996	Erickson
5,588,439	A		12/1996	Hollub
5,591,216	A		1/1997	Testerman et al.
5,605,151	A		2/1997	Lynn
5,645,053	A		7/1997	Remmers et al.
5,671,733	A		9/1997	Raviv et al.
5,797,852	A		8/1998	Karakasoglu et al.
5,823,187	A		10/1998	Estes et al.
5,843,135	A		12/1998	Weijand et al.
5,895,360	A		4/1999	Christopherson et al.
5,904,141	A		5/1999	Estes et al.
5,919,221	A		7/1999	Miesel
5,944,680	A		8/1999	Christopherson et al.
5,999,846	A		12/1999	Pardey et al.
6,015,389	A		1/2000	Brown
6,021,352	A		2/2000	Christopherson et al.
6,025,624	A		2/2000	Figura
6,041,780	A		3/2000	Richard et al.
6,099,479	A		8/2000	Christopherson et al.
6,120,441	A		9/2000	Griebel
6,125,290	A		9/2000	Miesel
6,125,291	A		9/2000	Miesel et al.
6,126,611	A		10/2000	Bourgeouis et al.
6,132,384	A		10/2000	Christopherson et al.
6,134,459	A		10/2000	Roberts et al.
6,144,866	A		11/2000	Miesel et al.
6,175,767	B1		1/2001	Doyle, Sr.
6,181,961	B1		1/2001	Prass
6,198,952	B1		3/2001	Miesel
6,223,064	B1		4/2001	Lynn et al.
6,240,316	B1		5/2001	Richmond et al.
6,248,080	B1		6/2001	Miesel et al.
6,249,703	B1		6/2001	Stanton et al.
6,251,126	B1		6/2001	Ottenhoff et al.
6,269,269	B1		7/2001	Ottenhoff et al.
6,307,481	B1		10/2001	Lehrman et al.
6,309,350	B1		10/2001	Tassel et al.
6,314,324	B1		11/2001	Lattner et al.
6,342,039	B1		1/2002	Lynn et al.
6,345,202	B2		2/2002	Richmond et al.
6,361,494	B1		3/2002	Lindenthaler
6,393,325	B1		5/2002	Mann et al.
6,449,507	B1		9/2002	Hill et al.
6,450,957	B1		9/2002	Yoshimi et al.
6,456,866	B1		9/2002	Tyler et al.
6,509,164	B1		1/2003	Guirguis
6,522,928	B2		2/2003	Whitehurst et al.
6,532,388	B1		3/2003	Hill et al.
6,572,543	B1		6/2003	Christopherson et al.
6,574,507	B1		6/2003	Bonnet
6,587,725	B1		7/2003	Durand et al.
6,609,016	B1		8/2003	Lynn
6,609,032	B1		8/2003	Woods et al.
6,629,527	B1		10/2003	Estes et al.
6,641,542	B2		11/2003	Cho et al.
6,645,143	B2		11/2003	Tassel et al.
6,647,289	B2		11/2003	Prutchi
6,651,652	B1		11/2003	Ward
6,654,634	B1		11/2003	Prass
6,665,560	B2		12/2003	Becker et al.
6,666,830	B1		12/2003	Lehrman et al.
6,689,068	B2		2/2004	Hale et al.
6,703,939	B2		3/2004	Lehrman et al.
6,718,208	B2		4/2004	Hill et al.
6,719,708	B1		4/2004	Jansen
6,731,976	B2		5/2004	Penn et al.
6,731,984	B2		5/2004	Cho et al.
6,735,471	B2		5/2004	Hill et al.
6,752,765	B1		6/2004	Jensen et al.
6,770,022	B2		8/2004	Mechlenburg et al.
6,773,404	B2		8/2004	Poezevera et al.
6,805,667	B2		10/2004	Christopherson et al.
6,811,538	B2		11/2004	Westbrook et al.
6,842,647	B1		1/2005	Griffith et al.
6,881,192	B1		4/2005	Park
6,890,306	B2		5/2005	Poezevera
6,893,405	B2		5/2005	Kumar et al.
6,904,320	B2		6/2005	Park et al.
6,907,293	B2		6/2005	Grill et al.
6,928,324	B2		8/2005	Park et al.
6,935,335	B1		8/2005	Lehrman et al.
6,936,011	B2		8/2005	Sheldon
6,964,641	B2		11/2005	Cho et al.
6,978,171	B2		12/2005	Goetz et al.
6,988,498	B2		1/2006	Berthon-Jones et al.
7,025,730	B2		4/2006	Cho et al.
7,041,049	B1		5/2006	Raniere
7,054,692	B1		5/2006	Whitehurst et al.
7,077,810	B2		7/2006	Lange et al.
7,081,095	B2		7/2006	Lynn et al.
7,082,331	B1		7/2006	Park et al.
7,082,336	B2		7/2006	Ransbury et al.
7,087,053	B2		8/2006	Vanney
7,117,036	B2		10/2006	Florio
7,128,717	B1		10/2006	Thach et al.
7,145,461	B2		12/2006	Lehrman et al.
7,149,573	B2		12/2006	Wang
7,155,278	B2		12/2006	King et al.
7,160,252	B2		1/2007	Cho et al.
7,160,255	B2		1/2007	Saadat
7,167,743	B2		1/2007	Heruth et al.
7,174,215	B2		2/2007	Bradley
7,186,220	B2		3/2007	Stahmann et al.
7,187,978	B2		3/2007	Malek et al.
7,189,204	B2		3/2007	Ni et al.
7,195,594	B2		3/2007	Eigler et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,200,440 B2 4/2007 Kim et al.
7,206,635 B2 4/2007 Cho et al.
7,212,862 B2 5/2007 Park et al.
7,214,197 B2 5/2007 Prass
7,252,640 B2 8/2007 Ni et al.
7,269,457 B2 9/2007 Shafer et al.
7,269,459 B1 9/2007 Koh
7,277,749 B2 10/2007 Gordon et al.
7,330,760 B2 2/2008 Heruth et al.
7,336,996 B2 2/2008 Hartley et al.
7,340,302 B1 3/2008 Falkenberg
7,351,208 B2 4/2008 Brodnick et al.
7,366,572 B2 4/2008 Heruth et al.
7,371,220 B1 5/2008 Koh et al.
7,387,608 B2 6/2008 Dunlop et al.
7,395,113 B2 7/2008 Heruth et al.
7,396,333 B2 7/2008 Stahmann et al.
7,398,115 B2 7/2008 Lynn
7,422,015 B2 9/2008 Delisle et al.
7,438,686 B2 10/2008 Cho et al.
7,447,545 B2 11/2008 Heruth et al.
7,454,250 B1 11/2008 Bjorling et al.
7,453,928 B2 12/2008 Lee et al.
7,468,040 B2 12/2008 Hartley et al.
7,469,697 B2 12/2008 Lee et al.
7,473,227 B2 1/2009 Hsu et al.
7,491,181 B2 2/2009 Heruth et al.
7,510,531 B2 3/2009 Lee et al.
7,526,341 B2 4/2009 Goetz et al.
7,542,803 B2 6/2009 Heruth et al.
7,572,225 B2 8/2009 Stahmann et al.
7,590,455 B2 9/2009 Heruth et al.
7,591,265 B2 9/2009 Lee et al.
7,596,413 B2 9/2009 Libbus et al.
7,603,170 B2 10/2009 Hatlestad et al.
7,610,094 B2 10/2009 Stahmann et al.
7,634,315 B2 12/2009 Cholette
7,644,714 B2 1/2010 Atkinson et al.
7,662,105 B2 2/2010 Hatlestad
7,672,728 B2 3/2010 Libbus et al.
7,678,061 B2 3/2010 Lee et al.
7,680,538 B2 3/2010 Durand et al.
7,702,385 B2 4/2010 Moffitt et al.
7,717,848 B2 5/2010 Heruth et al.
7,720,541 B2 5/2010 Stahmann et al.
7,725,195 B2 5/2010 Lima et al.
7,734,340 B2 6/2010 De Ridder
7,734,350 B2 6/2010 Dubnov et al.
7,742,819 B2 6/2010 Moffitt
7,747,323 B2 6/2010 Libbus et al.
7,751,880 B1 7/2010 Cholette
7,775,993 B2 8/2010 Heruth et al.
7,783,353 B2 8/2010 Libbus et al.
7,792,583 B2 9/2010 Miesel et al.
7,809,442 B2 10/2010 Bolea et al.
7,818,063 B2 10/2010 Wallace et al.
7,853,322 B2 12/2010 Bourget et al.
7,881,798 B2 2/2011 Miesel et al.
7,908,013 B2 3/2011 Miesel et al.
7,917,230 B2 3/2011 Bly
7,942,822 B1 5/2011 Koh
7,957,797 B2 6/2011 Bourget et al.
7,957,809 B2 6/2011 Bourget et al.
7,979,128 B2 7/2011 Tehrani et al.
8,016,776 B2 9/2011 Bourget et al.
8,021,299 B2 9/2011 Miesel et al.
8,150,531 B2 4/2012 Skelton
8,160,711 B2 4/2012 Tehrani et al.
8,160,712 B1 4/2012 Freed
8,175,720 B2 5/2012 Skelton et al.
8,233,987 B2 7/2012 Gelfand
8,265,759 B2 9/2012 Tehrani
8,280,513 B2 10/2012 Tehrani
8,718,776 B2 5/2014 Mashiach et al.
8,731,678 B2 5/2014 DeRidder
8,781,587 B2 7/2014 Alt et al.
9,737,708 B2 8/2017 Kobayashi
9,895,540 B2 2/2018 Mashiach
2001/0010010 A1 7/2001 Richmond et al.
2002/0010495 A1 1/2002 Freed et al.
2002/0049479 A1 4/2002 Pitts
2002/0156507 A1 10/2002 Lindenthaler
2003/0093128 A1 5/2003 Freed et al.
2003/0114905 A1 6/2003 Kuzma
2003/0224895 A1 6/2003 Gordon et al.
2003/0163059 A1 8/2003 Poezevera et al.
2003/0195571 A1 10/2003 Bumes et al.
2003/0216789 A1 11/2003 Deem et al.
2004/0015204 A1 1/2004 Whitehurst et al.
2004/0073272 A1 4/2004 Knudson et al.
2004/0111139 A1 6/2004 McCreery
2004/0215288 A1 10/2004 Lee et al.
2004/0230278 A1 11/2004 Dahl et al.
2004/0254612 A1 12/2004 Ezra
2005/0004628 A1 1/2005 Goetz et al.
2005/0010265 A1 1/2005 Baru Fassio et al.
2005/0042589 A1 2/2005 Hatlestad et al.
2005/0043765 A1 2/2005 Williams et al.
2005/0043772 A1 2/2005 Stahmann et al.
2005/0074741 A1 4/2005 Lee et al.
2005/0076908 A1 4/2005 Lee et al.
2005/0080348 A1 4/2005 Stahmann et al.
2005/0080461 A1 4/2005 Stahmann et al.
2005/0081847 A1 4/2005 Lee et al.
2005/0085865 A1 4/2005 Tehrani
2005/0085866 A1 4/2005 Tehrani
2005/0085868 A1 4/2005 Tehrani et al.
2005/0085869 A1 4/2005 Tehrani et al.
2005/0085874 A1 4/2005 Davis et al.
2005/0101833 A1 5/2005 Hsu et al.
2005/0113710 A1 5/2005 Stahmann et al.
2005/0115561 A1 6/2005 Stahmann et al.
2005/0145246 A1 7/2005 Hartley et al.
2005/0148897 A1 7/2005 Cho et al.
2005/0165457 A1 7/2005 Benser et al.
2005/0182457 A1 8/2005 Rope et al.
2005/0209513 A1 9/2005 Heruth et al.
2005/0209643 A1 9/2005 Heruth et al.
2005/0222503 A1 10/2005 Dunlop et al.
2005/0234523 A1 10/2005 Levin et al.
2005/0251216 A1 11/2005 Hill et al.
2005/0261747 A1 11/2005 Schuler et al.
2005/0267380 A1 12/2005 Poezevera
2005/0277844 A1 12/2005 Strother et al.
2005/0277999 A1 12/2005 Strother et al.
2005/0278000 A1 12/2005 Strother et al.
2006/0052836 A1 3/2006 Kim et al.
2006/0058852 A1 3/2006 Koh et al.
2006/0064029 A1 3/2006 Arab (Abboud)
2006/0079802 A1 4/2006 Jensen et al.
2006/0095088 A1 5/2006 De Ridder
2006/0103407 A1 5/2006 Kakizawa et al.
2006/0135886 A1 6/2006 Lippert et al.
2006/0142815 A1 6/2006 Tehrani et al.
2006/0155341 A1 7/2006 Tehrani et al.
2006/0167523 A1 7/2006 Tehrani et al.
2006/0212096 A1 9/2006 Stevenson
2006/0224209 A1 10/2006 Meyer
2006/0241708 A1 10/2006 Boute
2006/0247729 A1 11/2006 Tehrani et al.
2006/0259079 A1 11/2006 King
2006/0264777 A1 11/2006 Drew
2006/0266369 A1 11/2006 Atkinson et al.
2006/0271137 A1 11/2006 Stanton-Hicks
2006/0276701 A1 12/2006 Ray
2006/0293720 A1 12/2006 DiLorenzo
2006/0293723 A1 12/2006 Whitehurst et al.
2007/0021785 A1 1/2007 Inman et al.
2007/0027482 A1 2/2007 Pamis et al.
2007/0038265 A1 2/2007 Tcheng et al.
2007/0150022 A1 6/2007 Ujhazy et al.
2007/0233204 A1 10/2007 Lima et al.
2007/0255379 A1 11/2007 Williams et al.
2008/0009685 A1 1/2008 Kim et al.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2008/0039904	A1	2/2008	Bulkes et al.	
2008/0046055	A1	2/2008	Durand et al.	
2008/0064977	A1	3/2008	Kelleher et al.	
2008/0103545	A1	5/2008	Bolea et al.	
2008/0103570	A1	5/2008	Gerber	
2008/0109046	A1	5/2008	Lima et al.	
2008/0109048	A1	5/2008	Moffitt	
2008/0132802	A1	6/2008	Ni et al.	
2008/0154330	A1	6/2008	Tehrani	
2008/0161878	A1	7/2008	Tehrani	
2008/0294060	A1	11/2008	Haro et al.	
2009/0024047	A1	1/2009	Shipley et al.	
2009/0062882	A1	3/2009	Zhang et al.	
2009/0112116	A1	4/2009	Lee et al.	
2009/0118787	A1	5/2009	Moffitt et al.	
2009/0216293	A1	8/2009	Sasaki et al.	
2009/0234427	A1	9/2009	Chinn et al.	
2009/0287279	A1	11/2009	Parramon et al.	
2009/0308395	A1	12/2009	Lee et al.	
2009/0326408	A1	12/2009	Moon	
2010/0010566	A1	1/2010	Thacker et al.	
2010/0016749	A1	1/2010	Atsma et al.	
2010/0094379	A1	4/2010	Meadows	
2010/0125310	A1	5/2010	Wilson et al.	
2010/0125314	A1	5/2010	Bradley et al.	
2010/0125315	A1	5/2010	Parramon et al.	
2010/0137931	A1	6/2010	Hopper et al.	
2010/0152553	A1	6/2010	Ujhazy et al.	
2010/0174341	A1	7/2010	Bolea et al.	
2010/0198103	A1	8/2010	Meadows et al.	
2010/0198289	A1	8/2010	Kameli et al.	
2010/0228133	A1	9/2010	Averina et al.	
2010/0228310	A1	9/2010	Shuros et al.	
2010/0228317	A1	9/2010	Libbus et al.	
2010/0241195	A1	9/2010	Meadows et al.	
2010/0262210	A1	10/2010	Parramon et al.	
2011/0060380	A1	3/2011	Gelfand et al.	
2011/0093032	A1 *	4/2011	Boggs, II	A61N 1/3611 607/42
2011/0093036	A1	4/2011	Mashiach	
2011/0112601	A1	5/2011	Meadows et al.	
2011/0152706	A1	6/2011	Christopherson et al.	
2011/0152965	A1	6/2011	Mashiach et al.	
2011/0160794	A1	6/2011	Bolea et al.	
2011/0172733	A1	7/2011	Lima et al.	
2011/0264164	A1	10/2011	Christopherson et al.	
2011/0288609	A1	11/2011	Tehrani	
2012/0158091	A1	6/2012	Tehrani et al.	
2012/0192874	A1	8/2012	Bolea	
2012/0232611	A1	9/2012	Sasaki et al.	
2012/0253249	A1	10/2012	Wilson	
2012/0290036	A1	11/2012	Karamanoglu	
2013/0253627	A1	9/2013	Meadows et al.	
2014/0135868	A1	5/2014	Bashyam	
2014/0188185	A1	7/2014	Tesfayesus et al.	
2014/0194793	A1 *	7/2014	Nakata	G01S 13/825 601/48
2014/0228905	A1 *	8/2014	Bolea	A61F 5/566 607/42
2014/0364919	A1	12/2014	Doan	
2015/0039045	A1 *	2/2015	Ni	A61B 5/4836 607/42
2015/0328451	A1	11/2015	Kobayashi	
2016/0022204	A1	1/2016	Mostov	
2016/0193468	A1	7/2016	Rondoni et al.	
2016/0354602	A1	12/2016	Keenan	
2016/0354603	A1	12/2016	Keenan	
2016/0354608	A1	12/2016	Keenan	
2017/0368337	A1	12/2017	Steier	
2020/0147376	A1 *	5/2020	Dieken	A61N 1/36139

FOREIGN PATENT DOCUMENTS

JP	H11514557	12/1999
JP	4960704	8/2008
JP	2010502276	1/2010
JP	2011520526	7/2011
JP	2013509943	3/2013
JP	5636129	12/2015
JP	2015217108 A	12/2015
WO	9749455	12/1997
WO	9750049	12/1997
WO	2006047264	5/2006
WO	2006057734	6/2006
WO	2006102591	9/2006
WO	2007068284	6/2007
WO	2008048471	4/2008
WO	2008027297	6/2008
WO	2009048580	4/2009
WO	2009048581	4/2009
WO	2009135138	11/2009
WO	2009135140	11/2009
WO	2009140636	11/2009
WO	2009140636	3/2010
WO	2010039853	4/2010
WO	2010057286	5/2010
WO	2010059839	5/2010
WO	2010117810	10/2010
WO	2013023218	2/2013

OTHER PUBLICATIONS

Eisele Article—David W. Eisele, MD et al., "Tongue neuromuscular and direct hypoglossal nerve stimulation for obstructive sleep apnea," Otolaryngologic Clinics of North America, Otolaryngol Clin N Am 36 (2003) 501-510 (10 pages).

Goodall Article—Eleanor V. Goodhall et al., "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode," IEEE Transaction on Biomedical Engineering, vol. 43, No. 8, Aug. 1996, pp. 851-856.

Oliven Article—Arie Oliven et al., "Upper airway response to electrical stimulation of the genioglossus in obstructive sleep apnea," Journal of Applied Physiology, vol. 95, pp. 2023-2029, Nov. 2003, www.jap.physiology.org on Sep. 18, 2006. (8 pages).

Schwartz Article—Alan R. Schwartz MD et al., Theraputic Electrical Stimulation of the Hypoglossal Nerve in Obstructive Sleep Apnea, Arch Otolaryngol Headand Neck Surg., vol. 127, Oct. 2001, pp. 1216-1223. Copyright 2001 American Medical Association. (8 pages).

Park, "Preoperative Percutaneous Cranial Nerve Mapping in Head and Neck Surgery," Arch Facial Plast Surg/vol. 5, Jan./Feb. 2003, www.archfacial.compages 86-91.

Stanescu, "Expiratory flow limitation during sleep in heavy snorers" European Respiratory Journal, 1996, 9, 2116-2121.

J Sleep Res., "Hypoglossal nerve stimulation improves obstructive sleep apnea: 12-month outcomes" Journal, 2014, 23, 77-83.

The Laryngoscope, "Implanted Upper Airway Stimulation Device for Obstructive Sleep Apnea" Journal, 2012, 122, 1626-1633.

* cited by examiner

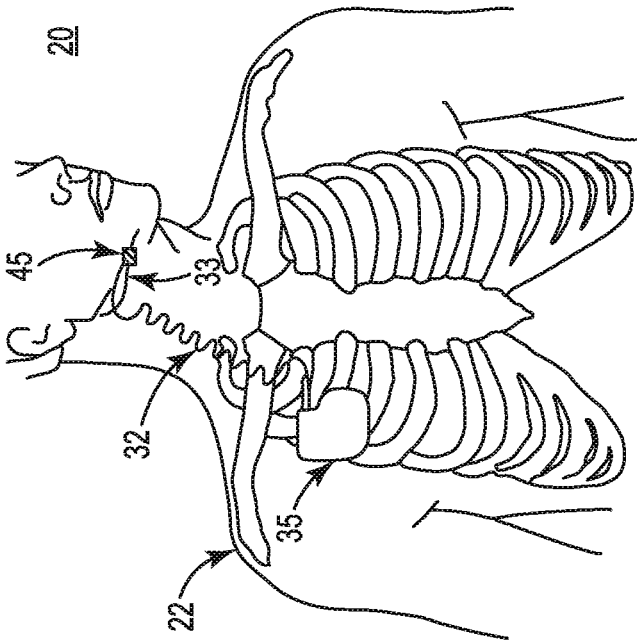


Fig. 2A

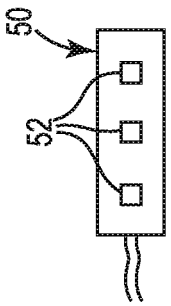


Fig. 2E



Fig. 1B

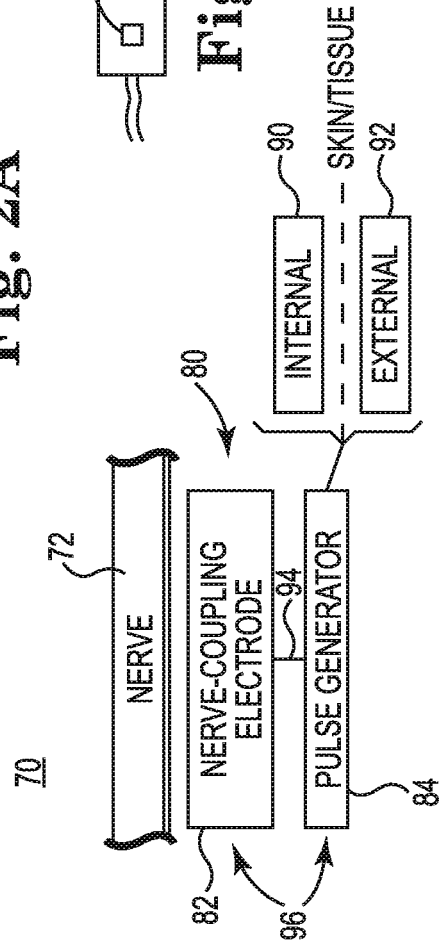


Fig. 2D

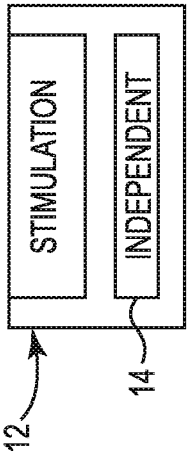


Fig. 1A

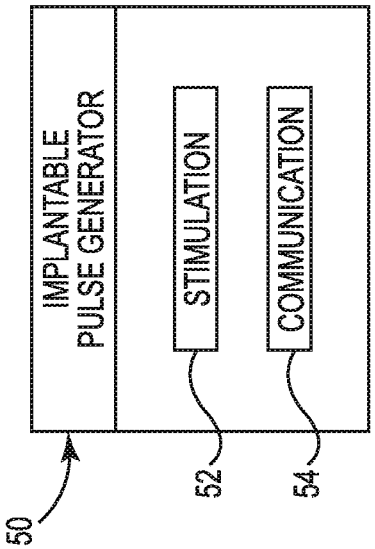


Fig. 2B

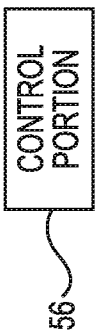


Fig. 2C

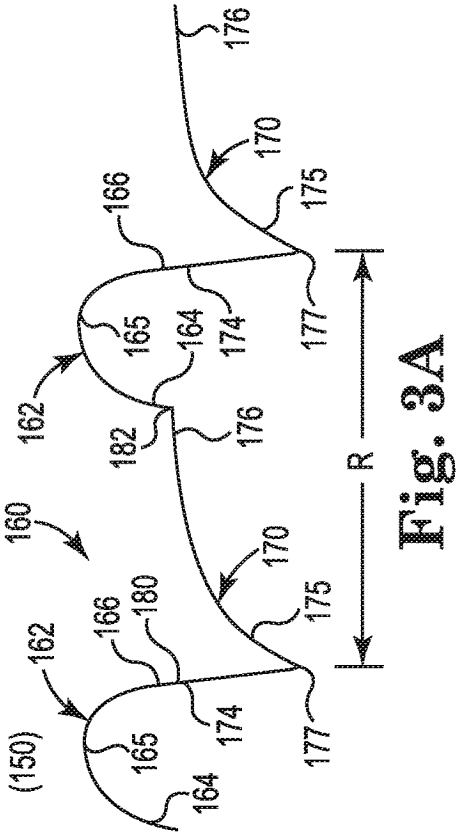

160
(150)
162
166
180
165
164
174
177
175
170
176
182
R

Fig. 3A

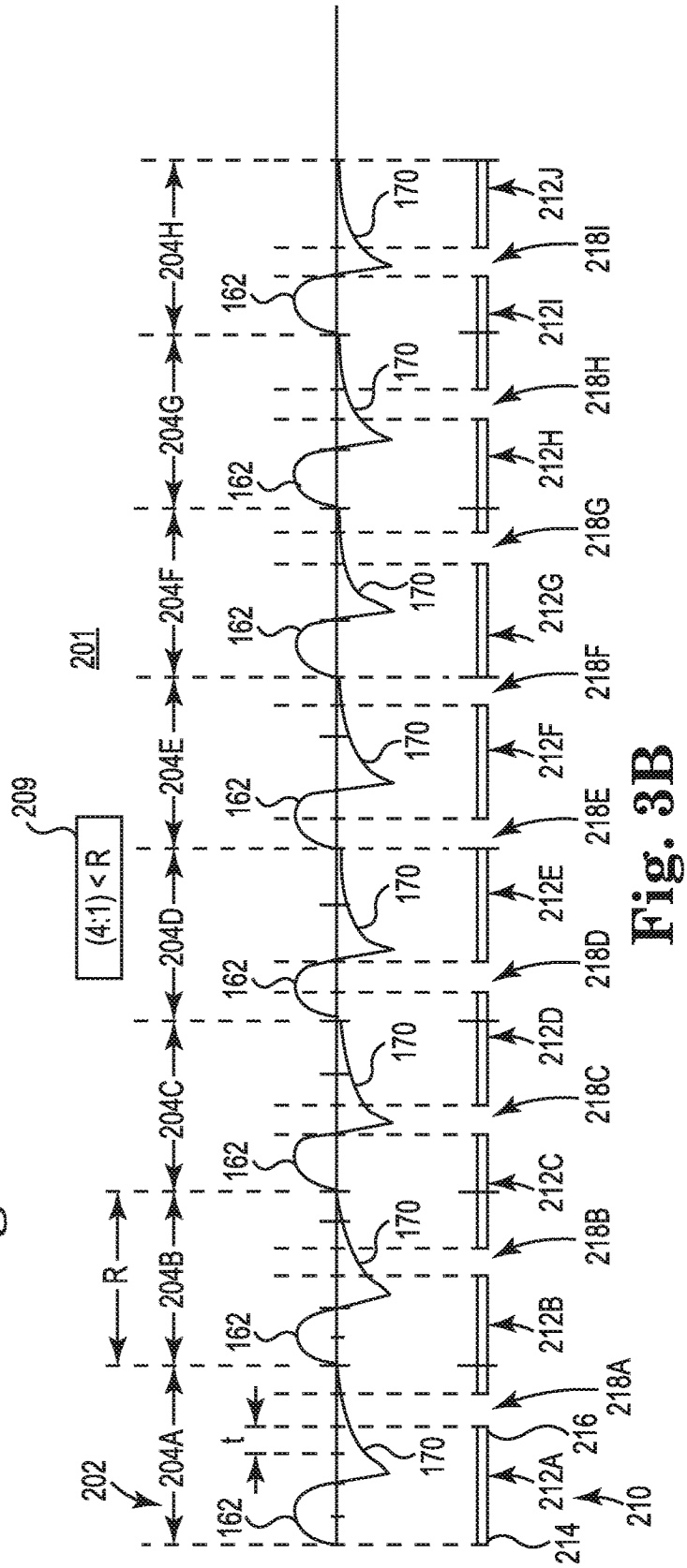

209
(4:1) < R
201
R
t
202
204A
204B
204C
204D
204E
204F
204G
204H
162
170
212A
212B
212C
212D
212E
212F
212G
212H
212I
212J
214
216
218A
218B
218C
218D
218E
218F
218G
218H
218I
210

Fig. 3B

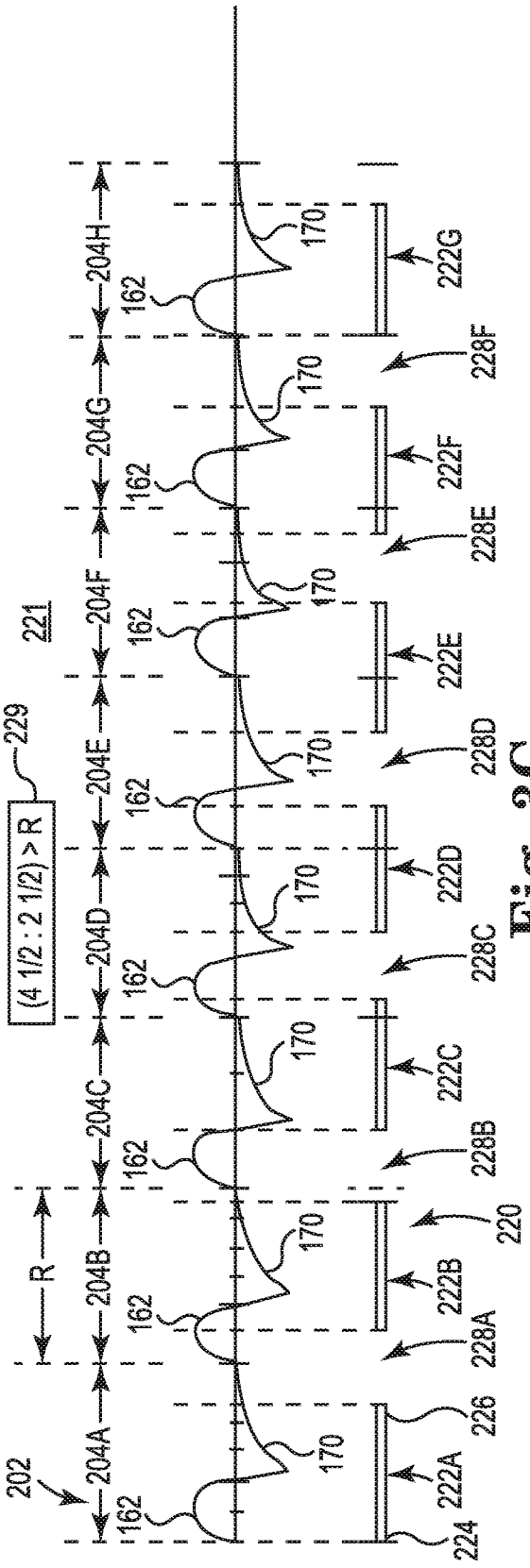

202
204A
204B
204C
204D
204E
204F
204G
204H
R
(4 1/2 : 2 1/2) > R
229
221
162
170
222A
222B
222C
222D
222E
222F
222G
224
226
228A
228B
228C
228D
228E
228F
220

Fig. 3C

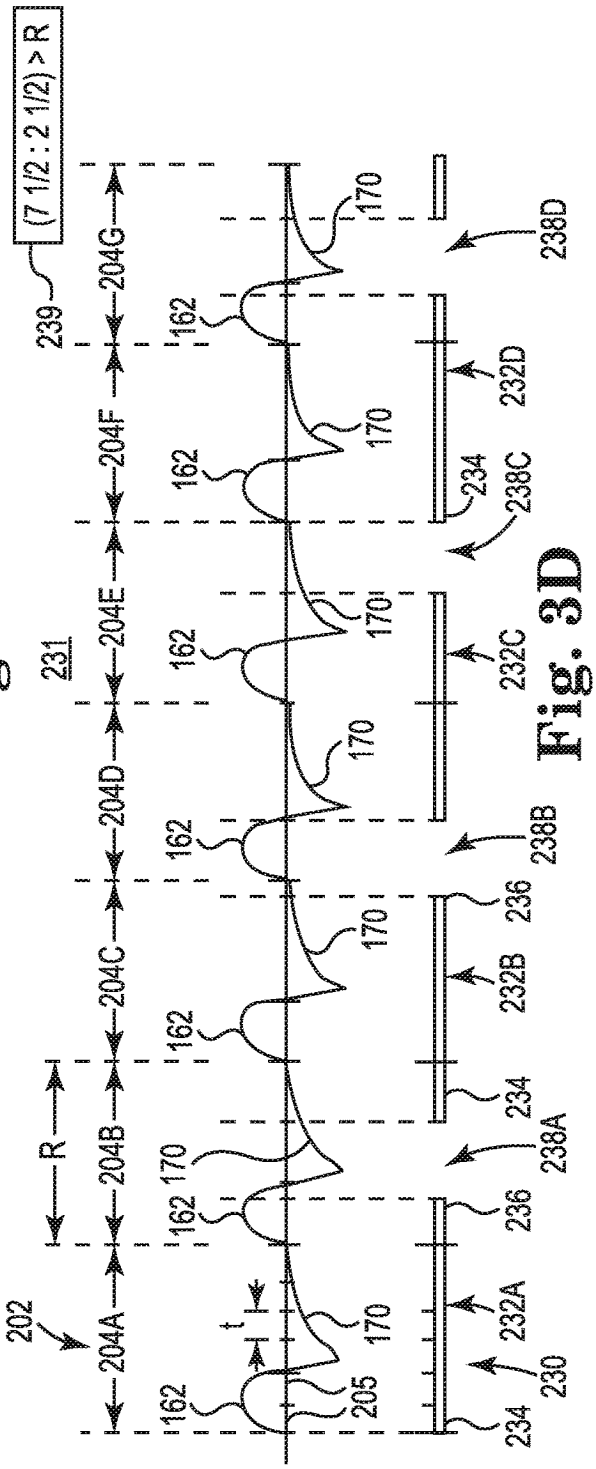

202
204A
204B
204C
204D
204E
204F
204G
R
(7 1/2 : 2 1/2) > R
239
231
162
170
205
t
230
232A
232B
232C
232D
234
236
238A
238B
238C
238D

Fig. 3D

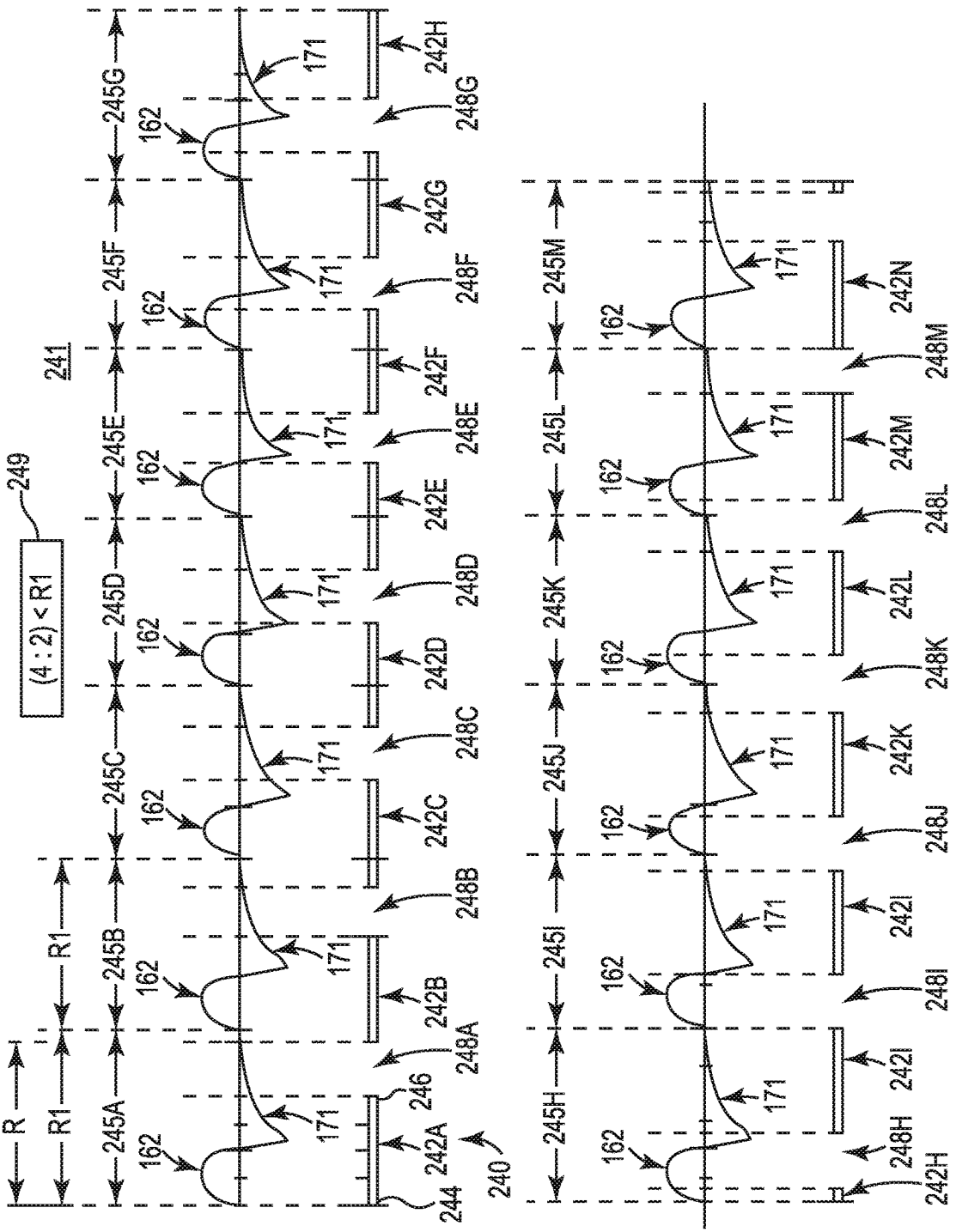

R
R1
R1
245A
245B
245C
245D
245E
245F
245G
245H
245I
245J
245K
245L
245M
241
249
(4 : 2) < R1
162
171
242A
242B
242C
242D
242E
242F
242G
242H
242I
242K
242L
242M
242N
244
246
240
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248J
248K
248L
248M

Fig. 3E

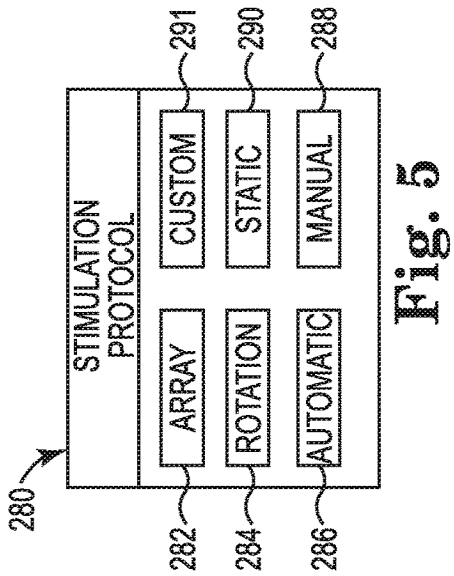


Fig. 5

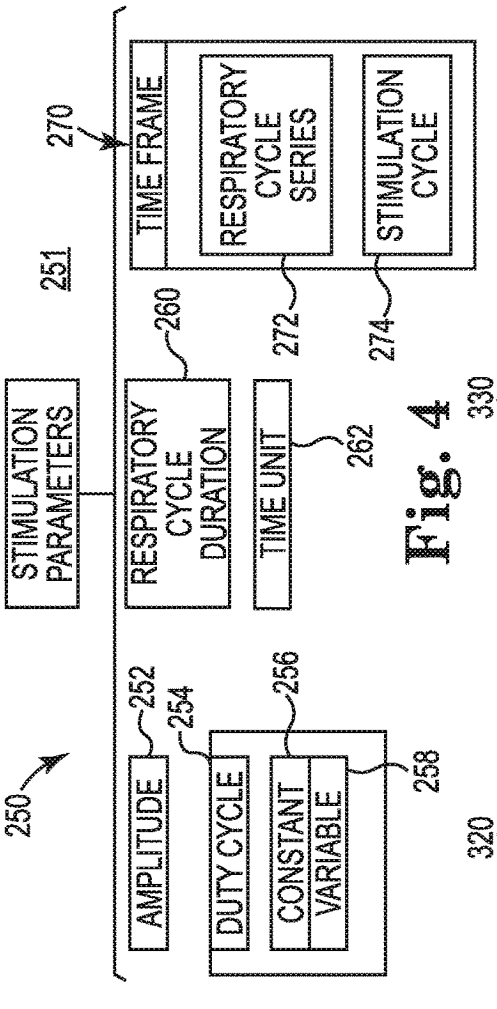


Fig. 4

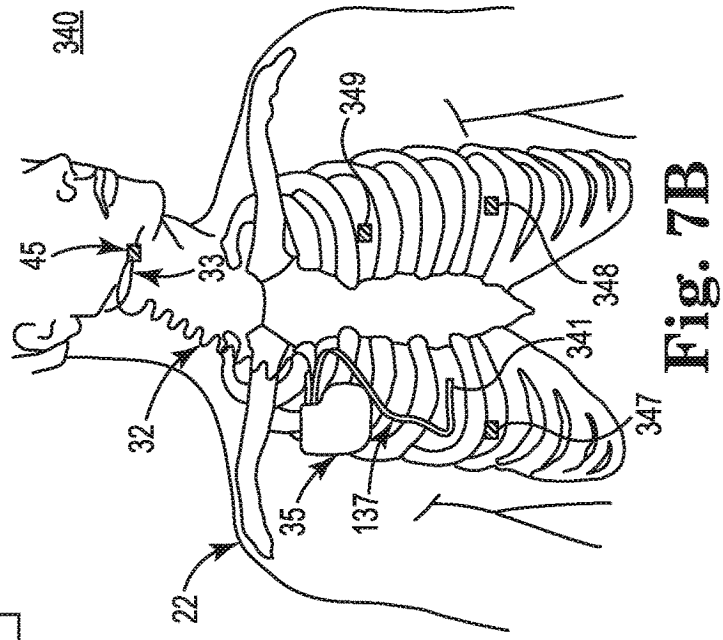


Fig. 7B

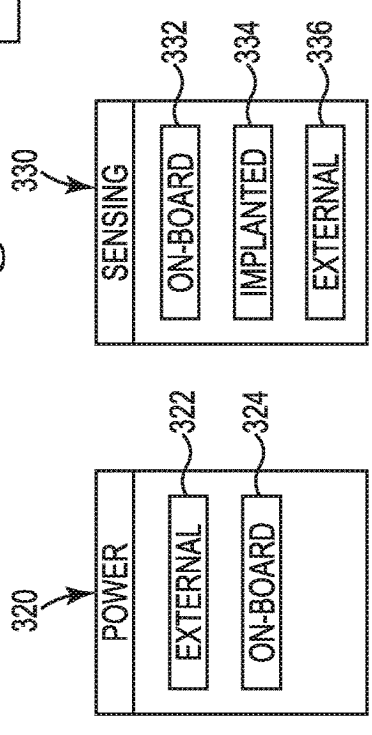


Fig. 7A

Fig. 6

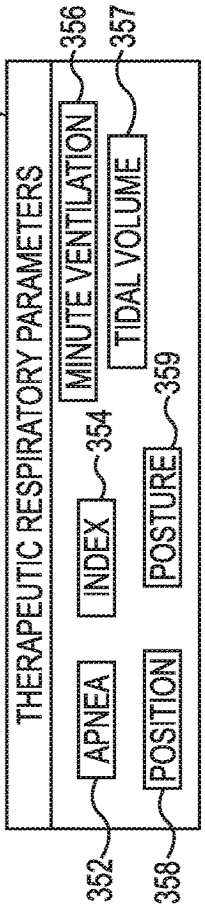


Fig. 8

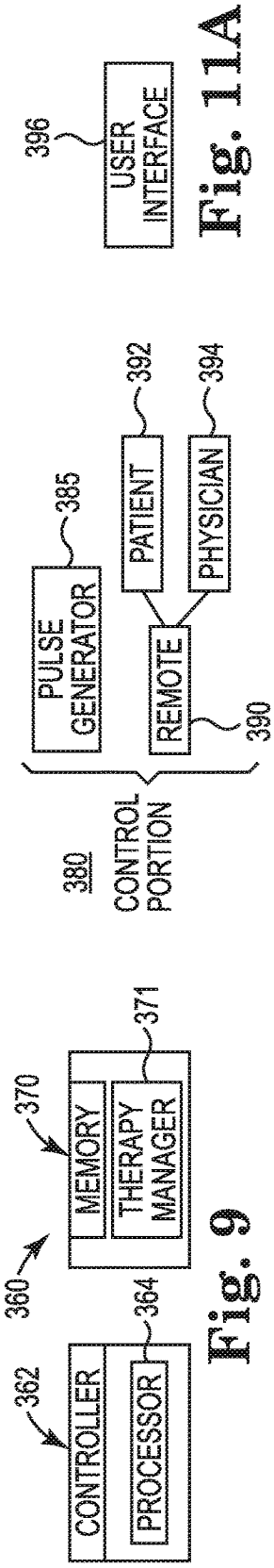


Fig. 9

Fig. 10

Fig. 11A

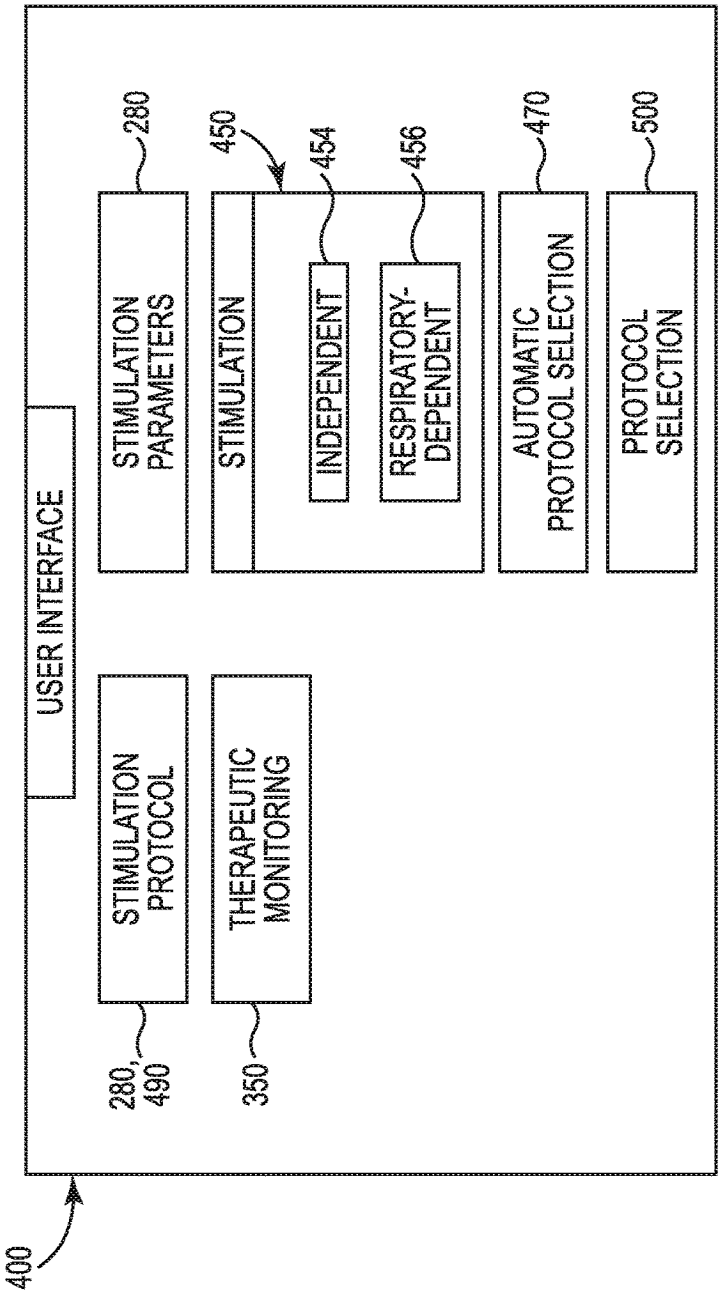


Fig. 11B

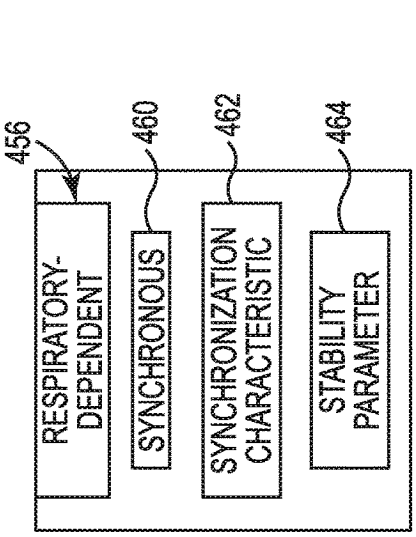


Fig. 13

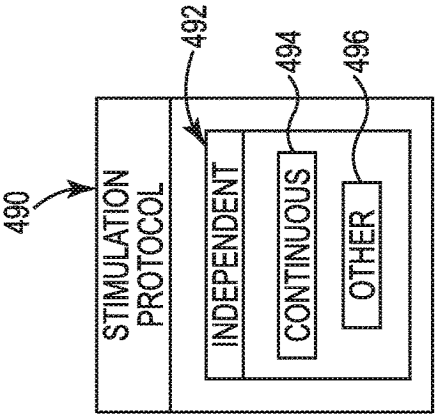


Fig. 15A

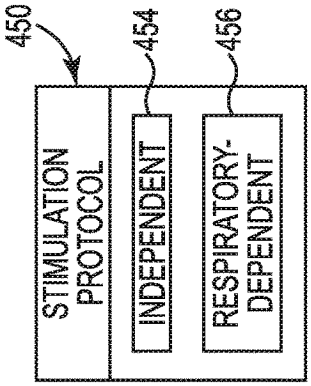


Fig. 12

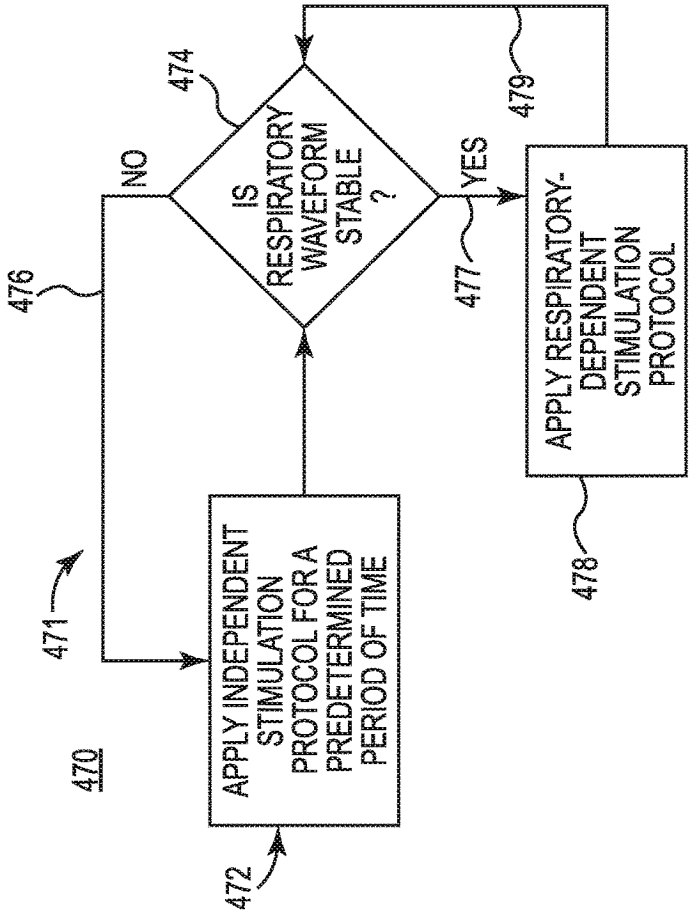


Fig. 14

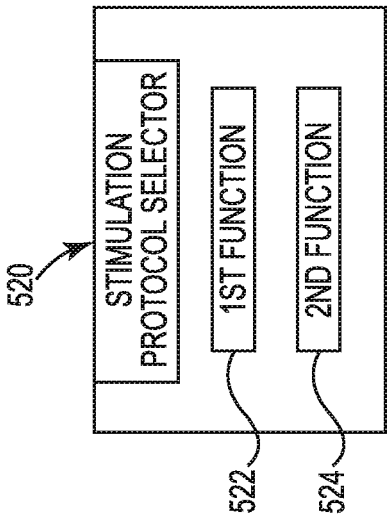


Fig. 15C

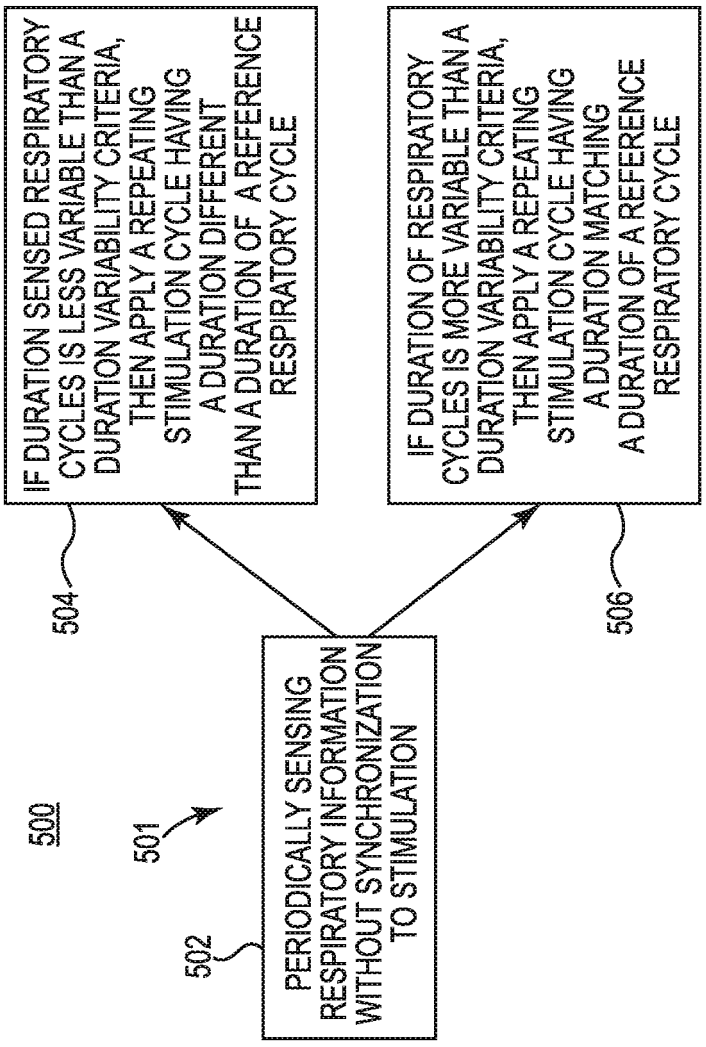


Fig. 15B

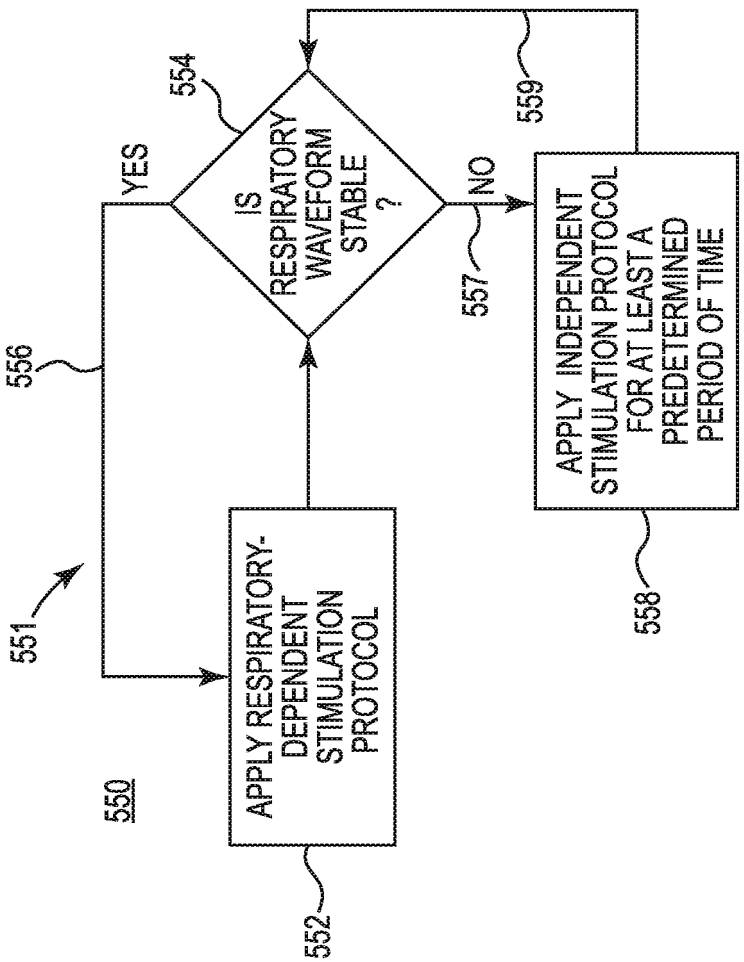

550
551
552
554
556
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558
559
IS RESPIRATORY WAVEFORM STABLE ?
YES
NO
APPLY RESPIRATORY-DEPENDENT STIMULATION PROTOCOL
APPLY INDEPENDENT STIMULATION PROTOCOL FOR AT LEAST A PREDETERMINED PERIOD OF TIME

Fig. 15D

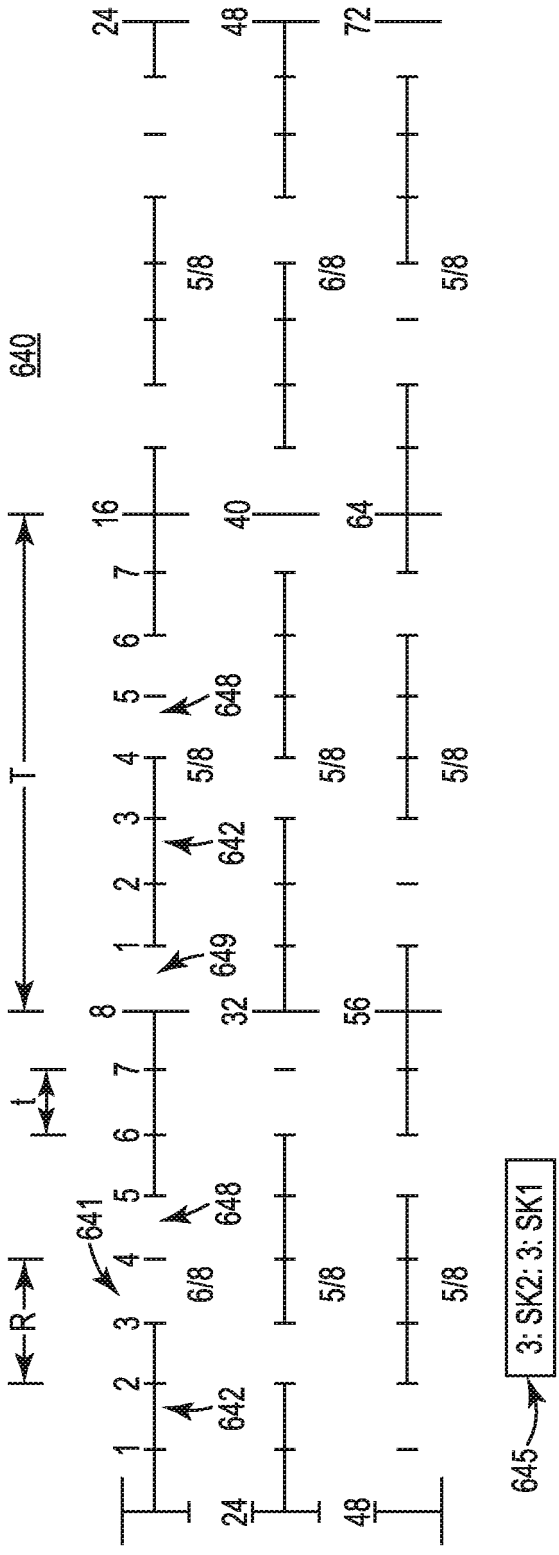

640
T
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642
648
649
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6/8
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64
72
645
3: SK2: 3: SK1

Fig. 16A

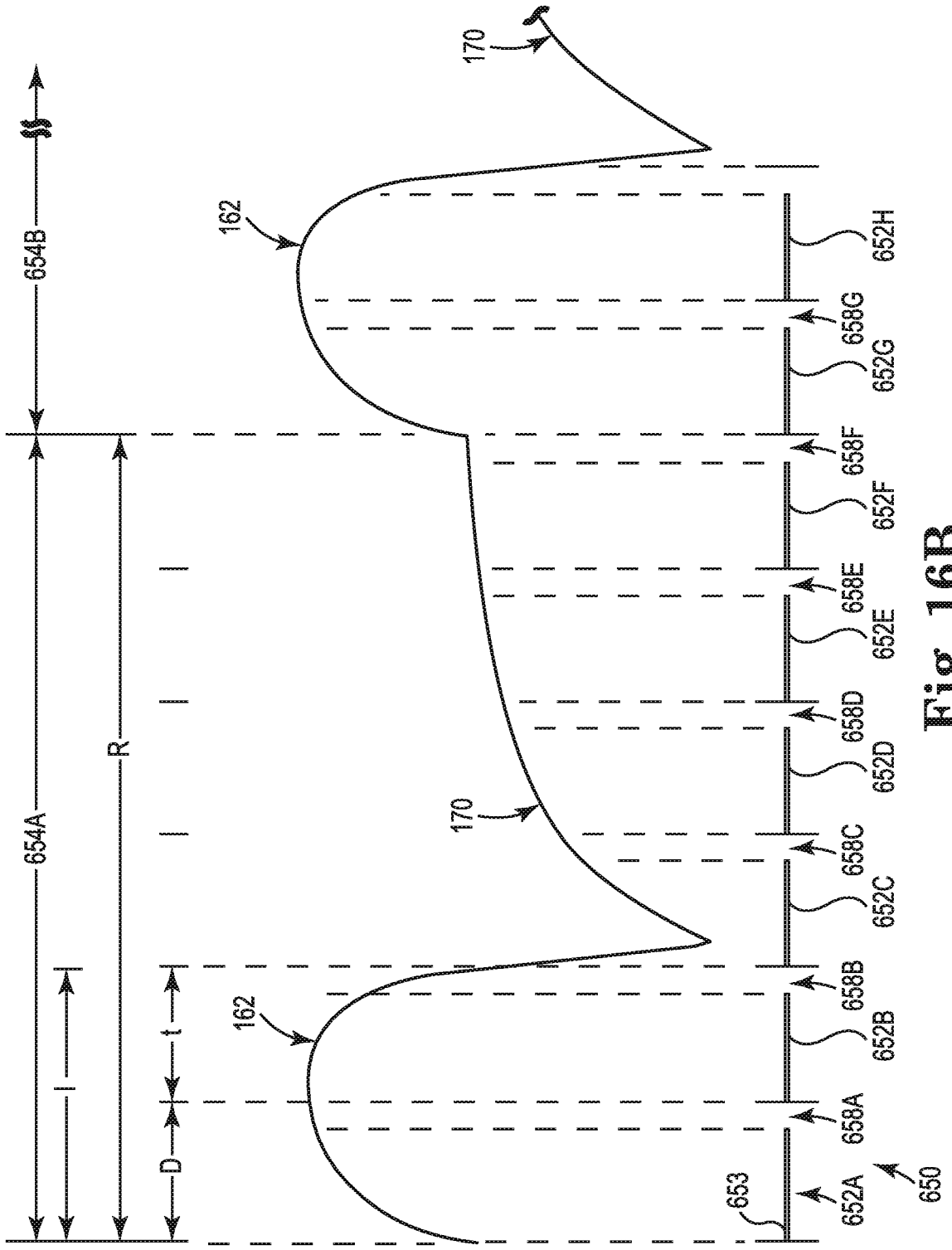

654B
654A
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162
170
652A
652B
652C
652D
652E
652F
652G
652H
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658F
658G
653
650

Fig. 16B

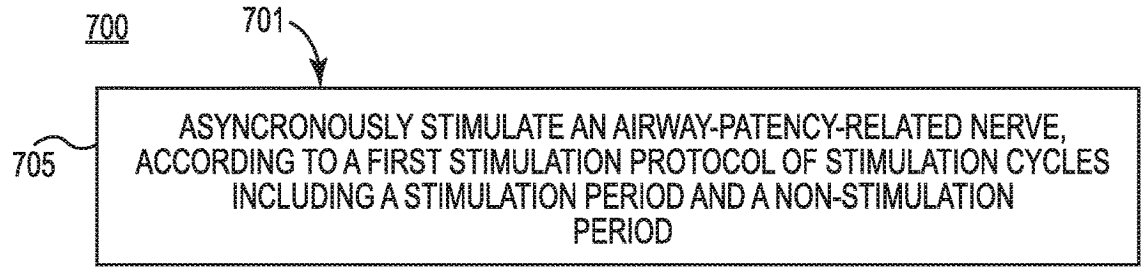


Fig. 17A

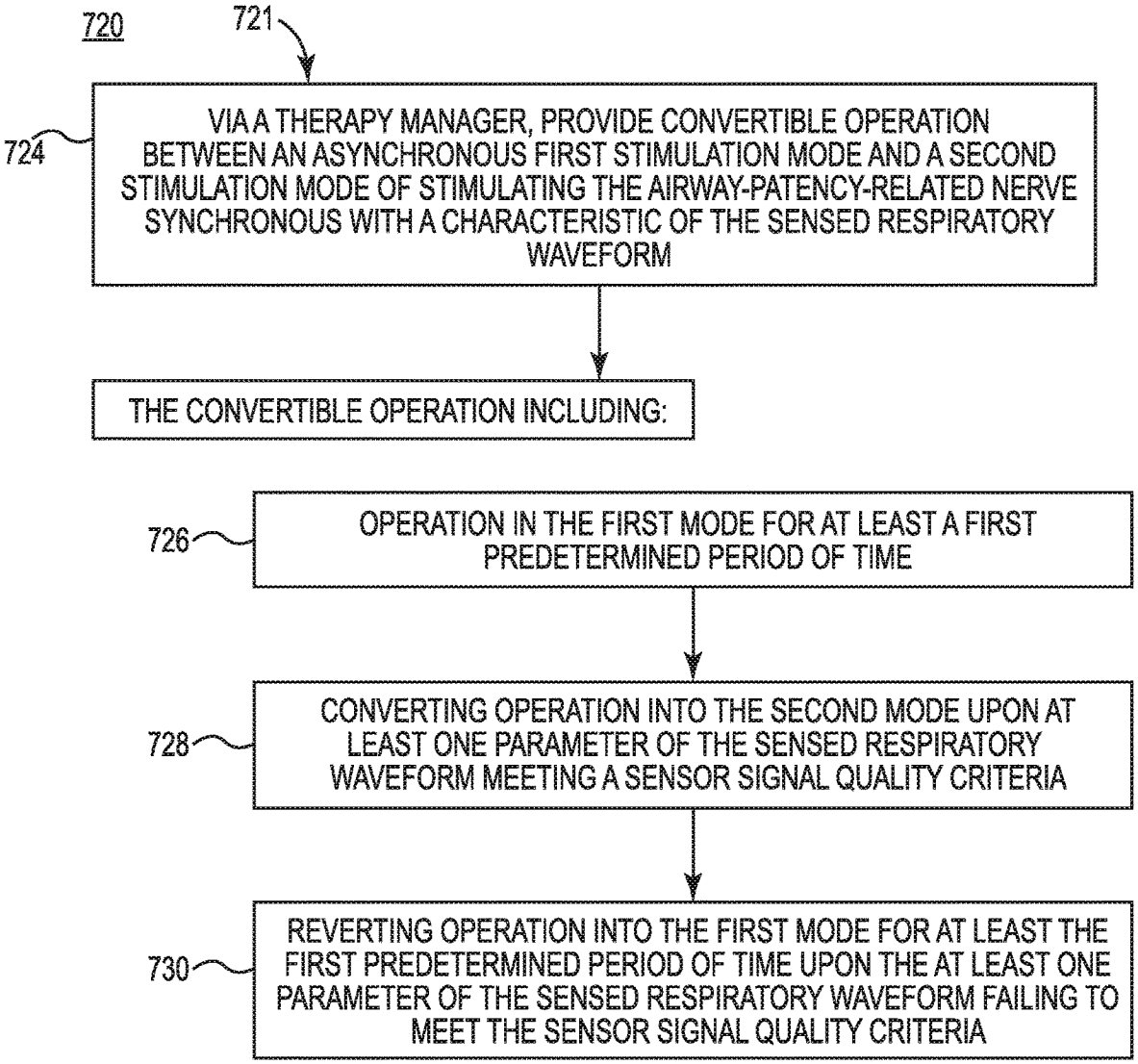


Fig. 17B

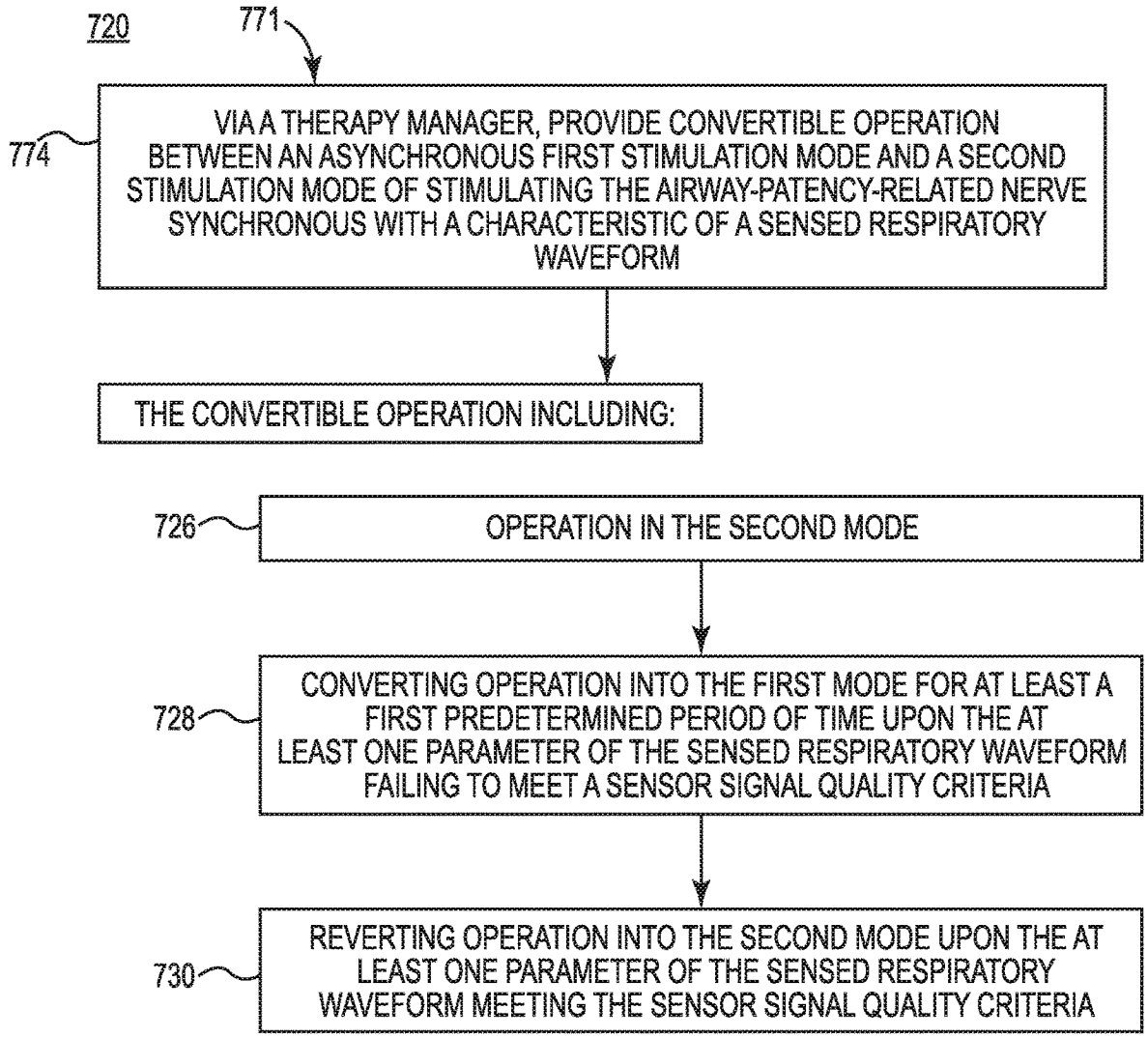


Fig. 17C

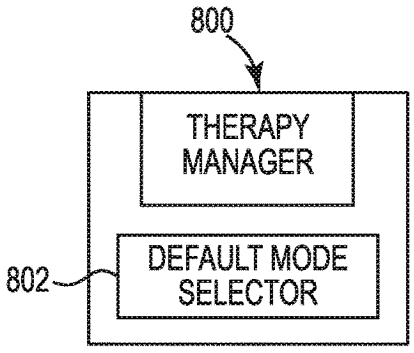


Fig. 18

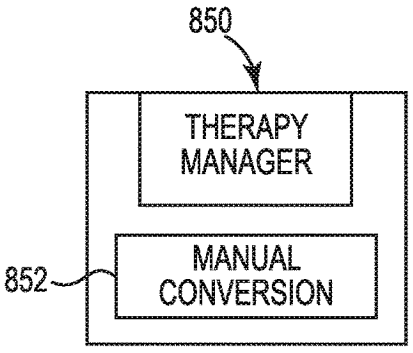


Fig. 19

STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of utility application Ser. No. 15/562,714, filed Sep. 28, 2017, now U.S. Pat. No. 10,898,709, which is a 371 National Phase Application of PCT Patent Application No. PCT/US20 16/022611, filed Mar. 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed Mar. 19, 2015, all of which are herein incorporated by reference.

BACKGROUND

Targeted electrical stimulation of a nerve shows great promise in a number of therapies. In one example, such stimulation of a hypoglossal nerve is known to alleviate obstructive sleep apnea by helping to maintain and/or restore upper airway patency.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1**A is a block diagram schematically illustrating a stimulation element, according to one example of the present disclosure.

FIG. **1**B is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

FIG. **2**A is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient, according to an example of the present disclosure.

FIG. **2**B is a block diagram schematically illustrating an implantable pulse generator, according to one example of the present disclosure.

FIG. **2**C is a block diagram schematically illustrating a control portion for the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **2**D is block diagram schematically illustrating a stimulation system, according to one example of the present disclosure.

FIG. **2**E is top view schematically illustrating a stimulation electrode, according to one example of the present disclosure.

FIG. **3**A is a diagram schematically illustrating a respiratory cycle in one example breathing pattern, according to one example of the present disclosure.

FIG. **3**B is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**C is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**D is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **3**E is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

FIG. **4** is a block diagram schematically illustrating a plurality of stimulation parameters, according to one example of the present disclosure.

FIG. **5** is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **6** is a block diagram schematically illustrating power source components of the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **7**A is a block diagram schematically illustrating a sensing element of the at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **7**B is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient and including sensing elements, according to an example of the present disclosure.

FIG. **8** is a block diagram schematically illustrating therapeutic respiratory parameters, according to one example of the present disclosure.

FIG. **9** is a block diagram schematically illustrating a control portion of an at least partially implantable stimulation system, according to one example of the present disclosure.

FIG. **10** is a block diagram schematically illustrating aspects of a control portion, according to one example of the present disclosure.

FIG. **11**A is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

FIG. **11**B is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

FIG. **12** is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **13** is a block diagram schematically illustrating a respiratory-dependent stimulation element, according to one example of the present disclosure.

FIG. **14** is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **15**A is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

FIG. **15**B is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **15**C is a block diagram schematically illustrating a stimulation protocol selector, according to one example of the present disclosure.

FIG. **15**D is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

FIG. **16**A is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

FIG. **16**B is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

FIG. **17**A is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **17**B is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **17**C is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

FIG. **18** is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

FIG. **19** is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

DETAILED DESCRIPTION

In the following Detailed Description, reference is made to the accompanying drawings, which form a part hereof, and in which is shown by way of illustration specific examples in which the invention may be practiced. In this regard, directional terminology, such as "top," "bottom," "front," "back," "leading," "trailing," etc., is used with reference to the orientation of the Figure(s) being described. Because components of examples can be positioned in a number of different orientations, the directional terminology is used for purposes of illustration and is in no way limiting. It is to be understood that other examples may be utilized and structural or logical changes may be made without departing from the scope of the present disclosure. The following detailed description, therefore, is not to be taken in a limiting sense.

At least some examples of the present disclosure are directed to methods of treating obstructive sleep apnea via applying nerve stimulation. By doing so, upper airway patency may be maintained and/or increased while preventing or minimizing collapse of the upper airway. At the same time, by using targeted stimulation, one can limit the overall volume of stimulation applied to a given nerve or set of nerves.

In some examples, nerve stimulation is applied during a treatment period. In some examples, a treatment period corresponds to the patient engaging in sleeping behavior, and during which sleep disordered breathing is to be avoided. The treatment period can be manually initiated by the patient or automatically initiated by a device that applies the nerve stimulation.

In some examples, an at least partially implantable stimulation system for treating sleep disordered breathing includes an independent stimulation element to stimulate an airway-patency-related nerve without synchronization relative to characteristics of respiratory wave form. Accordingly, in some examples, the independent stimulation element forms part of a system that omits any sensing elements. In some examples, the stimulation element comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator. In some examples, the pulse generator is implantable and in some examples, the pulse generator is external to the patient's body. In some examples, the stimulation element is in communication with a therapy manager or is incorporated within a therapy manager. In some examples, the therapy manager is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

In some examples, the at least partially implantable stimulation system includes sensing element(s) to receive and/or obtain respiratory information but that information is not employed to trigger stimulation by synchronizing the stimulation relative to characteristics of the sensed respiratory waveform. Rather, in these examples, the sensed respiratory information is used to detect and evaluate sleep disordered breathing behavior. When the detected behavior meets or exceeds a severity threshold, the therapy manager generally activates stimulation via the independent stimulation element. In some examples, the severity threshold is based on at least a frequency and/or an intensity of apneic events. In some instances, the severity threshold also may be expressed as an obstructive sleep apnea (OSA) burden, i.e. a quantity and/or intensity of apneas which are occurring. In some examples, the severity threshold or OSA burden is expressed as an Apnea-Hypopnea Index (AHI). However, despite the respiratory sensing occurring in these examples, the stimulation is performed via a protocol that remains independent of the particular characteristics of a real-time sensed respiratory waveform. In other words, individual stimulation periods are not triggered and/or synchronized relative to respiratory characteristics, such as the inspiratory phase.

In some examples, the independent stimulation element is configured to asynchronously stimulate an airway-patency-related nerve, according to a first stimulation protocol independent of sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. In some instances, the first stimulation protocol is referred to as being independent because the first stimulation protocol is not synchronized relative to sensed respiratory information. In some instances, the independence of the first stimulation protocol also may be referred to as being an asynchronous stimulation protocol because the first stimulation protocol is not synchronized relative to the sensed respiratory information.

In some examples, each stimulation period within a stimulation cycle includes continuous stimulation. In some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. **56** in FIG. **2**C).

In some examples, during the above-described continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

In some examples, the stimulation period has a minimum duration equal to or greater than an inspiratory reference. In some examples, the inspiratory reference corresponds to a duration of an inspiratory phase of a reference respiratory cycle. In some examples, each stimulation cycle of the first stimulation protocol includes the stimulation period having a duration greater than a duration of the inspiratory reference followed by the non-stimulation period, which has a duration less than the duration of the stimulation period.

In some examples, the reference respiratory cycle is defined by a historical patient-specific average respiratory cycle for stable respiration. In some examples, the reference

respiratory cycle is defined by a multi-patient average respiratory cycle for stable respiration.

Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) intentionally does not match the duration (R) of the reference respiratory cycle in at least some examples, the stimulation protocol ensures that each successive stimulation period within the series of stimulation cycles will fall along a different portion of each of the successive reference respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of reference respiratory waveform (which includes the series of reference respiratory cycles), no matter where the stimulation protocol is started relative to the ongoing pattern of reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period of the initial stimulation cycle at least partially overlaps with the inspiratory phase of a reference respiratory cycle, the stimulation periods of the successive stimulation cycles will at least partially overlap the inspiratory phase of the next reference respiratory cycles. Moreover, at least some of the later successive stimulation periods will significantly overlap (e.g. overlap at least a majority of the inspiratory phase) the inspiratory phase of the at least some of the respective successive reference respiratory cycles. In some instances, such significant overlap may include a complete overlap of the inspiratory phase.

Via this arrangement, it becomes feasible to stimulate an airway-related-nerve to treat sleep disordered breathing either without any sensing elements at all or with minimal use of sensing elements. In this sense, the stimulation is performed asynchronously, i.e. without synchronization relative to sensed respiratory information. Among other benefits, this may reduce the cost of the stimulation system, may simplify its implantation, and may simplify operation of the stimulation system. Moreover, the presence of non-stimulation periods helps to minimize potential muscle fatigue that might otherwise be caused. Finally, providing asynchronous stimulation via the independent stimulation element may help to overcome situations in which sensor-based systems or synchronous systems are unable to achieve synchronization and/or the sensing signal become unstable (or is unavailable).

However, it will be understood that in some examples, an asynchronous independent stimulation protocol is implemented while still performing sensing respiratory information for non-synchronization purposes, such as evaluating stimulation therapy effectiveness and/or provide information to adjust parameters of the independent stimulation protocol.

In another aspect, providing stimulation asynchronously via the independent stimulation element may enable leveraging a greater number of different stimulation protocols because of fewer constraints on how the stimulation cycles of the stimulation protocols relate to characteristics of a respiratory waveform. Moreover, in some examples, the stimulation element applies nerve stimulation while rotating application through the plurality of different stimulation protocols, which in some instances provides a more robust therapy than using a single stimulation protocol. In some examples, this rotation also can be used to sort through the relative effectiveness of the different stimulation protocols and select the most effective stimulation protocol for a particular patient.

In some examples, an independent stimulation protocol is implemented in which the inspiratory phase of a majority of reference respiratory cycles are at least partially overlapped by a stimulation period, with more occurrences of such overlapping being preferred over fewer such occurrences. Similarly, in some examples, it is generally preferred to implement such an independent stimulation protocol via providing the sequence of stimulation periods to result in a greater degree of overlap with the inspiratory phase of the reference respiratory cycles rather than a lesser degree of overlap.

In some examples, the therapy manager includes a stimulation protocol element that provides convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. In this arrangement, the therapy manager causes: operation in the first stimulation mode for at least a first predetermined period of time; conversion of operation into the second stimulation mode upon at least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria; and reversion of operation into the first stimulation mode for at least the first predetermined period of time upon the at least one parameter of the sensed respiratory waveform failing to meet the sensor signal quality criteria. Accordingly, in one aspect, the first stimulation mode comprises the default mode of stimulation.

In some examples, the conversion between the first stimulation mode and the second stimulation mode is automatic. In some examples, the therapy manager includes a user selection function to enable user selection of either the first mode or the second mode as a default mode.

In some examples, the therapy manager includes an operator selection function to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented manually during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient.

In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc. In some examples, the first predetermined period of time does not correspond to a test mode for evaluating the operational fitness of the stimulation system. Stated differently, activities occurring during the first predetermined period of time may sometimes be referred to as a non-test mode.

Via this arrangement, the independent stimulation element first establishes a stable respiratory pattern. This arrangement therapeutically achieves airway patency while simultaneously increasing the likelihood of later successful synchronization of a respiratory-dependent stimulation protocol. In particular, because some examples dictate that stimulation is not implemented until or unless sleep disordered breathing behavior (above a severity threshold) is detected, the available respiratory signal will likely be a poor signal which attempt synchronization of a stimulation signal.

Accordingly, rather than attempt a likely problematic synchronization, at least some examples of the present disclosure first establish independent nerve stimulation that does not depend on synchronization. This independent stimulation, in turn, helps to establish a stable respiratory pattern or signal, which then in turn, significantly increases

the success of later synchronizing a respiratory-dependent stimulation protocol relative to the respiratory signal. Once a robust synchronization is established, then the system is well positioned to maintain a stable respiratory period using less overall stimulation by stimulating on a synchronized basis in which stimulation is limited to generally coinciding with an inspiratory phase (or other characteristic of the sensed respiratory waveform).

Of course, in the event the sensed respiratory signal changes in a way that hinders synchronization and/or delivery of effective therapeutic stimulation, then in at least some examples, the therapy manager will cause operation to revert to the independent stimulation mode.

With this arrangement, the independent stimulation mode enables initially applying a higher intensity stimulation to establish and ensure a stable respiratory pattern, which in turn, increases the likelihood of being able to later establish and maintain a lower intensity stimulation via the synchronized, respiratory-dependent stimulation mode. In this way, it is expected that overall muscle fatigue is minimized because of the likelihood of the synchronization mode successfully operating for a longer period of time than if the independent stimulation mode were not applied first.

Accordingly, in some examples, an independent stimulation element is implemented alone to treat sleep disordered breathing. However, in some examples, treatment is accomplished via a complementary combination of an independent (i.e. asynchronous) stimulation mode and a synchronous stimulation mode.

As noted above, in some examples, a stimulation protocol element may provide convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. However, in one example arrangement, the therapy manager causes: operation in the second stimulation mode and conversion of operation into the first stimulation mode upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria. Later, reversion of operation into the second stimulation mode is made upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria. Accordingly, in one aspect, the second stimulation mode comprises the default mode of stimulation.

These examples, and other examples, are further described in association with at least FIGS. **1**-**19**.

FIG. **1**A is block diagram schematically illustrating a stimulation element **12**, according to one example of the present disclosure. In some examples stimulation element **12** directs and controls nerve stimulation to treat obstructive sleep apnea. In some examples, stimulation element **12** includes an independent stimulation function **14**, which in general terms, applies electrical stimulation via a stimulation protocol to an airway-patency-related nerve to treat upper airway obstructions. In some examples, such airway-patency-related nerves include at least the protrusor branches of the hypoglossal nerve.

In some examples, the independent stimulation function **14** operates to stimulate an airway-patency-related nerve, according to a first stimulation protocol not synchronized relative to sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. Accordingly, in some examples, via the independent stimulation function **14**, nerve stimulation is applied independent of characteristics of sensed respiratory information. In other words, once the independent stimulation function **14** has been activated, the initiation and termination of individual nerve stimulation periods is not synchronized relative to a characteristic, such as onset of the inspiratory phase of the patient respiratory cycle and/or other characteristics. In at least this context, operation of independent stimulation function **14** (FIG. **1**A) may be referred to as an asynchronous stimulation function or mode.

In some examples, once a treatment period begins, such as when the patient is engaging in sleeping behavior (and during which sleep disordered breathing is to be avoided), the nerve stimulation function **14** is always in an "on" or active mode, and therefore stimulation cycles are applied to the nerve. In such examples, activation or deactivation of the independent stimulation function **14** is independent of whether or not apneas are occurring. For instance, the general activation and/or deactivation of the independent stimulation function **14** can be controlled according to a selectable time schedule, such as a predetermined start time (e.g. 10 p.m.) and predetermined end time (e.g. 6 a.m.).

FIG. **1**B is a block diagram schematically illustrating a therapy manager **16**, according to one example of the present disclosure. In general terms, therapy manager **16** directs a therapeutic regimen for controlling sleep disordered breathing such as, but not limited to, obstructive sleep apnea. The therapy manager **16** operates as part of, or in cooperation with, an at least partially implantable nerve stimulation system. In some examples, therapy manager **16** forms at least part of a control portion such as, but not limited to, control portion **360** as later described in association with at least FIGS. **9**-**10**, and as such, in some examples, therapy manager **16** includes at least some of substantially the same features and attributes as therapy manager **371** described in association with at least FIG. **9**.

In some examples, therapy manager **16** is in communication with and/or incorporates at least some aspects of stimulation element **12**. In some examples, the therapy manager has access to physiologic sensing information via sensing elements (e.g. at least FIGS. **7**A-**7**B). In such examples, general activation and/or general deactivation of the independent stimulation function **14** is controlled according to a likelihood of sleep behavior, which is determined according to at least body position, body posture, body motion, and/or body activity parameters, which can be sensed via an accelerometer or other sensing elements. In some examples, determining likelihood of sleep behavior is supplemented via additional sensed physiologic information, including but not limited to sensed respiratory information.

In some of the examples in which the therapy manager **16** has access to sensed physiologic information (at least FIGS. **7**A-**8**), once a treatment period begins, the nerve stimulation function **14** is not generally activated and/or deactivated to stimulate a nerve until prompted to do so based on respiratory behavior criteria (e.g. whether apneas are likely or are occurring, etc.). This determination is separate from, and independent of, timing or synchronizing individual stimulation periods relative to particular characteristics (e.g., inspiration, expiration, etc.) of sensed respiratory information. Accordingly, in these examples, whether or not a patient receives any stimulation at all is governed by whether or not the patient experiences a sufficient quantity, frequency, or intensity of apneas.

In other words, in some examples, therapy manager **16** operates to apply stimulation when the patient is experiencing apneas or likely to experience apneas. In this way, nerve stimulation is limited to an as needed basis, thereby conserving energy of the stimulation system **20** and reducing

potential muscle fatigue. As to the particular strength of the stimulation signal and whether it is applied in view of the relative severity of the sleep disordered respiratory behavior, at least some examples of automatic adjustment of a level of stimulation therapy is described in at least Christopherson, METHOD OF TREATING SLEEP DISORDERED BREATHING, published on Oct. 27, 2011 as US 2011-0264164.

In some examples, the detection of flow limitations and/or associated apneas, as well as the detection of the beginning and end of the respective inspiratory and expiratory phases of the respiratory cycle, is performed according to, or in cooperation with, known methods and devices for doing so. Some non-limiting examples of such devices and methods to recognize and detect the various features and patterns associated with respiratory effort and flow limitations include, but are not limited to: PCT Publication WO/2010/059839, titled A METHOD OF TREATING SLEEP APNEA, published on May 27, 2010; Christopherson U.S. Pat. No. 5,944,680, titled RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS; and Testerman U.S. Pat. No. 5,522,862, titled METHOD AND APPARATUS FOR TREATING OBSTRUCTIVE SLEEP APNEA.

In some examples, the stimulation element **12** comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element **12** further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve, such as later described in association with at least FIGS. **2**A-**2**D and **7**B. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator.

In some examples, the therapy manager **16** is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager **16** are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

Details regarding particular stimulation protocols implemented via the independent stimulation function **14** are later described in association with at least FIGS. **3**B-**3**E. In particular, at least some details are provided regarding how asynchronous stimulation may increase therapeutic effectiveness in treating sleep disordered breathing.

FIG. **2**A is a schematic diagram of an at least partially implantable stimulation system **20**, according to an example of the present disclosure. In general terms, the stimulation element **12** of FIG. **1**A (and/or therapy manager **16** of FIG. **1**B) is incorporated within and/or operates in association with stimulation system **20** to deliver stimulation.

As illustrated in FIG. **2**A, in one example system **20** includes an implantable pulse generator (IPG) **35** and a stimulation lead **32** electrically coupled with the IPG **35** via a connector (not shown) positioned within a connection port of the IPG **35**. In some examples, the IPG **35** is surgically positioned within a pectoral region of a patient **22**. The lead **32** includes a stimulation electrode portion **45** and extends from the IPG **35** so that the stimulation electrode portion **45** is positioned in contact with a desired nerve, such as an airway-patency-related nerve **33** of the patient **10**, to enable stimulation of the nerve **33**, as described below in detail. In some examples, the stimulation electrode portion **45** comprises a self-sizing cuff such as described in U.S. Pat. No. 8,340,785 to Bonde et al. In some examples, in association with electrode **45**, lead **32** includes at least some of the features and attributes described in U.S. Patent Publication 20110160827 to Bonde et al. In some examples, lead **32** includes features and attributes at least consistent for use in an implantable stimulation system as described in U.S. Pat. No. 6,572,543 to Christopherson et al.

As later described more fully in association with at least FIGS. **9**-**10**, in some examples the therapy manager **16** controls the IPG **35**, and is implemented externally of the IPG **35**, entirely within the IPG **35**, or partially within the IPG **35**.

In some examples, stimulation electrode portion **45** comprises a cuff electrode including a single operative contact group of at least two electrodes through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. FIG. **2**E is a top view schematically illustrating one example of such an electrode **50** including a single operative contact group of at least two electrodes **52**. In some examples, the stimulation electrode portion **45** comprises a cuff electrode including at least one operative contact group through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. Accordingly, more than one operative contact group of electrodes can be incorporated in a single cuff electrode. In some examples, the stimulation electrode portion **45** can include multiple, separate cuff electrodes with each having at least one operative contact group of electrodes.

In some examples, the stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, in some examples, one or more components of the system are not implanted in a body of the patient, thereby providing an at least partially implantable system. A few non-limiting examples of such non-implanted components include an external processing unit and/or an external power source, as later noted in association with at least FIG. **6**.

In some examples, the at least partially implantable stimulation system **20** does not include any sensing elements. Accordingly, to the extent that the system **20** and its therapy manager **16** apply stimulation protocols to treat respiratory behavior, any patient-specific respiratory information would be received and/or obtained prior to, and/or during, implantation of the system **20**. Alternatively, a temporary external sensing system could be employed to periodically calibrate and/or evaluate therapeutic efficacy of the at least partially implantable stimulation system **20** operating according to an independent stimulation function **14** (FIG. **1**A).

At least some examples of the sensor-less stimulation system **20** use significantly less power than some sensor-based systems and are easier to implant. Moreover, in such examples, the system **20** is significantly easier to construct and/or operate because the sensors, certain sensing-related circuitry, and certain operational programming can be omitted.

However, it will be understood that in some examples, the stimulation system **20** includes sensing elements, at least in the manner later described in association with at least FIGS. **7**A-**7**B. In at least some of these examples, the sensing elements are used to evaluate therapy and particular stimulation protocols but are not used to synchronize stimulation relative to characteristics of the sensed respiratory waveforms.

FIG. **2**B is block diagram of an implantable pulse generator (IPG) **50**, according to one example of the present disclosure. In some examples, IPG **50** includes at least some of substantially the same features and attributes as IPG **35** (FIG. **2**A). However, in some examples, IPG **50** includes at least some features and attributes different than those in IPG **35** (FIG. **2**A). As such, in some examples, IPG **50** can take

different forms and be implanted in locations other than those shown in FIG. **2**A (and also FIG. **7**B).

With further reference to FIG. **2**B, in some examples the implantable pulse generator **50** includes a stimulation element **52** and a communication element **54**. The stimulation element **52** generates and applies a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) **45** in FIG. **2**A) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager **16**. In some examples, stimulation element **52** comprises at least some of substantially the same features and attributes as stimulation element **12** as previously described in association with FIG. **1**A.

The communication element **54** provides a communication pathway to enable transmission of data, power, and/or controls signals both to and from the implanted portions of the system **20** relative to the external portions of the system **20**. For instance, in some examples, the communication element **54** is configured to report activities of the IPG **50** (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG **50** from an external source, such as a patient programmer, clinician programmer, etc. as later noted in association with at least FIG. **10**. In some examples, the communication element **54** utilizes a radiofrequency (RF) telemetry link or other wireless communication protocols.

In some examples, the implantable pulse generator **50** includes a control portion or at least part of a control portion such as control portion **56** shown in FIG. **2**C. In general terms, control portion **56** directs operation of the pulse generator **50** and the at least partially implantable stimulation system. Further details regarding such a control portion **56** are described later in association with at least FIGS. **9**-**10**. Moreover, in some examples, control portion **56** is operable in association with a user interface, such as described later in association with at least FIGS. **11**A-**11**B.

FIG. **2**D is a block diagram **70** schematically illustrating an at least partially implantable stimulation system **80**, according to an example of the present disclosure. In some examples, system **80** includes at least some of substantially the same features and attributes as system **20** (FIG. **2**A), pulse generator **50** (FIG. **2**B), and control portion **56** (FIG. **2**C), except for system **80** having some portions in a non-pectoral location and located in close proximity to a target nerve to be stimulated, as further illustrated in association with at least FIG. **2**D.

In some examples, system **80** is a sensor-less system in a manner substantially similar to the above-described system **20**. In other words, as at least partially implanted in the patient's body, system **80** omits a sensor.

As shown in FIG. **2**D, in some examples system **80** includes a nerve-coupling electrode portion **82** and a pulse generator **84**. In some examples, the nerve-coupling electrode portion **82** comprises an element which is at least electrically coupled relative to a target nerve **72** suitable to maintain or restore airway patency, such as but not limited to, the hypoglossal nerve.

In some examples, the electrode portion **82** comprises a cuff, such as one of the stimulation electrode portions **45** described in association with FIG. **2**A in which the electrode portion is both mechanically and electrically coupled relative to the nerve **72**. However, in some examples, the nerve-coupling electrode portion **82** comprises a cuff-less structure that is both mechanically and electrically coupled relative to the nerve **72**.

In some examples, the nerve-coupling electrode portion **82** is not mechanically coupled to the nerve **72**, but is mechanically coupled or secured in a location in close proximity to the nerve **72** and that enables electrically coupling of the electrode portion **82** relative to the nerve **72**. In one instance, such examples include the electrode portion **82** being delivered to the target nerve **72** via a percutaneous access delivery. In one instance, such examples include the electrode portion **82** being delivered to the target nerve **72** via a transvenous delivery method in which the electrode portion **82** is delivered on a lead maneuvered within and through the vasculature of the patient.

In some examples, in a manner consistent with the previously described pulse generator **50** (FIG. **2**B) pulse generator **84** includes a stimulation element **52** and a communication element **54**. In some examples, pulse generator **84** includes solely internal components **90**, which are internally within the body below the skin/tissue. However, in some examples, pulse generator **84** includes a combination of some internal components **90** and some external components **92**, which are external to the body being above or outside the skin/tissue.

In some examples, via communication element **54** (FIG. **2**B), system **80** includes a wired communication path **94** and/or a wireless communication path **96** between the pulse generator **84** and the nerve-coupling electrode portion **82**, as shown in FIG. **2**D. In some examples, either or both such communication pathways **94**, **96** are also employable for communication between internal and external components **90**, **92** of a pulse generator **84**.

In some examples, in order to utilize and/or evaluate sensed respiratory information, the therapy manager **16** uses a reference point, such as a normal breathing pattern **150**, as shown in FIG. **3**A. Of course, variances may exist from patient-to-patient so it will be understood that the normal breathing pattern **150** is a representative example provided for illustrative purposes and is not intended to strictly define a breathing pattern that is universally normal for all patients. With this in mind, in some examples, the system **20** uses the particular breathing pattern of a specific patient (to which the method is applied) as the reference point to utilize and/or evaluate sensed respiratory information.

In the example of normal breathing pattern **150** shown in FIG. **3**A, a respiratory cycle **160** includes an inspiratory phase **162** and an expiratory phase **170**. The inspiratory phase **162** includes an initial portion **164**, intermediate portion **165**, and end portion **166** while expiratory phase **170** includes an initial portion **174**, intermediate portion **175**, end portion **176**, and an expiratory peak **177**. A first transition **180** occurs at a junction between the end inspiratory portion **166** and the initial expiratory portion **174** while a second transition **182** occurs at a junction between the end expiratory portion **176** and the initial inspiratory portion **164**. In some instances, end expiratory portion **176** includes and/or is referred to as an expiratory pause that occurs just prior to onset of the initial inspiratory portion **164**.

FIG. **3**B is a diagram **200** schematically illustrating a stimulation protocol **210** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In some examples, after initializing the system according to the known/applicable respiratory cycle for that patient and after general activation of the independent stimulation function **14**, the initiation, operation, and termination of the stimulation protocol **210** operates without regard to sensed respiratory information. In one aspect, FIG. **3**B illustrates a respiratory pattern **202** including a series of reference respiratory cycles **204**A-**204**H, with

each cycle having substantially the same features and attributes as the respiratory cycle **160**. Accordingly, each reference respiratory cycle **204**A-**204**H has a duration R.

In one aspect, the pattern **202** represents a stable respiratory pattern that occurs during normal daytime breathing and/or that results from application of stimulation protocol **210**.

In some examples, because stimulation via the stimulation protocol **210** is not synchronized relative to characteristics of actively-sensed respiratory cycles (such as via real-time measure of respiratory effort), the stimulation protocol **210** operates based on a reference respiratory cycle. In some examples, the reference respiratory cycle includes at least one of a historical patient-specific average respiratory cycle for stable respiration and a multi-patient average respiratory cycle for stable respiration. This historical and/or predictive information is employed in at least some examples in which the therapy manager **16** (FIG. **1**B) is not actively sensing respiratory waveforms during operation of the at least partially implantable stimulation system **20**.

As shown in FIG. **3**B, stimulation protocol **210** includes a series of separate stimulation periods (e.g. pulses) **212**A-**212**J spaced apart by a non-stimulation periods **218**A-**281**I, each of which are interposed between an adjacent pair of stimulation periods. For instance, non-stimulation period **218**B is interposed between stimulation periods **212**B, **212**C. In one aspect, each stimulation period (**212**A-**212**I) has a first end **214** and an opposite second end **216**.

In some examples, in order to demonstrate the manner in which the stimulation protocol **210** is juxtaposed relative to the respiratory pattern **202**, FIG. **3**B further illustrates each respiratory cycle being apportioned into a discrete number (e.g. 3, 4, 5, 6, 7, 8, etc.) time units, with each time unit having a duration t. In the example shown in FIG. **3**B, each respiratory cycle has a duration R and is divided into six time units t.

In some examples, the duration R is patient specific and is based on a long term average duration of a respiratory cycle. In some examples, the duration R is not patient specific and is based on an average duration of a respiratory cycle for many different patients. In some examples, duration R is about 3 to about 6 seconds. In some examples, via therapy manager **16**, the duration R can be adjusted to a preferred duration. In some examples, the therapy manager **16** uses the patient-specific information regarding durations.

However, in some examples, where such information is not available or is problematic, the therapy manager **16** uses multi-patient information. For instance, for at least some patient populations a duration of an entire respiratory period is about 3 to 6 seconds, which corresponds to a general respiratory rate of about 10-18 breaths/minute. Moreover, generally speaking inspiration (e.g. an inspiratory phase) is a minority of the entire respiratory period which includes inspiration, expiration, and expiratory pause.

In at least some patient populations, an apnea and/or hypopnea has a minimum duration of about 10 seconds, which corresponds to a minimum duration about 2-3 breaths.

In some examples, an apnea may be avoided via implementation of a stimulation protocol which avoids missing (either completely missing or significantly missing) stimulation for more than one breath (e.g. one inspiratory phase).

With further reference to FIG. **3**B, as represented by the legend **209**, the stimulation protocol **210** operates according to a stimulation cycle in which the duration of the stimulation cycle is less than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of 3. In some examples, as shown by legend **209**, the stimulation period and the non-stimulation period are in a proportion of 4 to 1. In such examples, each stimulation cycle includes a continuous stimulation period of 4 time units followed by a non-stimulation period of 1 time units, with this stimulation cycle being repeated continuously when nerve stimulation is generally activated. The total duration of the stimulation cycle (e.g. 4 time units of stimulation and 1 time unit of non-stimulation) is 5 time units, which is less than the duration R of the respiratory period, which is 6 time units in this example. In one aspect, this example arrangement in which the stimulation period is in much greater proportion to the non-stimulation period may benefit some patients by minimizing tongue rubbing by minimizing the frequency or total volume of tongue motion incident to tongue protrusion intentionally caused by the stimulation therapy to restore airway patency.

In FIG. **3**B, the first end **214** of stimulation period **212**A is shown as coinciding with the beginning of an inspiratory phase **162** of the respiratory cycle **204**A. However, it will be understood that the beginning **214** of the stimulation period **212**A is not synchronized relative to the inspiratory phase **162**. Rather, the beginning **214** of stimulation period **212**A is shown as coinciding with the beginning of inspiratory phase **162** for illustrative simplicity in juxtaposing the stimulation protocol **210** relative to the respiratory cycles **204**A-**204**H. Accordingly, it will be understood that when stimulation (according to stimulation protocol **210**) is initiated during a treatment period, the beginning of the stimulation period **212**A may coincide with a different portion of the respiratory cycle (e.g. **204**A) than shown in FIG. **3**B.

With further reference to the stimulation protocol **210** in FIG. **3**B, in one aspect, each respective non-stimulation period **218**A-**218**I has a duration less than a duration of each respective stimulation periods **212**A-**212**J. In one aspect, the duration of the stimulation period **212**A is less than a duration (R) of the reference respiratory cycle **204**A. In one aspect, the relative duration of the respective stimulation periods (e.g. **212**A) and non-stimulation periods (e.g. **218**A) causes each successive stimulation period (e.g. **212**B) to begin at a different place along a successive respiratory cycle, such that the stimulation pattern is independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. For instance, it can be seen from FIG. **3**B that the first end **214** of stimulation period **212**D coincides with a portion of the expiratory phase **170** of respiratory cycle **204**C while the first end **214** of stimulation period **212**E coincides with a portion of inspiratory phase **162** of the successive respiratory cycle **204**D.

As shown in FIG. **3**B, each of the respective stimulation periods **212**A, **212**B, **212**C overlaps the entire inspiratory phase **162** of the respective respiratory cycles **204**A-**204**C while stimulation period **212**D at least partially overlaps the inspiratory phase **162** of respiratory cycle **204**D.

Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) does not match the duration (R) of the reference respiratory cycle, the stimulation protocol **210** ensures that each successive stimulation period within the series of stimulation cycles will fall along a different portion of the successive respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **210** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference

respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol **210** happens to be initiated at a time that the non-stimulation period (e.g. **218**D, **218**E) at least partially overlaps with the inspiratory phase **162** of a respiratory cycle (e.g. **204**D, **204**E), the succeeding stimulation periods **212**F, **212**G, etc. at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**F, **204**G, etc., with these later successive stimulation periods significantly overlapping (e.g. stimulation period **212**F, which overlaps by at least a majority) or even completely overlapping (e.g. stimulation period **212**G) the inspiratory phase **162** of the respective successive respiratory cycles (e.g. **204**F, **204**G).

In one aspect, in stimulation protocol **210** the duration of each stimulation period (e.g. **212**A-**212**J) is less than a duration (R) of the reference respiratory cycles (**204**A-**204**H) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle for the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **204**A, **204**B, **204**C, **204**D, **204**F, **204**G, **204**H the duty cycle is 5 time units of continuous stimulation and 1 time unit of non-stimulation, which equals about 83%. However, during respiratory cycle **204**E, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 5 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**F, at which the first end **214** of the stimulation period **212**G once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**F in a manner similar to respiratory cycle **204**A. Accordingly, in one aspect, the long term duty cycle over an indefinite number of respiratory cycles (or average duty cycle over a sufficient number of time frames) is about 80%.

In some examples, via stimulation protocol **210**, no sequence of four respiratory cycles occurs without a stimulation period significantly overlapping the inspiratory phase **162** (e.g. overlapping at least majority of the inspiratory phase **162**) of respiratory cycles in FIG. **3**B. This criteria is based on the longest period of time, in at least some examples, that a patient can go without a breath while avoiding a respiratory-event related arousal and/or to maintain near normal blood oxygenation.

In some examples, via stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) a clinician can implement a stimulation protocol in which a quantity (e.g. 2, 3, 4) is selected by the operator regarding how many respiratory cycles can pass without a significantly overlapping stimulation period, according to a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

It will be understood that each inspiratory phase **162** of each respiratory cycle (**204**A-**204**H) is shown in its ideal form in FIG. **3**B, and that in some instances where the inspiratory phase **162** at least partially coincides with one of the respective non-stimulation periods (e.g. **218**D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in FIG. **3**B.

Accordingly, via stimulation protocol **210**, the independent stimulation function **14** of stimulation element **12** (FIG. **1**A) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

With the example of pattern **202** and stimulation protocol **210** as a foundation, it will be understood that in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 50 percent of the duration of the reference respiratory cycle. In at least some contexts, this arrangement may ensure that the probability of entirely missing inspiration in an asynchronous stimulation protocol is less than 50%, such that a majority of the treatment period, stimulation will be delivered during at least a portion of inspiration, which may be sufficient to minimize or prevent sleep disordered breathing (e.g. apneas).

In some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is 80 percent of the duration of the reference respiratory cycle. For instance, such an arrangement might be employed in some example patients having severe obstructive sleep apnea in which an inspiration can be missed for no more than 1 of 5 breaths. When applied asynchronously, such a duty cycle may likely ensure effective treatment (assuming other stimulation parameters are effective) while still allowing the protrusor muscles to rest sufficiently.

While not depicted in FIG. **3**B, in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 25 percent of the duration of the reference respiratory cycle. When employed in an asynchronous arrangement, such an arrangement will likely ensure that at least one stimulation period significantly overlaps with the inspiratory phase at least one breath (e.g. one respiratory cycle) out of every three breaths (i.e. three respiratory cycles). For some patients which exhibit less severe apneas, this arrangement can be sufficient to prevent obstructive events.

FIG. **3**C is a diagram **221** schematically illustrating a stimulation protocol **220** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **221** includes at least some of substantially the same features and attributes as diagram **201**, except for having a different stimulation protocol **220**.

Moreover, as represented by the legend **229**, the stimulation protocol **220** operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 1.5. As represented via legend **229**, in some examples stimulation protocol **220** includes a stimulation cycle including a stimulation period of 4½ time units and a non-stimulation period of 2½ time units, with the overall stimulation cycle of 7 time units having a duration greater than the duration R of the respiratory cycle (e.g. **204**A) of 6 time units.

In a manner substantially the same as previously noted for stimulation protocol **210**, even though stimulation protocol **220** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **220** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. For instance, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **228**B generally coincides with the inspiratory phase **162** of a respiratory cycle **204**C, the succeeding stimulation period **222**C at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**D, and with later successive stimulation periods significantly overlapping (e.g. stimulation period **222**D, exhibiting at

least a majority overlap) or completely overlapping (e.g. stimulation period **222**E) the inspiratory phase **162** of the respective successive respiratory cycles (e.g. **204**E, **204**F).

In some examples, a stimulation protocol is applied in which a total duration of stimulation via the first stimulation protocol during a treatment period is greater than 30 percent of the total duration of the treatment period.

In one aspect, in stimulation protocol **220** the duration of each stimulation period (e.g. **222**A-**222**G) is less than a duration (R) of the respiratory cycles **204**A-**204**H) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **204**D, **204**E, **204**F, **204**G the stimulation duty cycle is 3½ time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 58%. However, during respiratory cycles **204**A and **204**B the stimulation duty cycle is 4½ time units of continuous stimulation and 1½ time units of non-stimulation, which equals about 75%. Meanwhile, during respiratory cycles **204**C, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 8 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**H, at which the first end **224** of the stimulation period **222**G once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**H in a manner similar to respiratory cycle **204**A. Accordingly, in one aspect, the long term or average duty cycle over a long period of time is about 64%.

In some examples, via stimulation protocol **220** no more than four respiratory cycles occur without a stimulation period significantly overlapping (e.g. at least a majority of the) inspiratory phase **162** of respiratory cycles in FIG. **3**C.

FIG. **3**D is a diagram **231** schematically illustrating a stimulation protocol **230** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **231** includes at least some of substantially the same features and attributes as diagram **201** (FIG. **3**B) or diagram **221** (FIG. **3**C), except for having a different stimulation protocol **230**.

Moreover, as represented by the legend **239**, the stimulation protocol **220** operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 3. As represented via legend **239** in FIG. **3**D, in some examples stimulation protocol **230** includes a stimulation cycle including a continuous stimulation period of 7½ time units and a non-stimulation period of 2½ time units, with the overall stimulation cycle of 10 time units having a duration greater than the duration R of the respiratory cycle (e.g. **204**A) of 6 time units.

In a manner substantially the same as previously noted for stimulation protocols **210**, **220**, even though stimulation protocol **230** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **230** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **238**B generally coincides with the inspiratory phase **162** of a respiratory cycle **204**D, the succeeding stimulation period **232**C at least partially overlaps the inspiratory phase **162** of the next respiratory cycle **204**E.

In one aspect, in stimulation protocol **230** the duration of each stimulation period (e.g. **232**A-**232**D) is greater than a duration (R) of the respiratory cycles **204**A-**204**G) and greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **204**A).

In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycle **204**A, the duty cycle is 6 time units of continuous stimulation, which equals 100%. However, during respiratory cycles **204**B and **204**E the stimulation duty cycle is 3½ time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 58%. Meanwhile, during respiratory cycle **204**C, the duty cycle is 5½ time units of continuous stimulation and ½ time units of non-stimulation, which equals about 92 percent. Meanwhile, during respiratory cycle **204**D, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 66 percent.

Every 5 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **204**F, at which the first end **234** of the stimulation period **232**D once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **204**F in a manner similar to respiratory cycle **204**A.

In one aspect, the long term (i.e. average) duty cycle over a sufficient number of respiratory cycles is about 75 percent.

In one aspect, this stimulation protocol provides an occasional 100% duty cycle (e.g. stimulation period **232**D) to ensure that an inspiratory phase will be not missed during a stimulation period, while the overall average duty cycle is 75 percent. In some examples, such stimulation protocols are suitable for a patient in which the pattern of the respiratory waveform varies considerably but where effective therapy can be achieved without using continuous stimulation.

In some examples via stimulation protocol **230** no sequence of four respiratory cycles occurs without a stimulation period at least significantly overlapping the inspiratory phase **162** of respiratory cycles in FIG. **3**D.

FIG. **3**E is a diagram **241** schematically illustrating a stimulation protocol **240** implemented via independent stimulation function **14** (FIG. **1**A), according to one example of the present disclosure. In one example, diagram **241** includes at least some of substantially the same features and attributes as diagram **201**, except for having a different stimulation protocol **240**.

As represented via legend **249** in FIG. **3**E, stimulation protocol **240** includes a stimulation cycle including a continuous stimulation period of 4 time units and a non-stimulation period of 2 time units, with the overall stimulation cycle of 6 time units having a duration generally matching the duration R of the reference respiratory cycle (e.g. **204**A) of 6 time units. As in the prior examples associated with FIGS. **3**A-**3**E, the stimulation protocol **240** is independent, i.e. not synchronized relative to sensing of respiratory information.

In some patients the duration (R) of their respiratory cycle may vary slightly over time as the respiratory cycle might shorten or lengthen. Diagram **241** schematically illustrates just one example in which the reference respiratory cycle represents a situation in which the duration of the respiratory cycle lengthens to R1 due to lengthening of the expiratory phase **171** of the respiratory cycles of the patient. It will be understood that other characteristics, parameters, features of

the respiratory cycle often change as well, but these changes are not depicted in FIG. **3**E for illustrative simplicity and clarity.

It will be further understood that such changes may develop gradually over time and that FIG. **3**E provides a snapshot of one such change after it has already at least partially developed. Moreover, because this arrangement of independent stimulation operates without synchronization relative to sensed respiratory information, FIG. **3**E schematically represents at least some aspects regarding how stimulation protocol **240** may provide therapeutic effectiveness in this situation of lengthening respiratory cycles (or shortened respiratory cycles) as represented by the reference respiratory cycles **204**A-**245**M in FIG. **3**E.

Accordingly, in this example, the stimulation cycle repeats itself in what otherwise would be exactly matching each reference respiratory cycle, but the elongated duration of the reference respiratory cycle causes the stimulation cycle to no longer coincide with various portions of the respiratory cycle.

It will be understood, of course, as previously noted elsewhere that at the time the stimulation protocol is initiated and while not shown in FIG. **3**E, the first end **244** of the initial stimulation period **242**A may not necessarily coincide with the beginning of an inspiratory phase **162** of a respiratory cycle **245**A.

In some examples, even though stimulation protocol **240** is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **240** is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period **248**H **248**, **248**J generally coincides with the inspiratory phase **162** of a respiratory cycle **245**H, **245**, **245**J, at least some subsequent stimulation periods **242**L, **242**M, **242**N significantly overlap (at least a majority overlap) the inspiratory phase **162** of the next respiratory cycles **245**K, **245**L, **245**M. As further seen in FIG. **3**E, other example stimulation periods also significantly overlap (e.g. stimulation period **242**F) the inspiratory phase **162** of the corresponding respective respiratory cycle **245**F.

In some examples, the stimulation periods **242**A-**242**E, **242**N completely overlap the inspiratory phase **162** of the respective respiratory cycles (e.g. **245**A-**245**E, **245**M). However, it will be understood that in some examples, such complete overlap with the inspiratory phase of some respiratory cycles may not be exhibited, and a significant overlap would suffice to achieve adequate airway patency.

In one aspect, in stimulation protocol **240**, the duration of each stimulation period (e.g. **242**A-**242**M) is less than a duration (R) of the respiratory cycles (**245**A-**245**M) but greater than a duration of the inspiratory phase **162** of an individual respiratory cycle (e.g. **245**A).

In one aspect, the duty cycle associated with the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles **245**A, **245**B, **245**C, **245**D, **245**E, **245**F, **245**G, **245**H, **245**M the duty cycle is 4½ time units of continuous stimulation and 2 time units of non-stimulation, which equals about 75 percent. However, during respiratory cycles **245**, **245**J, **245**K, **245**L the duty cycle is 4 time units of continuous stimulation and 2½ time units of non-stimulation, which equals about 62 percent.

For at least the time that a particular duration (R1) of the elongated respiratory cycle persists (as represented by reference respiratory cycles), every 12 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle **245**M, at which the first end **244** of the stimulation period **242**N once again coincides with the beginning of the inspiratory phase **162** of the respiratory cycle **245**M in a manner similar to respiratory cycle **245**A.

In one aspect, the longterm, average stimulation duty cycle over a sufficient period of time is about 67 percent.

Accordingly, in some examples, via stimulation protocol **240** no sequence of four respiratory cycles occurs without a stimulation period at least partially overlapping or even significantly overlapping the inspiratory phase **162** of respiratory cycles in FIG. **3**E.

It will be further understood that the various stimulation protocols described and illustrated in association with at least FIGS. **3**B-**3**E are implemented via the at least partially implantable stimulation system **20** as described in association with at least FIGS. **1**-**14**. However, in some examples, the various stimulation protocols described and illustrated in association with at least FIGS. **3**B-**3**E are implemented via at least some components, elements, systems etc. other than those described in association with FIGS. **1**-**14**.

While the independent stimulation function **14** (FIG. **1**A) does not use sensed respiratory information to trigger each stimulation period or synchronize each stimulation period, in some examples the independent stimulation mode **14** uses sensed respiratory information to track how a stimulation protocol is matching up relative to the characteristics of the sensed respiratory waveform. Accordingly, upon elongation or shortening of the sensed respiratory cycles, the therapy manager **16** (including independent stimulation function **14**) can choose to maintain or modify which stimulation protocol is being applied in order to ensure that the desired amount and timing of stimulation is being applied. In addition, or as an alternative, the therapy manager **16** uses the sensed respiratory information to adjust or calibrate features of the reference respiratory cycle associated with a particular stimulation protocol.

In some examples, operation of the therapy manager **16** (as part of an at least partially implantable stimulation system **20**) is not limited to the specific stimulation protocols described in association with at least FIGS. **3**B-**3**E, as other stimulation protocols can be implemented with longer or shorter stimulation periods and with longer or shorter non-stimulation periods.

In some examples the independent stimulation function **14** (FIG. **1**A) includes a complex stimulation cycle in which at least two different length stimulation periods is employed and/or at least two different length non-stimulation periods is employed. As one non-limiting example to illustrate the principle, one stimulation protocol could include a first continuous stimulation period of three time units, a first non-stimulation period of two time units, a second continuous stimulation period of three time units, followed by a second non-stimulation period of one time unit. The example later described in association with FIG. **16**A illustrate some aspects of these features.

In some examples, and as illustrated in the diagrams of FIGS. **3**B-**3**E, the stimulation cycles are not centered relative to a characteristic or feature of a respiratory waveform. In other words, the respective continuous stimulation periods or non-stimulation periods (in the example stimulation protocols) are not fixed or tied to a particular landmark or fiducial of the respiratory waveform. Accordingly, the respective continuous stimulation periods and non-stimula-

tion periods within stimulation cycles (of a particular stimulation protocol) vary regarding which portion of a respiratory cycle (of a series of respiratory cycles) with which they coincide.

In some examples, the independent stimulation function **14** provides a stimulation protocol having a duty cycle of 80 percent, where a 100 percent duty cycle would correspond to continuous stimulation over a full respiratory cycle. In one example, a first portion of the duty cycle comprises a continuous stimulation period and a second portion of the duty cycle comprises a continuous non-stimulation period immediately following the first portion. In a non-limiting example in which a respiratory cycle has a duration of 5 seconds, the duty cycle includes applying continuous stimulation for 4 seconds immediately followed by continuous non-stimulation for 1 second, with the duty cycle being repeated.

FIG. **4** is a block diagram **251** schematically illustrating a plurality of stimulation parameters **250**, according to one example of the present disclosure. In general terms, these stimulation parameters may be employed as part of implementing one of the stimulation protocols described in association with FIGS. **3**B-**3**E and/or as part of general operation of stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1***i*). In one example, a single parameter is implemented, while in some examples, several of these parameters may be implemented. When several parameters are implemented, they are implemented separately but contemporaneously in some examples and in other examples, they are implemented in combination.

As shown in FIG. **4**, these stimulation parameters **250** include amplitude parameter **252**, a duty cycle parameter **254**, a respiratory cycle duration parameter **260**, a time unit parameter **262**, and a time frame parameter **270**. The amplitude parameter **252** controls an amplitude of the stimulation signal, which can be selected for a particular stimulation protocol.

In some examples, the duty cycle parameter **254** tracks and/or controls a duty cycle of stimulation. In some examples, the stimulation duty cycle is expressed relative to a duration (R) of one respiratory cycle (per parameter **260**) in the manner previously described regarding the stimulations protocols previously described in association with at least FIGS. **3**B-**3**E. The duty cycle parameter **254** comprises a constant function **256** and a variable function **258**. The constant function **256** implements a duty cycle in which the stimulation duty cycle is identical relative to each respiratory cycle, while the variable function **258** implements a duty cycle in which the stimulation duty cycle varies relative to at least some respiratory cycles within a series of respiratory cycles.

As previously described in association with at least FIGS. **3**B-**3**E, in some examples, the stimulation duty cycle is implemented according to a series of stimulation cycles in which each stimulation cycle includes at least one continuous stimulation period and at least one non-stimulation period. At least some stimulation protocols includes stimulation cycles in which the duration of the stimulation period(s) differs relative to the duration of the non-stimulation period(s) through a series of stimulation cycles such that an average duty cycle can be calculated.

Accordingly, the various stimulation protocols provide some duty cycles that vary from one respiratory cycle to the next, while simultaneously providing an overall or average duty cycle. By selecting a particular stimulation cycle, specific duty cycles are implemented on a respiratory-cycle by respiratory-cycle basis and an overall or average duty cycle is achieved.

In some examples, a respiratory cycle duration parameter **260** identifies a duration of a patient-specific average respiratory cycle during reasonably stable respiration (e.g. normal breathing) or a duration of a multi-patient average respiratory cycle during reasonably stable respiration. In some examples, the patient-specific average respiratory cycle is determined according to recent sensed respiration information while in some examples, the patient-specific average respiratory cycle is determined according to long term data gathered for that patient during reasonably stable respiration (e.g. normal breathing).

In some examples, the respiratory cycle duration parameter **260** tracks a duration of the sensed respiratory cycles of a patient and determines an average.

In some examples, the time unit parameter **262** tracks and controls a number of time units by which a stimulation cycle operates. In some examples, the time unit parameter **262** implements time units as a multiple of some natural time unit associated with a respiratory waveform. For instance, in some examples such as the stimulation protocols described and illustrated in association with FIGS. **3**B-**3**E, the time unit parameter **262** equates six time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle. However, it will be understood that in some examples, the time units (per parameter **262**) are unit-less. For instance, suppose the respiratory period has a duration R of five seconds, and a convention has been adopted that the respiratory cycle is divisible into six time units. Then, the six time units would be distributed across the five second duration of the respiratory cycle.

In some examples, the time unit parameter **262** implements time units which are entirely arbitrary relative to one or more natural time units associated with a respiratory waveform. For instance, in some examples such as the stimulation protocol described and illustrated in association with FIG. **16**A, the time unit parameter **262** equates eight time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle.

In some examples, the time frame parameter **270** in FIG. **4** identifies a respiratory cycle series parameter **272** and a stimulation cycle parameter **274**. The respiratory cycle series parameter **272** identifies and tracks the number of respiratory cycles that occur before a particular portion of a particular stimulation cycle (**274**) would coincide again with a particular portion of a respiratory cycle. For example, it was previously noted in association with at least FIG. **3**C that the stimulation protocol **220** operated based on a time frame of seven respiratory cycles such that a sequence of seven respiratory cycles would occur before a beginning of a stimulation period of a stimulation cycle would coincide with a beginning of an inspiratory phase of the repeating respiratory cycle. While the stimulation protocols associated with independent stimulation function **14** (FIG. **1**A) are not synchronized relative to characteristics (e.g. inspiratory phase) of a sensed respiratory waveform, the time frame parameter **270** enables tracking and adjusting how a given stimulation protocol is juxtaposed relative to sensed patient respiratory behavior.

FIG. **5** is a block diagram of a stimulation protocol element **280**, according to one example of the present disclosure. As shown in FIG. **5**, the stimulation protocol element **280** comprises an array parameter **282**, a rotation

parameter **284**, an automatic parameter **286**, a manual parameter **288**, a static parameter **290**, and a custom parameter **291**.

In some examples, stimulation protocol element **280** includes at least some of substantially the same features and attributes as stimulation protocol element **12**, as previously described in association with at least FIGS. **1**-**4**. In particular, as previously noted, in some examples the independent stimulation function **14** (FIG. **1**A) provides at least one stimulation protocol suitable for delivering electrical stimulation to a nerve of a patient, such as one of the stimulation protocols as previously described and illustrated in association with FIGS. **3**B-**3**E.

With this in mind, array parameter **282** of stimulation protocol element **280** provides an array of stimulation protocols that can be applied, such as but not limited to those illustrated in association with FIGS. **3**B-**3**E.

In some examples, via a rotation parameter **284**, the stimulation protocol **280** enables delivering therapeutic nerve stimulation to a patient while rotating through different stimulation protocols available via array parameter **282**. In some examples, such rotation enables identifying a stimulation protocol that works best for a particular patient on a particular day or on a long term basis. However, in some examples, rotation through different stimulation protocols is maintained for a particular day or on a long term basis to provide a large degree of variability in the overall stimulation pattern to thereby provide a robust therapy regimen when a patient's respiratory behavior is consistently erratic and/or when sensing of a patient's respiratory behavior is consistently problematic.

In some examples, in cooperation with an automatic parameter **286**, the rotation parameter **284** automatically rotates through the different stimulation protocols to achieve goals set by therapy manager **16** (FIG. **1**). In some examples, via automatic parameter **286**, the therapy manager **16** (FIG. **1**B) automatically selects at least one stimulation protocol suitable for a particular patient. In some examples, the automatic selection of which stimulation protocol(s) is best suited for a particular patient is based on a sensed respiratory waveform of the patient.

In some examples, via a static parameter **290** shown in FIG. **5**, therapy manager **16** (FIG. **1**B) enables selecting and then maintaining a single stimulation protocol indefinitely until and unless a user or operator selects a different stimulation protocol or parameters affecting the selected stimulation protocol. In some examples, if a particularly effective stimulation protocol is identified during operation of the rotation parameter **284**, the therapy manager **16** (FIG. **1**B) deactivates automatic rotation of the stimulation protocols and operates that single, "particularly effective" stimulation protocol, per the static parameter **290**.

In some examples, stimulation protocol element **280** includes custom parameter **291**, which enables adjusting a selected stimulation protocol or making a custom stimulation protocol by selecting a duration of respiratory cycle, duration of stimulation period(s), duration of non-stimulation periods, duration of stimulation cycle, and/or other parameters identified in the plurality of stimulation parameters **250** (FIG. **4**).

In some examples, the range of stimulation protocols available to a patient via stimulation protocol element **280** are selected and/or bounded according to the discretion of a physician or physician programmer.

FIG. **6** is a block diagram of a power element **320**, according to one example of the present disclosure. In one example, power element **320** represents IPG **35**, **50** (FIGS. **2**A-**2**B) as having an external power source **322** and/or an on-board power source **324**.

In some examples, an at least partially implantable stimulation system (according to examples of the present disclosure) operates in cooperation with and/or incorporates sensing functionality. With this in mind, in some examples, such systems include a sensing element **330**, according to one example of the present disclosure, as shown in FIG. **7**A. The sensing element receives and/or obtains respiratory information.

In some examples, the sensing element **330** includes an on-board sensing element **332**, which is physically incorporated into IPG **35** (FIG. **2**A) or IPG **50** (FIG. **2**B) in some manner such that communication between the on-board sensing element **332** and other elements of the IPG **35**, **50** will occur within the case or housing of the IPG. In some examples, the on-board sensing element **332** includes internal components, such as an accelerometer and in some examples, the on-board sensing element **332** includes surface components, such as the external surface of the case or housing of the IPG **35**, **50** acting as a sensing element alone or in combination with other sensing elements.

In some examples, the sensing element **330** includes an implanted sensing input **334** to receive signals from a sensor implanted within the body physically separate from the IPG **35**, **50**, with the sensing input **334** in communication with and/or connected to the IPG **35**, **50** via wired or wireless communication pathways.

In some examples, the sensing element **330** includes an external sensing input **336** to receive signals from a sensor external to the patient's body, with the sensing input **336** in communication with the IPG **35**, **50** via wireless communication pathways.

In some examples, sensing element **330** does not comprise a physically-embodied sensor but rather a sensing input to receive information sensed via sensors separate from, and independent of, sensing element **330** with such sensors in communication with sensing element **330**.

In some examples, sensing element **330** can comprise both a sensing input and a physically-embodied sensor.

Via these various sensing elements and inputs, the sensing element **330** receives and tracks signals from at least one physiologic sensor in order to gather information pertinent to treating sleep disordered breathing. In some examples, this information includes respiratory information such as, but not limited to, determining a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. In some examples, the type of sensed physiologic information received by, and/or the type of physiologic sensors embodied within, one of the sensing elements/inputs **332**, **334**, **336** (FIG. **7**A) include, but are not limited to, a pressure sensing, blood oxygenation sensing, acoustic sensing, posture sensing, motion/activity sensing, differential pressure sensing, electrocardiogram (ECG) sensing, or impedance sensing. Via such sensing modalities, the system can measure thoracic impedance, respiratory pressure, diaphragm-based parameters, electrocardiac monitoring, airflow monitoring, snoring, etc. Gathering of this respiratory information, including information regarding respiratory-related behaviors, may be implemented via either a single sensor or any combination of various physiologic sensors that can provide a reliable and accurate signal. In some examples, these various measures of respiratory-related behavior can be considered alone or together in combination to indicate

respiratory effort, which is at least one type of respiratory information receivable and/or obtainable by the sensing element.

In some examples, the therapy manager **16** (FIG. **1**B) maintains the sensing components of the sensing element **330** in a default, dormant mode (i.e. off or low power) and periodically activates one or more of the available sensing element(s) to gather patient data. After gathering the data, the sensing elements are deactivated, thereby resuming their dormant mode. In some examples, the gathered patient data is used to evaluate the effectiveness of the therapy, such as the number, intensity, and/or frequency of apneas occurring. After such data gathering, the therapy manager **16** (FIG. **1**B) deactivates the sensing element(s), thereby returning them to a dormant mode.

In some examples, the gathered patient data is used to measure the respiratory period to verify its duration and to determine or verify the relative durations (or absolute duration) of the inspiratory and expiratory phases. This information is used to assess a current stimulation protocol and potentially determine whether adjustments to the stimulation protocol are warranted or whether a different stimulation protocol should be employed. For instance, in some examples, the gathered patient data from the temporarily activated sensing elements is used to calibrate the reference respiratory cycle associated with implementation of a particular stimulation protocol.

FIG. **7**B is a schematic diagram of an at least partially implantable stimulation system **340**, according to an example of the present disclosure. In one example, the system **340** includes at least some of substantially the same features and attributes as system **20** (previously described in association with at least FIG. **2**A), except further including sensing functionality via at least one sensing element to sense respiratory information. In some examples, this sensing functionality is implemented via sensing element **330** (FIG. **7**A).

In some examples, the system **340** comprises an additional lead **137** including at least one sensor portion **341** (electrically coupled to the IPG **35** and extending from the IPG **35**) positioned in the patient **22** for sensing respiratory information, such as respiratory effort, respiratory pressure, etc. In some examples, this information includes identifying and tracking characteristics and parameters of sensed respiratory waveforms.

In some examples, the sensor portion **341** is a pressure sensor. In one example, the pressure sensor detects pressure in the thorax of the patient. In some examples, the sensed pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow). Via sensor portion **341**, therapy manager **16** (FIG. **1**B) is configured to analyze this pressure sensing information to identify, track, and evaluate the respiratory patterns of the patient.

In some examples, the respiratory sensor portion **341** comprises a bio-impedance sensor or forms one of a pair of bio-impedance sensors. In some examples, the respiratory sensor portion **341** is located in regions other than the pectoral region. In some examples, the sensor portion **341** is used to sense impedance in cooperation with other electrodes (e.g. a stimulation electrode) or with an electrically conductive exterior housing of the IPG **35**, **50** (FIGS. **2**A-**2**B, **7**B). In some examples, as shown in FIG. **7**B, additional sensors **347**, **348**, **349** are distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals. In some examples, sensor portion **341** is omitted and sensors **347**, **348**, **349** are implemented.

In some examples, the system **340** for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, as identified in various examples, in some examples, the system is partially implantable with some components (e.g. power source, sensing elements, or control circuitry) being at least partially or completely external to the patient's body.

In some examples, the previously-described at least partially implantable system **80** (FIG. **2**D) includes at least some of substantially the same features described and illustrated in association with FIGS. **4**-**7**B, except for system **80** having a non-pectoral location and those attributes specific to system **80** as described in association with FIG. **2**D.

In some examples, the respiratory information and/or other physiologic information gathered via the sensing element **330** (FIG. **7**A) and associated sensor schemes (FIG. **7**B) is used to identify, track, evaluate, etc. various therapeutic parameters. Accordingly, in some examples the at least partially implantable stimulation system includes a therapeutic monitoring element **350**, which as shown in FIG. **8**, includes a plurality of therapeutic parameters. In some examples, these parameters include identifying, tracking, and evaluating apnea events per parameter **352** and/or computing and tracking an apnea severity index **354**, such as AHI or other index. The index parameter **354** determines a frequency, intensity, duration, etc. of detected apneas to indicate the relative severity of sleep disordered breathing for the patient.

In some examples, one therapeutic parameter of monitoring element **350** includes a minute ventilation parameter **356** to track minute ventilation of the patient before, during, or after a therapy regimen. In some examples, one therapeutic parameter of monitoring element **350** includes a tidal volume parameter **357** to track the tidal volume of a patient before, during, or after a therapy regimen.

In some examples, one therapeutic parameter of monitoring element **350** includes a body position parameter **358**. In some examples, one therapeutic parameter of monitoring element **350** includes a posture parameter **359**. Together or separately, the body position parameter **358** and posture parameter **359** determine and track a body position of the patient and posture of the patient. Among other uses, such information can be used to activate or deactivate a therapy, to select a therapeutic regimen (e.g. stimulation protocol), and/or to adjust a therapeutic regimen. It will be understood that these example parameters are not exhaustive and can be employed separately from each other or in various combinations.

In some examples, this information obtained via anyone or several parameters **352**, **354**, **356**, **357**, **358**, **359** of the therapeutic monitoring element **350** is used to initiate, terminate, select, and/or adjust stimulation applied via the IPG **35**, **50** and stimulation electrode **45**. For instance, upon determining that the number and/or intensity of apneic events has met or exceeded a severity threshold, the therapy manager **16** (FIG. **1**B) can utilize control portion **56** (FIG. **2**C) to initiate application of stimulation to the airway-patency related nerves to open the airway and thereby reduce the associated sleep disordered breathing behavior. However, it will be understood that in at least some examples, this arrangement does not include causing (or depend on) the stimulation signal to become synchronized relative to a characteristic (e.g. inspiratory phase, expiratory phase, etc.) of the respiratory waveform. Rather, as noted in association with at least FIG. **1**A, in the examples described

thus far in association with FIGS. **1**-**8**, such stimulation is applied independent of such synchronization.

In some examples, the therapeutic parameters element **350** may be employed to select one of a plurality of stimulation protocols and/or to evaluate the therapeutic effectiveness of a particular stimulation protocol(s) for a particular patient for a given period of time or on a long term basis.

In at least this context and/or other contexts in at least some examples of the present disclosure, therapeutic effectiveness may correspond to alleviating sleep disordered breathing, which in some instances is measurable via a severity threshold, such as an apnea-hypopnea index (AHI) and/or other scoring mechanisms. In some examples, the therapeutic effectiveness may also be measured or evaluated relative to sensor signal quality, such as via sensor signal quality criteria as described in at least some of the examples of the present disclosure.

FIG. **9** is a block diagram schematically illustrating a control portion **360**, according to one example of the present disclosure. In some examples, control portion **360** includes a controller **362** and memory **370**. In some examples, therapy manager **371** is stored in memory **370**, and in some examples, therapy manager **371** includes at least some of substantially the same features and attributes as therapy manager **16** (FIG. **1**), as previously described in association with at least FIGS. **1**-**8**.

In general terms, controller **362** of control portion **360** comprises at least one processor **364** and associated memories that are in communication with memory **370** to generate control signals to direct operation of at least some components of the systems and components described throughout the present disclosure. In some examples, these generated control signals include, but are not limited to, employing therapy manager **371** to manage operation of the stimulation system to control sleep disordered breathing. In some examples, a control portion **360** is present in the IPG **35**, **50**, **84** (FIGS. **2**A, **2**B, **2**D) as control portion **56** (FIG. **2**C) and/or is accessible to the IPG **35**, **50**, **84**. In some examples, at least some aspects of stimulation element **12** (FIG. **1**A) are at least partially implemented via control portion **360** and/or in communication with control portion **360**, with at least some aspects of stimulation element **12** being storable in memory **370** with or as part of therapy manager **371**.

In particular, in response to or based upon commands received via a user interface **396**, **400** (FIGS. **11**A, **11**B) and/or machine readable instructions (including software), controller **362** generates control signals to implement a nerve stimulation protocol to control sleep disordered breathing, in accordance with at least some of the previously described examples and/or later described examples of the present disclosure. In some examples, controller **362** is embodied in a general purpose computer while in other examples, controller **362** is embodied in at least some of the components described throughout the present disclosure, such as IPG **35**, **50**, **84** or external components operatively coupled to implantable pulse generator **35**, **50**, **84**. For purposes of this application, in reference to the controller **362**, the term "processor" shall mean a presently developed or future developed processor (or processing resources) that executes sequences of machine readable instructions contained in a memory. In some examples, execution of the sequences of machine readable instructions, such as those provided via therapy manager **371** stored in memory **370** of control portion **360**, cause the processor to perform actions, such as operating controller **362** to implement stimulation protocols as generally described in (or consistent with) at least some examples of the present disclosure. The machine readable instructions may be loaded in a random access memory (RAM) for execution by the processor from their stored location in a read only memory (ROM), a mass storage device, or some other persistent storage (e.g., non-transitory tangible medium or non-volatile tangible medium), as represented by memory **370**. In some examples, memory **370** comprises a computer readable tangible medium providing non-volatile storage of the machine readable instructions executable by a process of controller **362**. In other examples, hard wired circuitry may be used in place of or in combination with machine readable instructions to implement the functions described. For example, controller **362** may be embodied as part of at least one application-specific integrated circuit (ASIC). In at least some examples, the controller **362** is not limited to any specific combination of hardware circuitry and machine readable instructions, nor limited to any particular source for the machine readable instructions executed by the controller **362**.

In some examples, user interface **396** shown in FIG. **11**A comprises a user interface or other display that provides for the simultaneous display, activation, and/or operation of at least some of the various components, functions, features, and of stimulation element **12** (FIG. **1**A), therapy manager **16** (FIG. **1**), control portion **360** (FIG. **9**), IPG **35**, **50**, **84** (FIGS. **2**A, **2**B, **2**D), and related elements, as described throughout the present disclosure. In some examples, at least some portions or aspects of the user interface **396** are provided via a graphical user interface (GUI) and may include an input and a display.

In some examples, user interface **396** includes at least some of the components illustrated in user interface **400** schematically depicted in FIG. **11**B.

As shown in FIG. **11**B, user interface **400** includes at least some of the various components, functions, elements, and features as described and illustrated in association with at least stimulation protocol elements **280** (FIG. **5**), **490** (FIG. **15**A), therapeutic monitoring element **350** (FIG. **8**), stimulation parameters **250** (FIG. **4**), stimulation protocol element **450** (including independent function **454**, respiratory-dependent function **456** in FIG. **12**), automatic protocol selector **470** (FIG. **14**), and stimulation protocol selection **500** (FIG. **15**B).

FIG. **10** is a diagram **380** schematically illustrating a manner in which the control portion **360** is implemented, according to one example of the present disclosure. In some examples, control portion **360** is entirely implemented within or by an implantable pulse generator **385**, which has at least some of substantially the same features and attributes as pulse generator (IPG) **35**, **50**, **84** as previously described in association with at least FIGS. **1**-**9**. In some examples, control portion **360** is entirely implemented within or by a remote control **390** (e.g. a programmer) external to the patient's body, such as a patient control **392** and/or a physician control **394**. In some examples, the control portion **360** is partially implemented in the pulse generator **385** and partially implemented in the remote control **390** (at least one of patient control **392** and physician control **394**).

In some examples, in association with control portion **360**, user interface (**396** in FIG. **11**A; **400** in FIG. **11**B) is implemented in remote control **390**.

FIG. **12** is a block diagram of a stimulation protocol element **450**, according to one example of the present disclosure. As shown in FIG. **12**, stimulation protocol element **450** includes an independent stimulation function **454** and a respiratory-dependent function **456**. In some examples, the independent stimulation function **454** includes

at least some of substantially the same features as independent stimulation function **14** associated with stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) as part of an at least partially implantable stimulation system, as previously described in association with FIGS. **1**-**11**B. Meanwhile, FIG. **13** is a block diagram of a respiration-dependent function **456**, according to one example of the present disclosure.

After describing the features and attributes associated with the respiration-dependent stimulation function **456**, at least some examples regarding the relationship and relative operation of the independent stimulation function **454** and respiratory-dependent stimulation function **456** will be addressed.

As shown in FIG. **13**, in some examples, the respiratory-dependent function **456** includes a synchronous parameter **460**, a synchronization characteristic parameter **462**, and a stability parameter **464**.

In some examples, via the synchronous parameter **460**, respiratory-dependent function **456** implements a stimulation protocol in which each individual nerve stimulation period (within a treatment period) is triggered by and/or synchronized relative to a synchronization characteristic of the patient's respiratory waveform. For instance, in some examples, respiratory-dependent function **456** causes individual stimulation periods to occur substantially simultaneous with the inspiratory phase (e.g. **162** in FIG. **3**B) of the patient's respiratory cycle (e.g. **204**A in FIG. **3**B) such that stimulation is considered to be synchronous with inspiration.

In some examples, per synchronization characteristic parameter **462**, one can select (or a therapy manager can automatically select) the characteristic to which stimulation will be synchronized. In some examples, via parameter **462** respiratory-dependent stimulation function **456** causes nerve stimulation periods to be synchronized relative to a junction or transition between expiratory pause and the onset of inspiration. In some examples, via parameter **462**, nerve stimulation periods are synchronized relative to a junction or transition between inspiration and the onset (i.e. beginning) of expiration. In some examples, the characteristic to which stimulation will be synchronized can be peak inspiration, peak expiration, or expiratory pause.

In some examples, stability parameter **464** of respiratory-dependent stimulation function **456** (FIG. **13**) tracks and determines at least one parameter of a sensed respiratory waveform to determine the relative stability of the respiratory waveform (e.g. sensor signal quality) to provide a reliable, accurate indication of respiratory behavior to the therapy manager (**371** in FIG. **9**). Without a reasonably stable respiratory waveform, the respiratory-dependent function **456** cannot be implemented. In such a situation, the independent stimulation function **454** is implemented until the control portion **360** determines via stability parameter **464** that a reasonably stable respiratory waveform is available (e.g. the sensor signal has sufficient quality) and by which stimulation can be triggered and/or synchronized relative to a characteristic of the respiratory waveform.

Via the stability parameter **464**, the control portion **56** of FIG. **2**C (control portion **360** in FIG. **9**) determines whether the respiratory waveform is stable enough (e.g. sensor signal quality is sufficient) to support synchronizing stimulation relative to characteristics (e.g. inspiratory phase) of the respiratory waveform. In some examples, the stability parameter **464** identifies and tracks parameters such as a peak-to-peak amplitude, a respiratory rate, sensor signal frequency content, signal morphology, and a duty cycle associated with at least one of inspiration, expiration, and expiratory pause, or various combinations of these parameters. In some examples, the at least one parameter comprises a statistical stability of these identified parameters. In some examples, a determination of such statistical stability may be performed relative to a known good state for the patient or a moving baseline of known good state for the patient. In some examples, a known good state corresponds to a period of respiration free from obstructive sleep apnea. In some examples, the determination of statistical stability may be performed relative to an independent threshold of statistical goodness.

In some examples, the inspiratory duty cycle is defined as the ratio of inspiration duration to the duration of respiratory period.

In some examples, the above-noted waveform signal stability or quality parameter may be evaluated after sufficient gain is applied to the signal to enable analysis. For instance, if the peak to peak amplitude is low and sensor signal quality is low, then signal gain can be increased to determine if signal quality analysis can be performed. In some examples, a sensed signal can be subject to a process in which a sensor obtains a physiologic signal, to which gain is applied prior to quality analysis, and then potentially used for synchronization of a stimulation protocol relative to the sensed respiratory waveform. In some examples, an automatic gain control mechanism is employed and queried to determine if the gain is stable so the signal may be reliably analyzed.

In some examples, via therapy manager **16**, **371** (FIGS. **1**, **9**), the respiratory-dependent stimulation function **456** can be disabled so that therapy is selectively applied entirely via the independent stimulation function **14** (FIG. **2**A), **454** (FIG. **12**). Of course, in some examples as previously described, the respiratory-dependent stimulation function **456** is not even present with the independent stimulation function **14**, **454** being the sole mechanism to apply nerve stimulation.

FIG. **14** is a diagram **470** schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol **454** (FIG. **12**) and the respiration-dependent stimulation protocol **456** (FIG. **12**), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection in diagram **470** can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram **470** can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least FIGS. **11**B-**13**.

In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols **454**, **456**. In some examples, an independent stimulation protocol **454** is applied for a predetermined period of time, as shown at **472** in FIG. **14**. The predetermined period of time corresponds at least to an amount of time for a stable respiration period to be established, which may be ensured based on the independent stimulation of the airway-patency-related nerve. In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc.

In some examples, operation of the first independent stimulation protocol during at least the first predetermined period of time is not a test mode, such as a mode that may otherwise be dedicated to diagnosing or evaluating the

operational fitness of the stimulation system. Rather, the first independent stimulation protocol operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

In some examples, by applying stimulation protocol(s) via the independent stimulation, a stable respiratory waveform is achieved, thereby increasing the likelihood of being able to transition to operation in the respiratory-dependent stimulation at **478** than if independent stimulation at **472** were not deployed prior to the activation of the respiratory-dependent function at **478**.

With further reference to FIG. **14**, based on monitoring of the sensed respiratory waveform, at repeating intervals, at **474** it is queried whether the respiratory waveform is sufficiently stable to support activation of the respiratory-dependent stimulation. If the answer to the query at **474** is NO, then pathway **476** directs continued operation of independent stimulation at **472**. However, if the answer to the query at **474** is YES, then pathway **477** directs initiation of operation of respiratory-dependent stimulation at **478** of FIG. **14**. During operation of respiratory-dependent stimulation at **478**, the query at **474** is periodically implemented. If the answer to the query (at **474**) is NO, then operation in respiratory-dependent stimulation n (**456** in FIG. **12**) at **478** in FIG. **14** is terminated as operation is returned (i.e. reverts) via pathway **476** to independent stimulation at **472** in FIG. **14** for at least the predetermined period of time.

For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in independent stimulation at **472** without converting to operation in respiratory-dependent stimulation **478**.

In some examples, the query at **474** is performed generally continuously by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc. Upon one or more of these parameters failing to meet the sensor signal quality criteria, then the answer to the query (at **474**) would be registered as NO. Upon meeting the sensor signal quality criteria, the answer to the query at **474** is YES.

In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a first parameter as an average peak-to-peak respiratory amplitude above a threshold, where the average is computed from the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a second parameter as a peak-to-peak respiratory amplitude variability below a threshold, where the threshold is referenced to an average computed over the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a third parameter as a respiratory duration variability below a threshold, where threshold is reference to an average computed of the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a fourth parameter as an average inspiratory phase duration above a threshold, where the average is computed of the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via various combinations of the respective first, second, third, and fourth parameters, including but not limited to, a combination of all four parameters. It will be understood that the sensor signal quality criteria and/or meeting the sensor signal quality criteria is not exclusively defined by the respective four parameters.

FIG. **15**A is block diagram of a stimulation protocol element **490**, according to one example of the present disclosure. In some examples, stimulation protocol element **490** includes at least some of substantially the same features and attributes as stimulation protocol element **450** as previously described in association with at least FIGS. **12**-**14**, while further including at least the features shown in FIG. **15**A.

As shown in FIG. **15**A, stimulation protocol element **490** includes an override function **492** to take abrupt and sustained action to achieve a stable respiratory pattern. For instance, in some examples, persistent sleep disordered breathing is observed, which includes a series of unresolvable/intractable respiratory events (e.g. persistent apnea) that occur despite stimulation via either the independent stimulation function **454** or the respiratory-dependent function **456**. In some examples, the override function **492** is activated when a stable respiratory pattern has not been detected for a predetermined period of time, such as 5 or 10 minutes. In some examples, the predetermined period of time is less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes.

Upon activation of the override function **492**, therapy that was being implemented via the independent stimulation function **454** or via the respiratory-dependent function **456** is terminated or converted over to operation via a continuous stimulation function **494** (FIG. **15**A) in which nerve stimulation is applied continuously (a 100% duty cycle) for a predetermined period of time. As previously described, in some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. **56** in FIG. **2**C). In some examples, during such continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

In some examples, the override function **492** is implemented via an "other" function, in which nerve stimulation is applied that is not continuous but which has an intensity and duration substantially greater than implemented via the stimulation protocols of one of the independent stimulation function **454** (FIG. **12**) or the respiratory-dependent function **456** (FIG. **12**).

In some examples, operation via the override function **492** is maintained until at least one of a time limit, and/or the therapy manager detecting (via the sensed respiratory waveform) at least one respiratory cycle exhibiting an absence of sleep disordered breathing behavior as measured by a number of respiratory cycles and/or a severity threshold (in one example). In some examples, the time limit is 100 seconds, such as about 20 breaths. However, in some examples, the time limit can be much lower, such as 30 to 40 seconds. In some examples, the continuous stimulation is applied until detected sleep disordered breathing is absent for at least three consecutive respiratory cycles, i.e. a successful inspi-

ration occurs for at least three consecutive respiratory cycles or some operator-selectable quantity (e.g. 2, 4) of consecutive respiratory cycles for a particular patient.

In some examples, the continuous stimulation is applied up to a predetermined maximum period. In some examples, the predetermined maximum period is at least 120 seconds. In some examples, the predetermined maximum period is selectable by an operator and can have values greater or less than 120 seconds, such as 130 seconds, 110 seconds, 90 seconds, etc. In general terms, the predetermined maximum period corresponds to an expired time by which fatigue of the stimulated muscle is complete or nearly complete.

In some examples, upon a determination that detected sleep disordered breathing behavior meets or exceeds the severity threshold, the therapy manager terminates operation in the respective independent and respiratory-dependent stimulation modes and initiates operation in a third mode including a stimulation protocol of a stimulation period and a non-stimulation period in a proportion of at least 3 to 1 wherein the stimulation period has a duration equal to or greater than a duration of at least four respiratory cycles.

In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 10 seconds. In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 5 seconds.

Upon determination that a stable respiratory period has been established, operation in the override function **492** terminates and operation is resumed via the independent stimulation function **454** (FIG. **12**) consistent with the functionality previously described in association with at least FIGS. **12**-**14**.

FIG. **15**B is a diagram **500** schematically illustrating aspects of selecting a stimulation protocol, according to one example of the present disclosure. In some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram **500** can be embodied as a method while in some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram **550** can be embodied as operational aspects of a stimulation protocol management associated with a therapy manager **16** as described in association with at least FIGS. **1**-**15**A.

As shown at **502**, respiratory information can be periodically sensed during a treatment period and without synchronization to stimulation. In other words, in at least some instances, this periodic sensing is not related to and/or does not result in synchronizing stimulation to sensed respiratory information. Rather, such periodic sensing can be used to enhance and/or evaluate the effectiveness of the stimulation, among other uses for such periodically sensed respiratory information.

As shown at **504** in FIG. **15**B, if the duration of the sensed respiratory cycles (among a sample of respiratory cycles) is less variable from cycle-to-cycle than a duration variability criteria, then a stimulation protocol is adopted in which a repeating stimulation cycle is applied and which has a duration different than a duration of the reference respiratory cycle for this patient. This arrangement introduces an intentional stagger or offset between the duration of the stimulation cycle and the duration of respiratory cycle, which may ensure overlap of at least some stimulation periods (of the stimulation cycles) with the actual inspiratory phases of the respiratory cycles of the patient a majority of the time.

In some examples, the duration variability criteria establishes a measure of the variability of a duration of sensed respiratory cycles. The variability can be measured by a frequency of changes in the duration during an observation period and/or a magnitude of change in such durations during the observation period. Further details regarding the observation period are identified below.

In some examples, the duration variability criteria is based on several factors, including but not limited to, a duration of a typical stable respiratory period (e.g. 3-6 seconds, depending on the patient), the minimum duration of an apnea (e.g. 10 seconds), and/or an observation period (e.g. 5 minutes) following a change in stimulation parameters. In some examples, the observation period can more than 5 minutes while in some examples, the observation period can be less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes. In some examples, the duration variability criteria is further based on a standard deviation of respiratory periods of less than 1 second and a sample period of at least 4 minutes.

With further reference to **504** in FIG. **15**B, in some examples, this arrangement is implemented via stimulation protocol **210** in FIG. **3**B in which a respiratory waveform is represented via a series **202** of respiratory cycles **204**A-**204**H. Moreover, in this example, the duration of the stimulation cycle (4 stimulation periods plus 1 non-stimulation period) is less than a duration (R) of the reference respiratory cycles, such that the repeating stimulation cycle has a duration different than a duration (R) of the reference respiratory cycle.

This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number (e.g. 2, 3, 4) of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase **162** of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

In some examples, other example stimulation protocols are used for implementation. For instance, example stimulation protocols **220**, **230** as described in association with at least FIGS. **3**C, **3**D can be used. It is noted that stimulation protocols **220**, **230** include stimulation cycles having a duration greater than a duration (R) of the reference respiratory cycle as shown in the respective legends **229**, **239** of FIGS. **3**C, **3**D, respectively.

As shown at **506** in FIG. **15**B, if the duration of the sensed respiratory cycle (of a sensed sample of respiratory cycles) is more variable than the duration variability criteria noted above, then a repeating stimulation cycle is applied and which has a duration generally matching a duration of a reference respiratory cycle. In this instance, the natural variability of the duration of the patient's respiratory cycle can be used to introduce a stagger or offset relative to the duration of the stimulation cycle, which may ensure an overlap of at least some stimulation periods relative to at least some of the inspiratory phases of the patient's live respiratory cycles at least a majority of the time.

In some examples, the reference respiratory cycle is defined by a patient-specific average respiratory cycle obtained at an earlier point in time. In some examples, the reference respiratory cycle is defined by a multi-patient specific average respiratory cycle obtained from a database.

In some examples, this arrangement is implemented via stimulation protocol **240** in FIG. **3**E in which a respiratory waveform is represented via a series **244** of respiratory cycles **245**A-**245**M. Accordingly, FIG. **3**E models the situation in which the duration (R1) of the respiratory cycles has

varied (relative to the duration R of its base/stable respiratory cycle) by more than a threshold. In some examples, the threshold includes R changing (increasing or decreasing) in duration by 5 percent. In this instance the duration R1 represents about an 8 percent change from the duration R because the respiratory cycles **245**A-**245**M have a duration R1 of 6½ time units whereas duration R is equal to 6 time units. It will be understood, of course, that other numeric values that are more or less than 5 percent can be used as the threshold.

While FIG. **3**E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in preceding respiratory cycles. Accordingly, at least with respect to the method of FIG. **15**B, duration R1 should not be viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

It will be further understood that variations in the duration of the respiratory cycle may be exhibited as decreases (instead of increases) and that variations in the duration of the respiratory cycle are not permanent but may last some finite number of respiratory cycles before reverting to a baseline or changing to yet another non-R duration.

In the example of FIG. **3**E, the duration of the stimulation cycle (4 stimulation periods plus 2 non-stimulation periods) is less than a duration (R1) of the respiratory cycles but with the duration of the stimulation cycles being equal to the duration (R) of the reference respiratory cycle (which is based on a historical baseline in at least some examples).

With this arrangement, because the duration (R1) of the sampled respiratory cycle (obtained via periodic sensing) has varied relative to a reference duration R, the therapy manager **16** utilizes a stimulation cycle having a duration to match the duration of the reference respiratory cycle, which in turn introduces the above-mentioned intentional stagger or offset.

This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

Accordingly, as represented at block **506**, when the duration of the periodically sensed respiratory cycle varies more than a duration variability criteria, the therapy manager ensures an appropriate level of stimulation coinciding with the inspiratory phases of the respiratory cycles by intentionally not adjusting the duration of the stimulation cycle to match the modified duration R1 exhibited by the periodically sensed respiratory cycles.

While FIG. **3**E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in at least some preceding respiratory cycles. Accordingly, at least with respect to the method of FIG. **15**B, duration R1 should not be viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

FIG. **15**C is a block diagram schematically illustrating a stimulation protocol selector element **520**, according to one example of the present disclosure. In some examples, the stimulation protocol selector element **520** includes, and enables, selection between a first function **522** and a second function **524**. In some examples, a selection via element **520** between first function **520** and second function **522** can be implemented in association with the aspects of block **502** in FIG. **15**B. In some examples, first function **520** can be implemented via at least some of the aspects of stimulation selection as described in association with block **504** in FIG. **15**B while second function **522** can be implemented via at least some of the aspects of stimulation selection as described in association with block **506** in FIG. **15**B.

FIG. **15**D is a diagram **550** schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol **454** (FIG. **12**) and the respiration-dependent stimulation protocol **456** (FIG. **12**), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection **551** in diagram **550** can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram **550** can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least FIGS. **1**B-**13**.

In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols **454**, **456** (at least FIGS. **11**B-**13**). Accordingly, as shown at **552** in FIG. **15**D, operation starts in a respiratory-dependent stimulation protocol.

With further reference to FIG. **15**D, based on monitoring of the sensed respiratory waveform, at repeating intervals, at **554** it is queried whether the respiratory waveform is sufficiently stable to support continued operation of respiratory-dependent stimulation at **552**. If the answer to the query at **554** is YES, then pathway **556** affirms continued operation of respiratory-dependent stimulation at **552**. However, if the answer to the query at **554** is NO, then pathway **557** directs initiation of operation of independent stimulation at **558** of FIG. **15**D for at least a predetermined period of time. The first predetermined period of time is defined in substantially the same manner as previously described in association with at least FIG. **14**, and the operation of the independent stimulation function at **558** is not a test mode. Rather, the independent stimulation (at **558**) operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

Upon operation of independent stimulation at **558** for at least the predetermined period of time, the query at **554** is periodically implemented. If the answer to the query (at **554**) is YES, then operation in independent stimulation at **558** in FIG. **15**D is terminated as operation is returned via pathway **556** to respiratory-dependent stimulation at **552** in FIG. **15**D. For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in the independent stimulation at **558** without reverting operation into respiratory-dependent stimulation at **552**.

In some examples, the query at **554** is performed by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc.

FIG. **16**A is diagram **640** schematically illustrating a nerve stimulation protocol **641**, according to one example of the present disclosure.

In one aspect, diagram **640** omits a representative respiratory waveform relative to the stimulation protocol because, in at least some examples, operation according to independent stimulation function **14** (FIG. **1**A) occurs regardless of whether a sensed respiratory waveform is available or reasonably stable. Accordingly, diagram **640** illustrates stimulation periods relative to predetermined time periods instead of relative to inspiratory and expiratory phases of a normal respiratory pattern, as further described and illustrated below.

As shown in FIG. **16**A, a nerve stimulation protocol **641** comprises stimulation segments **642** and non-stimulation segments **648**, **649** (i.e. rest periods), which may occur within a time frame (T). In this arrangement, the time frame T comprises a series of eight time units with each time unit having a duration t, as shown in FIG. **16**A. In some examples, a combination of two consecutive time units have a duration R that generally corresponds to a duration of a respiratory cycle. In one aspect, the duration of one time unit (t) comprises one-half of duration R.

As shown in diagram **640**, stimulation protocol **641** includes a repeating sequence of continuous stimulation segments **642** and non-stimulation segments **648**, **649**. Each stimulation segment **642** has a duration of 3 time units (t), each non-stimulation segment **648** has a duration of two time units, and each non-stimulation segment **649** has a duration of one time unit. This pattern is represented by legend **645** as 3:SK2:3:SK1, where SK represents "skip" to indicate skipping stimulation.

As further shown by diagram **640**, as this stimulation cycle pattern (3:SK 2:3:SK 1) is repeated through a series of time frames T (with each time frame T including 8 time units), one can identify the number of stimulation time units that occurs within each time frame T. For example, the first time frame includes 6 stimulation time units out of 8 total time units, followed by three time frames T including 5 stimulation time units out of 8 total time units, followed by two "six stimulation time unit" time frames T, and then three "five stimulation time unit" time frames T. With this in mind, one can express a pattern of the stimulation time units for the first twelve consecutive time frames as 6:5:5:5:6:6:5:5:5.

Via the stimulation protocol **641**, a therapeutic nerve stimulation regimen is applied in which no period of four consecutive respiratory cycles will transpire without a stimulation period coinciding with an expected inspiratory phase of a respiratory cycle. In this stimulation protocol, the duration of stimulation periods exceeds the duration of non-stimulation periods.

FIG. **16**B is a diagram **651** schematically illustrating a stimulation protocol **650**, according to one example of the present disclosure. In some examples, protocol **650** exhibits at least some of substantially the same features and attributes as the stimulation protocols, as previously described in association with at least FIGS. **3**B-**3**E. In general terms, via stimulation protocol **650**, via stimulation element **12** (FIG. **1**A) and/or therapy manager **16** (FIG. **1**B) the independent stimulation function **14** implements asynchronous nerve stimulation which to promote stable respiration despite potential sleep disordered breathing.

As illustrated in FIG. **16**B, the stimulation protocol **650** operates according to stimulation cycles in which the duration (D) of each stimulation cycle is less than the duration (R) of the reference respiratory cycles **654**A, **654**B. Moreover, in some examples, the stimulation cycle has a duration (D) which is significantly less (at least half or less) than the duration (R) of the reference respiratory cycles **654**A, **654**B. In one of these examples, a duration (D) of the stimulation cycle is less than 30 percent of the duration (R) of the reference respiratory cycles **654**A, **654**B. In one of these examples, a duration (D) of the stimulation cycle is less than 20 percent of the duration (R) of the reference respiratory cycle **654**A, **654**B. In one such instance, as illustrated in FIG. **16**B, the duration (D) of the stimulation cycle is about 1 second, whereas the duration (R) of the reference respiratory cycle is about 6 seconds.

In some examples of implementing stimulation protocol **650**, within a given stimulation cycle the stimulation period (e.g. **652**A, **652**B, etc.) and the non-stimulation period (e.g. **658**A, **658**B, etc.) are in a proportion of 4 to 1 to yield a stimulation duty cycle of 80 percent (for each stimulation cycle). In such examples, each stimulation cycle lasts about 1 time unit (t), including a continuous stimulation period of 4 "⅕" time units followed by a non-stimulation period of a single "⅕" time unit, with this stimulation cycle being repeated continuously when nerve stimulation via stimulation protocol **650** is implemented. Accordingly, in some examples, the duration of the entire stimulation cycle (e.g. 4 "⅕" time units of stimulation and a single "⅕" time unit of non-stimulation) is 1 time unit (t), which is significantly less than the duration R of the respiratory cycle, which is 6 time units in this example.

However, it will be understood that in some examples, the duration of the stimulation period need not coincide with a discrete number (e.g. 4) of fractional time units (e.g. "⅕" time units) and the duration of the non-stimulation period need not coincide with a discrete number (e.g. 1) of fractional time units (e.g. "⅕" time units).

In some examples, the duration (R) of the reference respiratory cycles (e.g. **654**A, **654**B, etc.) can be selected to be more or less than 6 time units (t), as shown in FIG. **16**B. In some examples, the duration (D) of each stimulation cycle (including a stimulation period, such as **652**A and a non-stimulation period, such as **658**A) can be selected to be more or less than one time unit (t).

In FIG. **16**B, the first end **653** of stimulation period **652**A is shown as coinciding with the beginning of an inspiratory phase **162** of the respiratory cycle **654**A. However, it will be understood that the beginning **653** of the stimulation period **652**A is not synchronized relative to the inspiratory phase **162**. Rather, the beginning **653** of stimulation period **652**A is shown as coinciding with the beginning of inspiratory phase **162** for illustrative simplicity in juxtaposing the stimulation protocol **650** relative to the reference respiratory cycles **654**A, **654**B, etc. Accordingly, it will be understood that when stimulation (according to stimulation protocol **650**) is initiated during a treatment period, the beginning of the stimulation period **652**A may coincide with a different portion of the reference respiratory cycle (e.g. **654**A) than shown in FIG. **16**B.

As further shown in FIG. **16**B, in one aspect, each respective non-stimulation period (e.g. **658**A, **658**B, etc.) has a duration significantly less than (e.g. at least less than half) a duration of each respective stimulation period (e.g. **652**A, **652**B, etc.). In one aspect, the duration of each stimulation period (e.g. **652**A, **652**B, etc.) is also significantly less than (e.g. at least less than 30%) a duration (R) of the respective reference respiratory cycles (e.g. **654**A, **654**B, etc.). In some examples, in stimulation protocol **650**, the duration (D) of each stimulation period (e.g. **652**A, **652**B, etc.) is significantly less than a duration (I) of the inspiratory phase **162** of an individual respiratory cycle (e.g.

654A) such that multiple, different stimulation periods occur during a single inspiratory phase **162**. Accordingly, with this arrangement, several stimulation cycles will be repeated within a single reference respiratory cycle.

In some examples, the relatively short duration of the stimulation cycle causes a successive stimulation period (e.g. **652**B) to begin at a different place within the inspiratory phase **162** of the reference respiratory cycle than prior stimulation period (e.g. **652**A), such that the stimulation pattern is considered to be independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. Rather, the asynchronous nature of stimulation protocol **650** is further exhibited via the stimulation periods **652**C-**652**F occurring during the expiratory phase **170** of respiratory cycle **654**A because the same stimulation cycle is repeated regardless of where the stimulation periods falls relative to different portions of the reference respiratory cycle.

Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol **650** is started relative to a series of respiratory cycles, the short duration (D) of the stimulation cycle (relative to the longer duration R of the respiratory cycle) ensures that at least a portion of two stimulation periods (e.g. **652**A, **652**B) will significantly overlap (at least a majority) the inspiratory phase **162** of the respective reference respiratory cycles throughout the portion of the treatment period during which stimulation protocol **650** is applied.

In some examples, via therapy manager **16** (FIG. **1**B) a clinician can set a criteria how many respiratory cycles through which the stimulation protocol **650** will be applied before stimulation terminates and/or before a different stimulation protocol is implemented. In some examples, the criteria are based on a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

It will be understood that each inspiratory phase **162** of each respiratory cycle (**204**A-**204**H) is shown in its ideal form in FIG. **3**B, and that in some instances where the inspiratory phase **162** at least partially coincides with one of the respective non-stimulation periods (e.g. **218**D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in FIG. **3**B.

Accordingly, via stimulation protocol **650**, the independent stimulation function **14** of therapy manager **16** (FIG. **1**B) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

In some examples, the stimulation protocol **650** (and similar protocols described above) is implemented via the "other" function **496** (FIG. **15**A) of override function **492** to help overcome the type of persistent sleep-disordered breathing that does not become controlled via less intensive stimulation protocols. Accordingly, stimulation protocol **650** provides stimulation, which is not continuous but which has an intensity substantially greater than implemented via the stimulation protocols of one of the independent stimulation function **454** (FIG. **12**) or the respiratory-dependent function **456** (FIG. **12**), as previously illustrated in association with at least FIGS. **3**B-**3**E.

However, unlike a continuous stimulation pattern such as provided via continuous function **494** (FIG. **15**A) of override function **492**, stimulation protocol **650** regularly provides non-stimulation periods to enable the targeted nerve and/or muscle to rest somewhat among the stimulation periods, while still achieving an overall 80% stimulation duty cycle. In this arrangement, multiple stimulation periods can occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase. In one aspect, such an arrangement may contribute to more favorable patient comfort or tolerance for the implementation of the "other" override function and/or contribute to diminishing any potential nerve or muscle fatigue.

In some examples, variations of stimulation protocol **650** are implemented in which the duration (D) of the stimulation cycle is significantly less than the duration (R) of the reference respiratory cycle, and the stimulation duty cycle is about 60 percent or 70 percent (instead of 80 percent). In such an arrangement, multiple stimulation periods can still occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase, but with more non-stimulation available. In one aspect, such an arrangement may provide more comfort for some patients and/or potentially less muscle fatigue, as compared to the illustrated example stimulation protocol **650** having an 80% stimulation duty cycle (with relatively short duration stimulation cycles).

As with the other example stimulation protocols described herein, stimulation protocol **650** can be modified by an operator via the various parameters, functions, and components as previously described in association with at least FIGS. **4**-**5** can be selected and/or adjusted via a control portion (**56** in FIG. **2**C; **360** in FIG. **9**; **380** in FIG. **10**) in association with user interface (**396** in FIG. **11**A; **400** in FIG. **11**B).

FIG. **17**A is a flow diagram **700** of a method **701** of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method **701** is performed using the components, elements, systems, etc. previously described and illustrated in association with FIGS. **1**-**16**B. In some examples, method **701** is performed using components, elements, systems, etc. other than those previously described and illustrated in association with FIGS. **1**-**16**B.

As shown in FIG. **17**A, at **705** method **701** includes asynchronously stimulating an airway-patency-related nerve, according to a first stimulation protocol of stimulation cycles including a stimulation period and a non-stimulation period.

FIG. **17**B is a flow diagram **720** of a method **721** of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method **721** is performed using the components, elements, systems, etc. previously described and illustrated in association with FIGS. **1**-**16**B. In some examples, method **721** is performed using components, elements, systems, etc. other than those previously described and illustrated in association with FIGS. **1**-**16**B.

As shown in FIG. **17**B, in cooperation with the method **701** of FIG. **17**A, method **721** includes performing nerve stimulation via the therapy manager providing automatic convertible operation between the independent stimulation mode/function of FIG. **17**A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at **724**. With this arrangement, the therapy manager causes operation in the first mode for at least a first predetermined period of time (**726**) and converts operation into the second mode upon at least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria (**728**). Upon the at least one parameter of the sensed

respiratory waveform failing to meet the sensor signal quality criteria (**730**), operation reverts into the first mode for at least the first predetermined period of time In this example, the first mode acts as the default mode of operation.

In some examples, the sensor signal quality criteria is indicative of the system's ability to actually deliver stimulation at the targeted portion of the respiratory period with a high degree of confidence. In some examples the system may define an obstructive event (e.g. apnea/hypopnea) as lasting at least 10 seconds, then the above-mentioned high degree of confidence would correspond to not missing the target portion of the respiratory period twice in consecutive respiratory cycles.

In some examples, the sensor signal quality criteria can be indicative of a patient's real-time condition either in the absence of or in the presence of stimulation. In some examples, the sensor signal quality criteria can be indicative of sensor noise, thereby indicating how well the sensor signal correlates with the patient's real-time condition.

However, in some examples, the second mode can act as the default mode of operation. Accordingly, as shown in FIG. **17**C, in cooperation with the method **701** of FIG. **17**A, method **771** includes performing nerve stimulation via the therapy manager providing convertible operation between the independent stimulation mode/function of FIG. **17**A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at **774**. With this arrangement, the therapy manager causes operation in the second mode (**776**), and upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria, operation converts into the first mode for at least a first predetermined period of time (**778**). At **780**, upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria, operation reverts back into the second mode.

In some examples, with respect to at least FIGS. **17**B and **17**C, the conversion between the first stimulation mode and the second stimulation mode is automatic.

With respect to selection of the first mode or the second mode in association with FIGS. **17**B and **17**C, in some examples a therapy manager **800** includes a default mode selector function **802** (as shown in FIG. **18**) to enable user selection of either the first mode or the second mode as a default mode. In some examples, the therapy manager **800** also comprises at least some of the features and attributes as therapy manager **16** (FIG. **1**B) and other examples of a therapy manager, as previously described in association with at least FIGS. **1**-**17**C.

With respect to selection of the first mode or the second mode in association with FIGS. **17**B and **17**C, in some examples a therapy manager **850** includes a manual conversion function **852** (as shown in FIG. **19**) to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient. In some examples, the therapy manager **850** also comprises at least some of the features and attributes as therapy manager **16** (FIG. **1**B) and other examples of a therapy manager, as previously described in association with at least FIGS. **1**-**17**C. Accordingly, at least some examples of the present disclosure provide for a robust scheme to increase the effectiveness of nerve stimulation to treat sleep disordered breathing.

Although specific examples have been illustrated and described herein, it will be appreciated by those of ordinary skill in the art that a variety of alternate and/or equivalent implementations may be substituted for the specific examples shown and described without departing from the scope of the present disclosure. This application is intended to cover any adaptations or variations of the specific examples discussed herein.

What is claimed is:

1. A device for treating obstructive sleep apnea, comprising: a non-cardiac stimulation means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter.

2. The device of claim **1**, wherein the asynchronous timing of the stimulation relative to patient breathing comprises the timing being not based on actively-sensed respiration during application of the first stimulation therapy protocol.

3. The device of claim **1**, wherein the reference respiratory-related parameter comprises a reference respiratory pattern.

4. The device of claim **3**, wherein the reference respiratory pattern comprises a reference respiratory cycle, and wherein a duration of each respective stimulation period is greater than a duration of an inspiratory phase of the reference respiratory cycle.

5. The device of claim **1**, wherein the reference respiratory-related parameter is based on stable respiration.

6. The device of claim **1**, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is less than a duration of the reference respiratory cycle.

7. The device of claim **1**, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is no greater than a duration of a reference respiratory cycle.

8. The device of claim **1**, wherein the duration of the respective stimulation periods remain uniform.

9. The device of claim **1**, wherein the reference respiratory-related parameter comprises a reference respiratory cycle, and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 30 percent of duration of a reference respiratory cycle.

10. The device of claim **1**, wherein a respective one of the stimulation periods and a respective one of the non-stimulation periods are in a proportion of at least 1.5 to 1.

11. The device of claim **10**, wherein a duration of a respective one of the stimulation periods exceeds the duration of a respective one of the non-stimulation periods by a factor of 3.

12. The device of claim **1**, wherein a combination of a respective one of the stimulation periods and a respective

one of the non-stimulation periods comprises a stimulation cycle, and wherein a duration of the respective one of the stimulation periods comprises at least 80 percent of a duration of the stimulation cycle.

13. The device of claim **1**, wherein each respective stimulation period comprises continuous pulsed stimulation.

14. The device of claim **1**, comprising:

a processor; and

a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation protocol.

15. The device of claim **1**, wherein the first stimulation therapy protocol is to be applied during a treatment period in which the patient is to engage in sleeping behavior.

16. A device for treating obstructive sleep apnea, comprising: a non-cardiac means for stimulating an upper airway patency-related nerve wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.

17. The device of claim **16**, wherein the duration of each respective non-stimulation period is at least less than half of the duration of each respective stimulation period.

18. The device of claim **16**, wherein the reference respiratory cycle comprises at least one of:

a historical patient-specific reference respiratory cycle; and

a multiple patient reference respiratory cycle.

19. The device of claim **16**, wherein the first stimulation therapy protocol is to deliver at least some of the multiple stimulation periods within a duration of an inspiratory phase of the reference respiratory cycle.

20. The device of claim **16**, wherein the duration of each respective stimulation period is at least less than 30 percent of a duration of the reference respiratory cycle.

21. The device of claim **16**, wherein a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein the first stimulation therapy protocol is to deliver more than one stimulation cycle within a duration of the reference respiratory cycle.

22. A device for treating obstructive sleep apnea, comprising: a non-cardiac means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle.

23. The device of claim **22**, wherein the duration of a respective one of the stimulation periods is greater than the duration of the reference respiratory cycle.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 11/07/2023

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EXAMINER	
LAU, MICHAEL J	

ART UNIT	PAPER NUMBER
3792	

NOTIFICATION DATE	DELIVERY MODE
11/07/2023	ELECTRONIC

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USPTO.PATENTS@dbclaw.com

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00067

UNITED STATES PATENT AND TRADEMARK OFFICE

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Address: COMMISSIONER FOR PATENTS
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APPLICATION NO.	ISSUE DATE	PATENT NO.
17/012,481	07-Nov-2023	11806526

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
MINNEAPOLIS, MN 55402

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at https://patentcenter.uspto.gov

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit https://www.uspto.gov/electronicgrants

UNITED STATES PATENT AND TRADEMARK OFFICE

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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	11/07/2023	11806526	I618.118.104	3270

25281 7590 10/18/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at https://patentcenter.uspto.gov/. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at https://certifiedcopycenter.uspto.gov/index.html. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment is 403 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (https://patentcenter.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00069

INVENTOR(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional inventors):

Darrell Wagner, Ham Lake, MN;
Quan Ni, Shoreview, MN;
John Rondoni, Plymouth, MN;
Dave Dieken, Minneapolis, MN;

APPLICANT(s) (Please see PATENT CENTER site https://patentcenter.uspto.gov for additional applicants):

INSPIRE MEDICAL SYSTEMS, INC., Golden Valley, MN;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit SelectUSA.gov.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00070

INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3700
Examiner Name	Fristoe Jr., John K.
Attorney Docket Number	I618.118.104

	163	7447545		2008-11-04	Heruth et al.	
	164	7454250		2008-11-18	Bjorling et al.	
	165	7453928		2008-12-09	Lee et al.	
	166	7468040		2008-12-23	Hartley et al.	
	167	7469697		2008-12-30	Lee et al.	
	168	7473227		2009-01-06	Hsu et al.	
	169	7491181		2009-02-17	Heruth et al.	
Change(s) applied to document, /C.S./ 7/11/2023	170	6509164		~~2009-03-24~~ 01/2003	~~Jensen et al.~~ Guirguis	
	171	7510531		2009-03-31	Lee et al.	
	172	7526341		2009-04-29	Goetz et al.	
	173	7542803		2009-06-02	Heruth et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25281 7590 07/06/2023
DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

Paul S. Grunzweig	(Typed or printed name)
/Paul S. Grunzweig/	(Signature)
September 27, 2023	(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

TITLE OF INVENTION: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	10/06/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
LAU, MICHAEL J	3792	607-042000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 Dicke, Billig & Czaja, PLLC
2
3

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE: INSPIRE MEDICAL SYSTEMS, INC.

(B) RESIDENCE: (CITY and STATE OR COUNTRY): Golden Valley , MN

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☒ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

☒ Electronic Payment via Patent Center or EFS-Web ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. 500471

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

☐ Applicant asserting small entity status. See 37 CFR 1.27

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

☐ Applicant changing to regular undiscounted fee status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /Paul S. Grunzweig/ Date September 27, 2023

Typed or printed name Paul S. Grunzweig Registration No. 37143

PTOL-85 Part B (08-18) Approved for use through 01/31/2020 OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00072

Electronic Patent Application Fee Transmittal

Application Number:	17012481
Filing Date:	04-Sep-2020
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Attorney Docket Number:	I618.118.104

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
UTILITY APPL ISSUE FEE	1501	1	1200	1200

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**1200**

Electronic Acknowledgement Receipt

EFS ID:	48647441
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	27-SEP-2023
Filing Date:	04-SEP-2020
Time Stamp:	14:12:21
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$1200
RAM confirmation Number	E20239QE12498050
Deposit Account	
Authorized User	
The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:	

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Issue Fee Payment (PTO-85B)	2023-09-27IssueFee.pdf	1747230 51782b90117f8484c9caf5845dec74e8d9a8ac2f	no	1
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	37844 f09c9e38a0386618d008323f1236893aa7dfff56	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	1785074		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 07/21/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	

ART UNIT	PAPER NUMBER
3792	

NOTIFICATION DATE	DELIVERY MODE
07/21/2023	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DBCLAW-Docket@dbclaw.com
USPTO.PATENTS@dbclaw.com

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00077

Corrected ***Notice of Allowability***	**Application No.** 17/012,481	**Applicant(s)** Wagner et al.	
	Examiner MICHAEL J LAU	**Art Unit** 3792	**AIA (FITF) Status** Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 3/2/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-9,11-14 and 16-25 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☑ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☐ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MICHAEL J LAU/ Examiner, Art Unit 3792	/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00078

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Response to Arguments

2. Applicant's arguments, see Pages 7-18, filed 3/2/2023, with respect to claims 1-24 have been fully considered and are persuasive. The rejection of claims 1-24 has been withdrawn.

EXAMINER'S AMENDMENT

3. Authorization for this examiner's amendment was given in an interview with Paul Grunzweig on 7/14/2023.

4. Para. 1 of the Specification is amended as follows:

5. [0001] This application is a continuation of utility application Serial Number 15/562,714, filed September 28, 2017, now US Patent 10,898,709, which is a 371 National Phase Application of PCT Patent Application No. PCT/US20 16/022611, filed March 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed March 19, 2015, all of which are herein incorporated by reference.

6. Claim 1 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac stimulation ~~element to stimulate~~ means for stimulating an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter, wherein, the non-cardiac stimulation means for

stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.

7. Claim 17 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non- stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.

8. Claim 23 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle, wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.

9. Claim 15 is cancelled.

10. Claim 16 is amended as follows: The device of claim 1, comprising: a processor; and a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation therapy protocol via the non-cardiac stimulation means for stimulating.

Allowable Subject Matter

11. Claims 1-9,11-14 and 16-25 are allowed.

Reasons for Allowance

12. The following is an examiner's statement of reasons for allowance: Claims 1-9,11-14 and 16-25 are allowed over the prior art because the Examiner found that none of the cited prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing.

13. Examiner found closest prior art would be Bolea, cited previously, that the asynchronous is used for familiarization (eg. Para. 514-515), but does not use it as a therapy for sleep apnea.

14. Another close prior art found was US 2011/0093032 A1 that discloses asynchronous stimulation with pulse trains (eg. Para. 39, 42, 162, and 171) but does not disclose the duration of each respective stimulation period is based on a reference respiratory-related parameter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J LAU whose telephone number is (571)272-2317. The examiner can normally be reached 8-5:30 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on (571) 272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL J LAU/

Examiner, Art Unit 3792

/CARL H LAYNO/
Supervisory Patent Examiner, Art Unit 3792

Applicant-Initiated Interview Summary	**Application No.** 17/012,481	**Applicant(s)** Wagner et al.		
	Examiner MICHAEL J LAU	**Art Unit** 3792	**AIA (First Inventor to File) Status** Yes	**Page** 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	**Title**	**Type**
MICHAEL J LAU	Examiner	Telephonic
Paul Grunzweig	Attorney	

Date of Interview: 14 July 2023

Issues Discussed:

Other

Discussed corrections to the Examiner's amendments in the NoA

/MICHAEL J LAU/ Examiner, Art Unit 3792	/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792

Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04
Please further see:
MPEP 713.04
Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b)
37 CFR § 1.2 Business to be transacted in writing

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00083

Doc Code: ECOMM.AUTH/ECOMM.WTDW
Doc Description: Internet Communications Authorization/Internet Communications Authorization Withdrawal

PTO/SB/439 (11-15)

AUTHORIZATION FOR INTERNET COMMUNICATIONS IN A PATENT APPLICATION OR REQUEST TO WITHDRAW AUTHORIZATION FOR INTERNET COMMUNICATIONS		
	Application No.	17/012,481
	Filing Date	September 04, 2020
	First Named Inventor	Darrell Wagner
	Art Unit	3792
	Examiner Name	LAU, Michael J.
	Practitioner Docket No.	I618.118.104

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I. To authorize permission for Internet Communications.

☒ Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned and practitioners in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application via video conferencing, instant messaging, or electronic mail. I understand that a copy of these communications will be made of record in the application file. (MPEP 502.03)

II. To withdraw authorization for Internet Communications.

☐ The authorization given on _____, to the USPTO to communicate with the undersigned and any practitioner in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application via Internet communications such as video conferencing, instant messaging, or electronic mail is hereby withdrawn. I understand that the withdrawal is effective when approved rather than when received.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 37,143.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/Paul S. Grunzweig/ — Signature

7/12/2023 — Date

Paul S. Grunzweig — Typed or printed name

612-767-2504 — Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Juristic entities must be represented by a patent practitioner (see 37 CFR 1.31, which is applicable to any paper filed on or after September 16, 2012, that is presented on behalf of a juristic entity, regardless of application filing date). Submit multiple forms if more than one signature is required, see below*.

☒ * Total of 1 forms are submitted.

Privacy Act Statement

The **Privacy Act of 1974 (P.L. 93-579)** requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Acknowledgement Receipt

EFS ID:	48285777
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	12-JUL-2023
Filing Date:	04-SEP-2020
Time Stamp:	14:27:18
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Internet Communications Authorization	2023-07-12AuthznInternetComm.pdf	213049 0e0258bf79bad0a39e7700fc427882b24cc690f8	no	2
Warnings:					

Information:	
Total Files Size (in bytes):	213049

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

25281 7590 07/06/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER
LAU, MICHAEL J

ART UNIT	PAPER NUMBER
3792	

DATE MAILED: 07/06/2023

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

TITLE OF INVENTION: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	10/06/2023

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PTOL-85 (Rev. 02/11)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00088

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

25281 7590 07/06/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

TITLE OF INVENTION: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	$1200	$0.00	$0.00	$1200	10/06/2023

EXAMINER	ART UNIT	CLASS-SUBCLASS
LAU, MICHAEL J	3792	607-042000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,
(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
2 _____
3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. Fees submitted: ❑ Issue Fee ❑ Publication Fee (if required)

4b. Method of Payment: *(Please first reapply any previously paid fee shown above)*

❑ Electronic Payment via Patent Center or EFS-Web ❑ Enclosed check ❑ Non-electronic payment by credit card (Attach form PTO-2038)

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

❑ Applicant certifying micro entity status. See 37 CFR 1.29
NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

❑ Applicant asserting small entity status. See 37 CFR 1.27
NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

❑ Applicant changing to regular undiscounted fee status.
NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

PTOL-85 Part B (08-18) Approved for use through 01/31/2020 OMB 0651-0033 U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00089

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 07/06/2023

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	
ART UNIT	PAPER NUMBER
3792	

DATE MAILED: 07/06/2023

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00090

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 17/012,481	Applicant(s) Wagner et al.	
	Examiner MICHAEL J LAU	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☑ This communication is responsive to 3/2/2023.
   ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☑ The allowed claim(s) is/are 1-9,11-14 and 16-25 . As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information , please see **http://www.uspto.gov/patents/init_events/pph/index.jsp** or send an inquiry to **PPHfeedback@uspto.gov.**

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

   Certified copies:

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____ .

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____ .

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☑ Notice of References Cited (PTO-892)
2. ☑ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____.
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. _____.
5. ☑ Examiner's Amendment/Comment
6. ☑ Examiner's Statement of Reasons for Allowance
7. ☐ Other _____.

/MICHAEL J LAU/ Examiner, Art Unit 3792	/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00092

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Response to Arguments

2. Applicant's arguments, see Pages 7-18, filed 3/2/2023, with respect to claims 1-24 have been fully considered and are persuasive. The rejection of claims 1-24 has been withdrawn.

EXAMINER'S AMENDMENT

3. Authorization for this examiner's amendment was given in an interview with Paul Grunzweig on 6/26/2023.

4. Para. 1 of the Specification is amended as follows:

5. [0001] This application is a continuation of utility application Serial Number 15/562,714, filed September 28, 2017, now US Patent 10,898,709, which is a 371 National Phase Application of PCT Patent Application No. PCT/US20 16/022611, filed March 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed March 19, 2015, all of which are herein incorporated by reference.

6. Claim 1 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac stimulation ~~element to stimulate~~ means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode according to a first stimulation therapy protocol including alternating stimulation periods and non- stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-

stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter.

7. Claim 17 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non- stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.

8. Claim 23 is amended as follows: A device for treating obstructive sleep apnea, comprising: a non-cardiac ~~stimulation element to stimulate~~ means for stimulating an upper airway patency-related nerve, wherein, the non-cardiac stimulation element comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle.

9. Claim 15 is cancelled.

Allowable Subject Matter

10. Claims 1-9,11-14 and 16-25 are allowed.

Reasons for Allowance

11. The following is an examiner's statement of reasons for allowance: Claims 1-9,11-14 and 16-25 are allowed over the prior art because the Examiner found that none of the cited prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing.

12. Examiner found closest prior art would be Bolea, cited previously, that the asynchronous is used for familiarization (eg. Para. 514-515), but does not use it as a therapy for sleep apnea.

13. Another close prior art found was US 2011/0093032 A1 that discloses asynchronous stimulation with pulse trains (eg. Para. 39, 42, 162, and 171) but does not disclose the duration of each respective stimulation period is based on a reference respiratory-related parameter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J LAU whose telephone number is (571)272-2317. The examiner can normally be reached 8-5:30 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on (571) 272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL J LAU/
Examiner, Art Unit 3792

/CARL H LAYNO/
Supervisory Patent Examiner, Art Unit 3792

Notice of References Cited	Application/Control No. 17/012,481	Applicant(s)/Patent Under Reexamination Wagner et al.	
	Examiner MICHAEL J LAU	Art Unit 3792	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20200147376-A1	05-2020	Dieken; David	A61N1/36139	1/1
*	B	US-5146918-A	09-1992	Kallok; Michael J.	A61N1/3601	607/42
*	C	US-20150039045-A1	02-2015	Ni; Quan	A61B5/4836	607/42
*	D	US-20140228905-A1	08-2014	BOLEA; Stephen L.	A61F5/566	607/42
*	E	US-20140194793-A1	07-2014	Nakata; Robert Haruo	G01S13/825	601/48
*	F	US-20110093032-A1	04-2011	Boggs, II; Joseph W.	A61N1/3611	607/42
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	**Art Unit**
	MICHAEL J LAU	3792

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/27/2022	06/22/2023							
1	1	✓	=							
2	2	✓	=							
3	3	✓	=							
4	4	✓	=							
5	5	✓	=							
6	6	✓	=							
7	7	✓	=							
8	8	✓	=							
9	9	✓	=							
	10	✓	-							
10	11	✓	=							
11	12	✓	=							
12	13	✓	=							
13	14	✓	=							
	15	✓	-							
14	16	✓	=							
16	17	✓	=							
17	18	✓	=							
18	19	✓	=							
19	20	✓	=							
20	21	✓	=							
21	22	✓	=							
22	23	✓	=							
23	24	✓	=							
15	25		=							

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00098

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	Art Unit
	MICHAEL J LAU	3792

CPC - Searched*		
Symbol	**Date**	**Examiner**
A61N1/3601,36146,3611,36171	10/27/2022	ML
A61B5/0826,0816,113,4818,4848,686,0205	10/27/2022	ML
G16H20/40	10/27/2022	ML

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**
607	42	10/27/2022	ML

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
inventor and prior art search on pe2e search	10/27/2022	ML
updated search on pe2e search	06/22/2023	ML

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**
	see pe2e search history for interference search	06/22/2023	ML

/MICHAEL J LAU/ Examiner, Art Unit 3792	

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00099

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	**Art Unit**
	MICHAEL J LAU	3792

CPC						
Symbol					**Type**	**Version**
A61N	/	1	/	3601	F	2013-01-01
A61B	/	5	/	0826	I	2013-01-01
A61B	/	5	/	4818	I	2013-01-01
A61B	/	5	/	4848	I	2013-01-01
A61N	/	1	/	3611	I	2013-01-01
A61B	/	5	/	686	I	2013-01-01
G16H	/	20	/	40	I	2018-01-01
A61B	/	5	/	0816	I	2013-01-01
A61B	/	5	/	113	I	2013-01-01
A61N	/	1	/	36146	A	2013-01-01
A61N	/	1	/	3614	A	2017-08-01
A61B	/	5	/	0205	A	2013-01-01
A61N	/	1	/	36171	A	2013-01-01

CPC Combination Sets							
Symbol					**Type**	**Set**	**Ranking**	**Version**
	/		/					

/MICHAEL J LAU/ Examiner, Art Unit 3792	22 June 2023	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	23	
/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792	26 June 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1A-B

U.S. Patent and Trademark Office — Part of Paper No.: 20230622

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00100

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	**Art Unit**
	MICHAEL J LAU	3792

INTERNATIONAL CLASSIFICATION				
CLAIMED				
A61N	/	1	/	36

NON-CLAIMED				
	/		/	

US ORIGINAL CLASSIFICATION	
CLASS	**SUBCLASS**

CROSS REFERENCES(S)						
CLASS	**SUBCLASS (ONE SUBCLASS PER BLOCK)**					

/MICHAEL J LAU/ Examiner, Art Unit 3792 (Assistant Examiner)	22 June 2023 (Date)	**Total Claims Allowed:** 23	
/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792 (Primary Examiner)	26 June 2023 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure 1A-B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00101

Issue Classification	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	**Art Unit**
	MICHAEL J LAU	3792

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIMS

Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
1	1	10	11	20	21										
2	2	11	12	21	22										
3	3	12	13	22	23										
4	4	13	14	23	24										
5	5	14	16	15	25										
6	6	16	17												
7	7	17	18												
8	8	18	19												
9	9	19	20												

/MICHAEL J LAU/ Examiner, Art Unit 3792	22 June 2023	**Total Claims Allowed:**	
(Assistant Examiner)	(Date)	23	
/CARL H LAYNO/ Supervisory Patent Examiner, Art Unit 3792	26 June 2023	O.G. Print Claim(s)	O.G. Print Figure
(Primary Examiner)	(Date)	1	1A-B

U.S. Patent and Trademark Office — Part of Paper No.: 20230622

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00102

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	57	((("INSPIRE") near3 ("MEDICAL") near3 ("SYSTEMS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2022/10/25 03:54 PM
L2	558	((("WAGNER") near3 ("Darrell")) OR (("NI") near3 ("Quan")) OR (("RONDONI") near3 ("John")) OR (("DIEKEN") near3 ("Dave"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 03:57 PM
L3	0	607/042.ccls.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:15 PM
L4	1065	607/42.ccls.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:15 PM
L5	6479	A61N1/3601,36146,3611,36171.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:27 PM
L6	44916	A61B5/0826,0816,113,4818,4848,686,0205.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:28 PM
L7	13477	G16H20/40.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:28 PM
L8	59691030	@pd<"20150319"	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 05:17 PM
L9	42	(Artificial Intelligence) Similar to: 17/012,481 with 0 CPC Selections and 0 Text Selections Text: (US-20200398051-A1 OR US-10898709-B2 OR US-20200147376-A1 OR AU-2016233377-B2 OR AU-2020210249-A1 OR CN-113908438-A OR US-20210308454-A1 OR AU-2020210249-B2 OR US-20180117316-A1 OR EP-3881892-A1 OR AU-2016233377-A1 OR EP-3271008-A1 OR WO-2016149344-A1 OR CA-3004583-A1 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN))	OR	ON	ON	2022/10/25 05:34 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00103

		AU-2021232791-A1 OR US-20170128002-A1 OR JP-6759227-B2 OR JP-2020203110-A OR CN-107864617-B OR US-20200146620-A9 OR US-10888267-B2 OR EP-2358268-B1 OR EP-0505195-A2 OR US-20200238084-A1 OR US-5146918-A OR US-7680538-B2 OR US-20180015281-A1 OR US-20160354603-A1 OR AU-649145-B2 OR CA-2084312-A1 OR WO-2016149176-A1 OR US-20150283383-A1 OR EP-0541763-A1 OR US-5174287-A OR WO-9221407-A1 OR JP-H05103839-A OR US-20160354602-A1 OR EP-0541763-B1 OR CA-2744269-C OR JP-2018508299-A OR US-9370657-B2 OR WO-2020102193-A1 OR US-10946195-B2 OR US-20020049479-A1 OR CN-107864617-A OR CA-2062171-A1 OR US-20220160295-A1 OR EP-3714771-A1 OR US-5215082-A OR US-20100131029-A1).did.					
L10	43	(Artificial Intelligence) Similar to: 17/012,481 with 0 CPC Selections and 1 Text Selection Text: (US-20200147376-A1 OR US-10888267-B2 OR US-5146918-A OR EP-0505195-A2 OR EP-2358268-B1 OR CA-2084312-A1 OR AU-649145-B2 OR EP-0541763-A1 OR WO-9221407-A1 OR EP-0541763-B1 OR US-5174287-A OR JP-H05103839-A OR US-20200238084-A1 OR CA-2744269-C OR US-7680538-B2 OR US-	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN))	OR	ON	ON	2022/10/25 05:34 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00104

		20200146620-A9 OR US-20170128002-A1 OR US-20020049479-A1 OR US-5215082-A OR CA-2062171-A1 OR US-20160354603-A1 OR US-20060167523-A1 OR US-8498712-B2 OR US-20150283383-A1 OR US-20080103407-A1 OR US-20160354602-A1 OR EP-0507580-A2 OR US-20120234332-A1 OR US-8626304-B2 OR US-5540733-A OR US-7225021-B1 OR US-20100125310-A1 OR US-8644939-B2 OR CA-2744269-A1 OR WO-2010057286-A1 OR EP-2358268-A1 OR US-5275159-A OR US-20170188940-A9 OR US-20140051938-A1 OR US-9370657-B2 OR US-20170119306-A1 OR EP-0702978-A3 OR AR-030368-A1 OR US-20200398051-A1 OR WO-2019088582-A1 OR US-20060149334-A1 OR US-7004908-B2 OR US-6770037-B2 OR US-10368800-B2 OR US-9402563-B2).did.					
L11	168300	L4 OR L5 OR L6 OR L7	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:07 PM
L12	51493	L8 AND L11	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA,	OR	ON	ON	2022/10/26 02:07 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00105

			EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L13	564	L12 AND upper ADJ air$1way WITH nerve	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:17 PM
L14	77	L12 AND upper ADJ air$1way WITH nerve WITH puls$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:17 PM
L15	72	L12 AND upper ADJ air$1way WITH nerve WITH puls$ AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO;	OR	ON	ON	2022/10/26 02:18 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00106

			JPO; DERWENT; IBM_TDB)				
L16	53	L12 AND upper ADJ air$1way WITH nerve WITH puls$ AND duration$ AND (independent$ OR a$1synchron$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:22 PM
L17	7	L12 AND upper ADJ air$1way WITH nerve WITH puls$ SAME (independent$ OR a$1synchron$) AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:23 PM
L18	11	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ SAME (independent$ OR a$1synchron$) AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:26 PM
L19	100	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS,	OR	ON	ON	2022/10/26 02:27 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00107

			IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L20	98	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$ SAME (signal$ OR stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:27 PM
L21	46	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$ SAME (signal$ OR stimulat$) AND (a$synchron$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:48 PM
L22	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (signal$ OR stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00108

L23	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM
L24	10	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ SAME (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM
L25	71	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:53 PM
L26	71	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL,	OR	ON	ON	2022/10/26 02:55 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00109

		(inspirat$)	NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L27	59	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (inspirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:56 PM
L28	19	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (inspirat$) AND duty ADJ cycle	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:58 PM
L29	1	"20140228905".pn. AND duration SAME (respirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 04:40 PM
L30	1	"20140228905".pn. AND duration SAME	(US-PGPUB; USPAT; USOCR; FIT (AP, AT,	OR	ON	ON	2022/10/27 12:35 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00110

		(respirat$) SAME (stimulat$ OR puls$ OR therap$ OR wave$form)	AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L31	1	"20140228905".pn. AND duration SAME (respirat$) SAME (stimulat$ OR puls$ OR therap$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:21 PM
L32	1	"20140228905".pn. AND duration SAME (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:23 PM
L33	1	"20140228905".pn. AND duration WITH (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE,	OR	ON	ON	2022/10/27 01:23 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00111

			SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L34	1	"20140228905".pn. AND (duration OR length$ OR period$ OR time$) WITH (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:40 PM
L35	1	"20140228905".pn. AND duty ADJ cycle	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 02:14 PM
L36	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$) WITH populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:37 PM
L37	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU,	OR	ON	ON	2022/10/27 03:37 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00112

		puls$ AND (signal$ OR stimulat$ OR pulse$) AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$)	CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L38	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:37 PM
L39	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:51 PM
L40	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN,	OR	ON	ON	2022/10/27 03:59 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00113

			WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L41	4	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:59 PM
L42	155	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:00 PM
L43	5	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$ SAME (stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:00 PM
L44	162	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB,	OR	ON	ON	2022/10/27 04:08 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00114

		templat$) SAME (populat$ OR multipl$ near2 patient$)	HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L45	10	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:08 PM
L46	10	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:23 PM
L47	30	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) AND (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT;	OR	ON	ON	2022/10/27 04:26 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00115

			IBM_TDB)				
L48	3	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:26 PM
L49	1	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$) WITH (populat$ OR multipl$ near2 patient$) SAME (duration OR period OR width OR length)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:30 PM
L50	11	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:31 PM
L51	27	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$ OR respirat$ OR inspirat$) WITH (populat$ OR multipl$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV,	OR	ON	ON	2022/10/27 04:32 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00116

		near2 patient$)	MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L52	1	"20140228905".pn. AND (duration OR length OR time OR width) SAME (breath$ OR respirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 05:11 PM

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	2	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (inspirat$) AND duty ADJ cycle	(US-PGPUB; USPAT)	OR	ON	ON	2023/06/22 04:26 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00117

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
Approved for use through 05/31/2024. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3792
Examiner Name	Lau, Michael J.
Attorney Docket Number	I618.118.104

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20120158091	A1	2012-06-21	TEHRANI et al.	

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	1							

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ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3792
	Examiner Name	Lau, Michael J.
	Attorney Docket Number	I618.118.104

	1		

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Examiner Signature	/MICHAEL J LAU/	Date Considered	06/22/2023

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3792
Examiner Name	Lau, Michael J.
Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2023-03-02
Name/Print	Paul S. Grunzweig	Registration Number	37143

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Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00121

Bibliographic Data

Application No: 17/012,481

Foreign Priority claimed: ○ Yes ◉ No

35 USC 119 (a-d) conditions met: ☐ Yes ☑ No ☐ Met After Allowance

Verified and Acknowledged: /MICHAEL J LAU/ Examiner's Signature | Initials

Title: STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
09/04/2020	607	3792	
RULE			

APPLICANTS

INSPIRE MEDICAL SYSTEMS, INC., Golden Valley, MN,

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John Rondoni, Plymouth, MN, UNITED STATES

Dave Dieken, Minneapolis, MN, UNITED STATES

CONTINUING DATA

This application is a CON of 15562714 09/28/2017 PAT 10898709

15562714 is a 371 of PCT/US2016/022611 03/16/2016

PCT/US2016/022611 has PRO of 62135305 03/19/2015

FOREIGN APPLICATIONS

IF REQUIRED, FOREIGN LICENSE GRANTED**

09/15/2020

STATE OR COUNTRY

UNITED STATES

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$2,280

PTO/SB/06 (09-11)
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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 17/012,481	Filing Date 09/04/2020	☐ To be Mailed

ENTITY: ☑ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $460 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT	07/03/2023	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 23	Minus	** 24	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 3	Minus	*** 3	= 0		x $480 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/DAWN BREWER/
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Electronic Patent Application Fee Transmittal

Application Number:	17012481
Filing Date:	04-Sep-2020
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Filer:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Extension - 1 month with $0 paid	1251	1	220	220
Miscellaneous:				
			Total in USD ($)	**220**

Electronic Acknowledgement Receipt

EFS ID:	47622866
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG
Filer Authorized By:	
Attorney Docket Number:	I618.118.104
Receipt Date:	02-MAR-2023
Filing Date:	04-SEP-2020
Time Stamp:	22:56:24
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
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RAM confirmation Number	E202332M57227000
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Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Amendment/Request for Reconsideration-After Non-Final Rejection	2023-03-02ResponseNFOA.pdf	539245 9b04d9ea8d04486a63f85cd4bdfc4d5f83a0efcd	no	18
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	38153 ee011c3bb64e026cf1e8b8b055bee300b2521686	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	577398		

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National Stage of an International Application under 35 U.S.C. 371

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New International Application Filed with the USPTO as a Receiving Office

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+IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Darrell Wagner et al.	Examiner:	LAU, Michael J.
Serial No.:	17/012,481	Group Art Unit:	3792
Filed:	September 04, 2020	Docket No.:	I618.118.104
Title:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING		

AMENDMENT AND RESPONSE

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This Amendment and Response is in reply to the Non Final Office Action mailed November 02, 2022. Please amend the above-identified patent application as follows:

IN THE CLAIMS

Please cancel claim 10 without prejudice.

Please add new claim 25.

Please amend claims 1, 2-5, 17, 20, and 22-23 as follows:

1. (Currently Amended) A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter.

2. (Currently Amended) The device of claim 1, wherein the asynchronous timing of the stimulation relative to patient breathing comprises the timing being not based on actively-sensed respiration during application of the first stimulation therapy protocol.

3. (Currently Amended) The device of claim 1, wherein the reference ~~respiration-related~~respiratory-related parameter comprises a reference respiratory pattern.

4. (Currently Amended) The device of claim 3, wherein the reference respiratory pattern comprises a reference respiratory cycle, and ~~where~~wherein a duration of each respective stimulation period is greater than a duration of an inspiratory phase of the reference respiratory cycle.

5. (Currently Amended) The device of claim 1, wherein the reference ~~respiration-related~~respiratory-related parameter is based on stable respiration.

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6. (Original) The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is less than a duration of the reference respiratory cycle.

7. (Original) The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is no greater than a duration of a reference respiratory cycle.

8. (Original) The device of claim 1, wherein the duration of the respective stimulation periods remain uniform.

9. (Original) The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle, and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 30 percent of duration of a reference respiratory cycle.

10. (Canceled)

11. (Original) The device of claim 1, wherein a respective one of the stimulation periods and a respective one of the non-stimulation periods are in a proportion of at least 1.5 to 1.

12. (Original) The device of claim 11, wherein a duration of a respective one of the stimulation periods exceeds the duration of a respective one of the non-stimulation periods by a factor of 3.

13. (Original) The device of claim 1, wherein a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation

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cycle, and wherein a duration of the respective one of the stimulation periods comprises at least 80 percent of a duration of the stimulation cycle.

14. (Original) The device of claim 1, wherein each respective stimulation period comprises continuous pulsed stimulation.

15. (Original) The device of claim 1, wherein the non-cardiac stimulation element comprises an implantable electrode and the device comprises an implantable pulse generator electrically connectable to the implantable electrode.

16. (Original) The device of claim 1, comprising:

a processor; and

a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation protocol.

17. (Currently Amended) A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.

18. (Original) The device of claim 17, wherein the duration of each respective non-stimulation period is at least less than half of the duration of each respective stimulation period.

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19. (Original) The device of claim 17, wherein the reference respiratory cycle comprises at least one of:

a historical patient-specific reference respiratory cycle; and

a multiple patient reference respiratory cycle.

20. (Currently Amended) The device of claim 17, wherein the first stimulation therapy protocol is to deliver at least some of the multiple stimulation periods within a duration of an inspiratory phase of the reference respiratory cycle.

21. (Original) The device of claim 17, wherein the duration of each respective stimulation period is at least less than 30 percent of a duration of the reference respiratory cycle.

22. (Currently Amended) The device of claim 17, wherein a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein the first stimulation therapy protocol is to deliver more than one stimulation cycle within a duration of the reference respiratory cycle.

23. (Currently Amended) A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle.

24. (Original) The device of claim 23, wherein the duration of a respective one of the stimulation periods is greater than the duration of the reference respiratory cycle.

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25. (New) The device of claim 1, wherein the first stimulation therapy protocol is to be applied during a treatment period in which the patient is to engage in sleeping behavior.

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REMARKS

The following remarks are made in response to the Non Final Office Action mailed November 02, 2022, in which claims 1-18 and 20-24 were rejected. With this Response, claims 1-2-5, 17, 20, and 22-23 have been amended, claim 10 has been canceled, and new claim 25 has been added. Claims 1-9 and 11- 25 remain pending in the application and are presented for reconsideration and allowance.

Claim Rejections under 35 U.S.C. § 103

Claims 1-18 and 20-24 stand rejected under 35 U.S.C. § 103 as being unpatentable over Bolea (US 2014/0228905).

Independent Claim 1

Applicants respectfully traverse the rejection regarding independent claim 1. Applicants submit that the cited portion of Bolea (US 2014/0228905) in Paragraphs 460, 473-474, 514 taken in context with the full passage of Paragraphs 466-474 regarding FIGS. 64A-64D, conflicts with at least the recitation "a non-cardiac stimulation element to engage and to stimulate an upper-airway-patency-related nerve, according to a **first stimulation therapy protocol (including alternating stimulation periods and non-stimulation periods) in which a timing of the stimulation periods is asynchronous relative to patient breathing**" in Applicants' independent claim 1. (Bolea Paragraphs 514-516 are discussed below)

Paragraphs 472-474 of Bolea (cited in the rejection of Applicants' independent claim 1) describe aspects of various stimulation duty cycles. In doing so, it would be apparent to one skilled in the art that such stimulation duty cycles relate to the embodiments of preceding Paragraphs 466-471 of Bolea, which depend on stimulation timing synchronized relative to a detected peak of the respiration signal "Z."

In particular, Paragraphs 466-467 relate to a bio-impedance respiration signal and triggering stimulation based on a fiducial (e.g. begin-expiration) within this respiration signal,

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among other details. As noted in Paragraph 468 of Bolea, "an algorithm is used to predict respiratory period and determine stimulation trigger time. The predictive algorithm is contained in software and executed by a microprocessor resident in the INS circuitry 1130, thus enabling the INS 1100 to generate stimulation synchronous with inspiration." Example predictive algorithms are described in Paragraphs 469, 470 in association with FIGS. 64B, 64C. As further noted in Paragraph 471:

> A feature common to the predictive algorithms is illustrated in FIG. 64D. This feature provides a sequence of predicted respiratory periods in case the respiration impedance signal ("Z") is temporarily lost (e.g. due to change in respiratory effort). Until a subsequent respiratory peak is detected, stimulation parameters which are based on the measured respiratory period (e.g. stimulation period) are unchanged. **Thus, stimulation timing remains synchronous to the last detected peak.** (emphasis added)

With this in mind, as the following Paragraphs 472-474 of Bolea (cited in the Office Action) describe aspects of various stimulation duty cycles, it would be apparent to one skilled in the art that such stimulation duty cycles relate to the embodiments of Paragraphs 466-471, which depend on stimulation timing synchronized relative to a detected peak of the respiration signal "Z."

Accordingly, at least this cited portion of Bolea conflicts with at least the recitation "a stimulation element to stimulate an upper-airway-patency-related nerve, according to a **first stimulation therapy protocol (including alternating stimulation periods and non-stimulation periods) in which a timing of the stimulation periods is asynchronous relative to patient breathing**" in Applicants' independent claim 1.

Applicants note that FIGS. 80A-80 and Paragraphs 489-499 of Bolea, also conflict with Applicants' independent claim 1 at least because such passages (particularly Paragraph 496) provide substantially similar information to Paragraphs 466-471 at least with respect to being conflicting relative to Applicants' independent claim 1.

Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' independent claim 1 and/or otherwise significantly conflicts with independent claim

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1. Therefore, Bolea fails to reasonably make obvious Applicants' independent claim 1. Claims 2-9 and 11-16 are patentable at least based on their dependency from independent claim 1.

Applicants further submit that Paragraphs 514-516 (cited in the Office Action), and particularly Paragraph 515, of Bolea fails to meet the recitations of Applicants' independent claim 1. In particular, while Paragraph 514-515 does refer to asynchronous stimulation, this Paragraph 515 explains that "the asynchronous mode (fixed mode) may be used during daytime familiarization", which is not a **therapy** for sleep apnea when a patient would be sleeping. Bolea further explains:

> This mode may be used to **test** the benefits of asynchronous stimulation compared to inspiratory synchronous stimulation. Asynchronous stimulation may be initiated by programming the device to fixed mode and starting a therapy session. Fixed mode stimulation may be in any available pulse train configuration.

In view of the particular context in which asynchronous stimulation is described (e.g. daytime familiarization, testing), and given that other portions of Bolea do not appear to directly address such asynchronous stimulation, it would appear to one skilled in the art that Bolea does not address asynchronous stimulation as a "**first stimulation therapy protocol**" in the manner recited in Applicants' independent claim 1. Rather, during a treatment period in which the patient would be sleeping, Bolea relies on inspiratory synchronous stimulation.

Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' independent claim 1 and/or otherwise significantly conflicts with independent claim 1. Therefore, Bolea fails to reasonably make obvious Applicants' independent claim 1. Claims 2-9 and 11-16 are patentable at least based on their dependency from independent claim 1.

Dependent Claim 3

First, Applicants submit that claim 3 is patentable for at least some of substantially the same reasons as previously presented for base independent claim 1, and therefore, the recitations of Claim 3 also stand in sharp contrast to the portions of Bolea cited regarding base independent claim 1. In particular, at least some of those cited portions of Bolea (e.g. Paragraphs 473-474 with

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preceding Paragraphs 466-472) address a predictive algorithm which is synchronized relative to a **detected** peak of inspiration, which therefore does not relate to a "reference respiratory pattern" in the manner recited in Applicants' claim 3.

Meanwhile Paragraph 326 of Bolea relates to a Patient PSG Titration Data block. Paragraph 326 addresses a Patient PSG Titration Data block, which includes conventional polysomnographic (PSG) data obtained in a sleep study. Paragraph 326 mentions "A *self-adjusting predictive algorithm utilizes a reference datum to which the algorithm can be adjusted,*" and then, among other things, describes that "**Onset** may be defined as onset of inspiration as measured by airflow or pressure sensor used in a sleep study" and mentions other onsets such as (but not limited to) Estimated Onset in the context of *enabling the predictive algorithm to be self-adjusting.*

Based on other preceding Paragraphs such as, for example, Paragraphs 296, 298, Bolea provides a "Description of Stimulus Trigger Algorithms." As stated in Paragraph 296,

> As mentioned previously with reference to FIG. 39, **the neurostimulation system described herein may operate in a closed-loop process wherein the step of delivering stimulation 390 to the targeted nerve may be a function of a sensed feedback parameter (e.g., respiration).** For example, stimulation of the hypoglossal nerve may be triggered to occur during the inspiratory phase of respiration. In a health human subject, the hypoglossal nerve is triggered about 300 mS before inspiration. **Accordingly, a predictive algorithm may be used to predict the inspiratory phase** and deliver stimulation accordingly. FIG. 48 schematically illustrates a system 480 including devices, data and processes for implementing a self-adjusting predictive trigger algorithm. (emphasis added)

Unlike the closed loop system of Bolea which relies on a predictive algorithm, Applicants' independent claim 1 recites "a first stimulation therapy protocol" in which "a timing of the stimulation periods is asynchronous relative to patient breathing.."

Moreover, while these cited portions of Bolea utilize onsets to trigger to stimulation, Applicants' claim 3 must be considered in context with the recitation from Applicants' independent claim 1 that "the **duration** of each respective stimulation period is based on a reference respiratory-related parameter" such that, when combined with claim 3, the **duration** of each respective stimulation period would be based on a reference respiratory pattern.

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Accordingly, claim 3 addresses a **duration** of each respective stimulation period while one skilled in the art likely would view Bolea (e.g. Paragraph 326) as addressing **predictively triggering** stimulation (versus duration).

Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' claim 3 and/or otherwise significantly conflicts with Applicants' claim 3. Therefore, Bolea fails to reasonably make obvious claim 3.

Dependent Claim 4

Applicants submit that claim 4 (depending from independent claim 1 and claim 3) is further patentably distinguishable over Bolea. In particular, Applicants' claim 4 recites that "the reference respiratory pattern comprises a reference respiratory cycle" and "a duration of each respective stimulation period is greater than a duration of an inspiratory phase of a reference respiratory cycle." (*At least some aspects of* the *term "inspiratory reference" are described in least Paragraph 46 of Applicants' specification.)*

First, these recitations stand in sharp contrast to the portions of Bolea cited regarding base independent claim 1. In particular, at least some of those cited portions of Bolea (e.g. Paragraphs 473-474 with preceding Paragraphs 466-472) address a predictive algorithm which is synchronized relative to a **detected** peak of inspiration, which therefore does not relate to a "reference respiratory cycle" in the manner recited in Applicants' claim 4 for "a first stimulation therapy protocol" in which "timing is asynchronous relative to patient breathing" (independent claim 1).

Applicants submit that claim 4 (depending from claims 1, 3) is further patentably distinguishable over Bolea. In particular, Applicants' claim 4 recites in part that "a duration of each stimulation period is greater than a duration of the inspiratory phase of the reference respiratory cycle", while base independent claim 1 recites "a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period." These recitations are directly supported by at least Paragraph 46 of Applicants' specification.

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Applicants further note that the phrase "inspiratory phase" of the "reference respiratory cycle" as defined in Applicants' specification does **not** correspond to actively-sensed respiration. See, for example, at least Paragraph 47 of Applicants' specification.

In contrast, Paragraph 420 of Bolea (cited in the Office Action against Applicants' claims) addresses ramping stimulation intensity, the number of pulses per second, amplitudes, and pulse width. The Paragraph concludes by stating that "Each of these ramp methods would require a predictive algorithm that would stimulate based on the previous inspiration cycle."

Accordingly, Paragraph 420 of Bolea does not address the recitation in Applicants' claim 4 of "the reference respiratory pattern comprises a reference respiratory cycle" and Paragraph 420 of Bolea does not address the recitation in Applicants' claim 1 of "a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period."

Meanwhile, Paragraph 357 of Bolea (cited in the Office Action) addresses measuring an inspiratory stage and related effort for comparison to a threshold, such as to identify a disordered breath if the inspiratory period is at least 40% of the entire respiratory period. However, this Paragraph 357 does not address a first stimulation therapy protocol as recited in claim 1, and more particularly, Paragraph 357 of Bolea does not address either the duration of a stimulation period or the duration of a non-stimulation period in the manner recited in Applicants' claim 1 (from which claim 4 depends).

Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' claim 4 and/or otherwise significantly conflicts with Applicants' claim 4. Therefore, Bolea fails to reasonably make obvious claim 4.

Dependent Claim 6

Applicants submit that Applicants' claim 6 (depending from dependent claim 1) is further patentably distinguishable over Bolea. First, claim 6 depends from independent claim 1, and is therefore patentable over Bolea for at least the reasons explained above regarding independent claim 1.

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In particular, Applicants' claim 6 recites that "the reference respiratory-related parameter comprises a reference respiratory cycle" and that "a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is **less than** a duration of the reference respiratory cycle."

Paragraphs 492-499 of Bolea (cited in the Office Action) appear in association with FIGS. 80A-80C. As shown in FIG. 80C and described in at least Paragraph 496, the duration of each (of several) predicted respiratory period coincides with (e.g. matches) a duration of a combination of a stimulation period and a period of no-stimulation.

This arrangement in Bolea directly conflicts with the recitation in Applicants' claim 6 that "a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods **is less than** a duration of the reference respiratory cycle." Via Applicant's claimed arrangement, the duration of the stimulation cycle (a stimulation period and a non-stimulation period) does not match or coincide with the duration of the reference respiratory cycle, such that upon the application of multiple stimulation cycles, the stimulation period will coincide with a different portion of each reference respiratory cycle of a sequence of reference respiratory cycles. This arrangement may ensure that "*no matter where the stimulation protocol is started relative to the pattern of ongoing reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the reference respiratory cycles for a significant majority of the treatment period.*" See, for example, Applicants' specification in a least Paragraph 0049.

Moreover, as previously noted in association with at least base independent claim 1, Applicants' arrangement "a first stimulation therapy protocol **in which a timing of the stimulation periods is asynchronous relative to patient breathing**" stands in sharp contrast to the arrangement in FIGS. 80A-80C of Bolea (Paragraphs 492-499, particularly Paragraph 496) in which "the stimulation timing remains **synchronous** to the last detected peak" and in which the stimulation period is centered at 75% of the respiratory period from the last detected peak, as shown in FIG. 80B of Bolea (Paragraph 495).

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Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' claim 6 and/or otherwise significantly conflicts with claim 6. Therefore, Bolea fails to reasonably make obvious Applicants' claim 6.

Independent Claim 17

Independent Claim 17 is patentable over Bolea for at least some of substantially the same reasons as previously presented in favor of the patentability of Applicants' independent claim 1. In addition, to reciting "a first stimulation **therapy** protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing," independent claim 17 further recites that "wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein each stimulation period comprises continuous pulsed stimulation, and **wherein the first stimulation therapy protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.**"

Per Applicants' specification, each stimulation period (within a stimulation cycle) comprises continuous pulsed stimulation such that each stimulation period comprises multiple pulses. See, for example, at least Paragraph 0044 of Applicants' specification which states:

> In some examples, each stimulation period within a stimulation cycle includes continuous stimulation. In some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second…..

Therefore, Applicants submit that it is unreasonable in the Office Action to assert equivalency between the term "multiple stimulation periods" and the term "multiple pulses", and in view of the recitation in Applicants' claim 17 of "wherein each stimulation period comprises continuous pulsed stimulation", the cited Paragraph 420 of Bolea cannot be reasonably said to meet this recitation.

For example, Paragraph 420 of Bolea (cited in the Office Action against Applicants' claim 17) addresses ramping stimulation intensity, the number of pulses per second, amplitudes, and

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pulse width. The Paragraph concludes by stating that "Each of these ramp methods would require a predictive algorithm that would stimulate based on the previous inspiration cycle."

Accordingly, Paragraph 420 of Bolea does not even remotely address the recitation in Applicants' claim 17 of "wherein the first stimulation therapy protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle" and Paragraph 420 does not address the recitation in Applicants' claim 1 of "a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period."

In addition to the above-mentioned previously presented arguments (and associated amendment of Claim 1), Applicants note that Paragraphs 492-499 of Bolea (cited in the Office Action) appear in association with FIGS. 80A-80C. As shown in FIG. 80C and described in at least Paragraph 496 of Bolea, the duration of each (of several) predicted respiratory period coincides with (e.g. matches) a duration of a combination of a stimulation period and a period of no-stimulation.

This arrangement in Bolea directly conflicts with the recitation in Applicants' claim 17 that "the first stimulation therapy protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle." Via Applicant's claimed arrangement, the duration of the stimulation cycle does not match or coincide with the duration of the reference respiratory cycle, such that upon the application of multiple stimulation cycles, the stimulation period will coincide with a different portion of each reference respiratory cycle of a sequence of reference respiratory cycles. This arrangement may ensure that "*no matter where the stimulation protocol is started relative to the pattern of ongoing reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the reference respiratory cycles for a significant majority of the treatment period.*" See, for example, Applicants' specification in a least Paragraph 0049.

Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' independent claim 17 and/or otherwise significantly conflicts with independent claim 17. Therefore, Bolea fails to reasonably make obvious Applicants' independent claim 17. Claims 18 and 20-22 are patentable at least based on their dependency from independent claim 17.

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Independent Claim 23

Independent Claim 23 is patentable over Bolea for at least some of substantially the same reasons as previously presented in favor of the patentability of Applicants' independent claim 1 and/or independent claim 17. In addition to reciting "a first stimulation **therapy** protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing," independent claim 23 further recites that "a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein **a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a duration of a stimulation cycle, which is greater than a duration of a reference respiratory cycle**.

In addition to the above-mentioned previously presented arguments (and associated amendment of Claim 1), Applicants note that Paragraphs 492-499 of Bolea (cited in the Office Action) appear in association with FIGS. 80A-80C. As shown in FIG. 80C and described in at least Paragraph 496 of Bolea, the duration of each (of several) predicted respiratory period coincides with (e.g. matches) a duration of a combination of a stimulation period and a period of no-stimulation.

This arrangement in Bolea directly conflicts with the recitation in Applicants' claim 23 that "a combined duration of a respective one of the stimulation *periods* and a respective one of the non-stimulation *periods* comprises a duration of a stimulation *cycle,* which is greater than a duration of a reference respiratory *cycle*." Via Applicant's claimed arrangement, the duration of the stimulation cycle does not match or coincide with the duration of the reference respiratory cycle, such that upon the application of multiple stimulation cycles, the stimulation period will coincide with a different portion of each reference respiratory cycle of a sequence of reference respiratory cycles. This arrangement may ensure that "*no matter where the stimulation protocol is started relative to the pattern of ongoing reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the reference respiratory cycles for a significant majority of the treatment period.*" See, for example, Applicants' specification in a least Paragraph 0049.

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Accordingly, for at least these reasons, Bolea fails to meet each and every recitation of Applicants' independent claim 23 and/or otherwise significantly conflicts with independent claim 23. Therefore, Bolea fails to reasonably make obvious Applicants' independent claim 23. Claim 24 is patentable at least based on its dependency from independent claim 23.

Claim 19 was rejected under 35 U.S.C. § 103 as being unpatentable over Bolea, in view of Nakata (US 2014/0194793).

Applicants submit that Nakata fails to cure the above-demonstrated deficiencies of Bolea regarding base independent claim 1, from which claim 19 depends, and therefore claim 19 is patentable over the cited combination of Bolea and Nakata.

New Claim 25

New claim 25 further defines independent claim 1 and recites that the first stimulation therapy protocol is to be applied during a treatment period in the patient is to engage in sleeping behavior." Favorable consideration and allowance of claim 25 is respectfully requested.

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CONCLUSION

In view of the above, Applicants respectfully submit that the pending claims 1-9 and 11-25 are in form for allowance and are not taught or suggested by the cited references.

Please consider this a Petition for Extension of Time for a sufficient number of months to enter these papers, if appropriate. At any time during the pendency of this application, please charge any additional fees or credit overpayment to Deposit Account No. 500471.

The Examiner is invited to contact the Applicants' representative at the below-listed telephone numbers to facilitate prosecution of this application.

Any inquiry regarding this Amendment and Response should be directed to Paul S. Grunzweig at Telephone No. (612) 767-2504, Facsimile No. (612) 573-2005. In addition, all correspondence should continue to be directed to the following address:

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Respectfully submitted,

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By their attorneys,

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Date: March 2, 2023

/Paul S. Grunzweig/
Paul S. Grunzweig
Reg. No. 37,143

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00145

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-22)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3792
Examiner Name	Lau, Michael J.
Attorney Docket Number	I618.118.104

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	1	20120158091	A1	2012-06-21	TEHRANI et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3792
	Examiner Name	Lau, Michael J.
	Attorney Docket Number	I618.118.104

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[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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00147

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3792
	Examiner Name	Lau, Michael J.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

☒ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2023-03-02
Name/Print	Paul S. Grunzweig	Registration Number	37143

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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00149

Electronic Patent Application Fee Transmittal

Application Number:	17012481
Filing Date:	04-Sep-2020
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Attorney Docket Number:	I618.118.104

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
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Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
SUBMISSION- INFORMATION DISCLOSURE STMT	1806	1	260	260
		Total in USD ($)		**260**

Electronic Acknowledgement Receipt

EFS ID:	47620315
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	02-MAR-2023
Filing Date:	04-SEP-2020
Time Stamp:	15:21:00
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$260
RAM confirmation Number	E202332F21529125
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1	Information Disclosure Statement (IDS) Form (SB08)	2023-03-02SIDS.pdf	1263316 cda3e85c326de18052a944499078d9c662f96c89	no	4
Warnings:					
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2	Fee Worksheet (SB06)	fee-info.pdf	37869 c3e8d911e205ede8546d9982f89a1de5df2475f8	no	2
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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

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ENTITY: ☑ LARGE ☐ SMALL ☐ MICRO

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA		RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A		N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A		N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A		N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*		x $100 =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*		x $460 =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).				
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))					
* If the difference in column 1 is less than zero, enter "0" in column 2.				TOTAL	

APPLICATION AS AMENDED - PART II

AMENDMENT	03/02/2023	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	* 24	Minus	** 24	= 0		x $100 =	0
	Independent (37 CFR 1.16(h))	* 3	Minus	*** 3	= 0		x $480 =	0
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	0

AMENDMENT		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA		RATE ($)	ADDITIONAL FEE ($)
	Total (37 CFR 1.16(i))	*	Minus	**	=		x $0 =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=		x $0 =	
	☐ Application Size Fee (37 CFR 1.16(s))							
	☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							
							TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.	LIE
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".	/VIKKI GRAY/
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".	
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.	

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
17/012,481	09/04/2020	Darrell Wagner	I618.118.104	3270

25281 7590 11/02/2022

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

EXAMINER	
LAU, MICHAEL J	

ART UNIT	PAPER NUMBER
3792	

NOTIFICATION DATE	DELIVERY MODE
11/02/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DBCLAW-Docket@dbclaw.com
USPTO.PATENTS@dbclaw.com
dmorris@dbclaw.com

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00155

Office Action Summary	Application No. 17/012,481	Applicant(s) Wagner et al.	
	Examiner MICHAEL J LAU	Art Unit 3792	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 9/4/2020.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 1-24 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 1-24 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00156

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Rejections - 35 USC § 103

2. In the event the determination of the status of the application as subject to AIA 35 U.S.C. 102 and 103 (or as subject to pre-AIA 35 U.S.C. 102 and 103) is incorrect, any correction of the statutory basis for the rejection will not be considered a new ground of rejection if the prior art relied upon, and the rationale supporting the rejection, would be the same under either status.

3. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-18 and 20-24 are rejected under 35 U.S.C. 103 as being unpatentable over multiple embodiments of Bolea (US 2014/0228905 A1).

6. Regarding claim 1, Bolea discloses a device for treating obstructive sleep apnea (eg. Abstract, Para. 2-4), comprising: a non-cardiac stimulation element to stimulate an upper airway patency-related nerve (Eg. Abstract, Para. 361), according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing in multiple embodiments (eg. Para. 473 and 514, asynchronous stimulation), wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period (eg. Para. 460, 473-474, duty cycle values are non-limiting examples), and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter (eg. Para. 473-474).

7. It would have been obvious to one of ordinary skill in the art before the effective filing date of the claimed invention to combine the embodiments of Bolea to allow for asynchronous/fixed stimulation to account for irregular and unpredictable breathing patterns (eg. Para. 516). Although the asynchronous method typically uses a 50% duty cycle, the prior art states that it can be used with a more manual method which gives more flexibility in setting parameters such as duty cycle (Eg. Para. 514-516). Combining this with previous embodiments that adjust duty cycles based on predicted respiratory periods (eg. Para. 472-474) would better tailor the treatment to the individual patient's most predictable breathing patterns.

8. Regarding claim 2, Bolea discloses the asynchronous timing of the stimulation relative to patient breathing comprises the timing being not based on actively-sensed respiration during application of the first stimulation protocol (eg. Para. 514-516, settings may be arbitrarily set).

9. Regarding claim 3, Bolea discloses the reference respiration-related parameter comprises a reference respiratory pattern (eg. Para. 326, 472-474).

10. Regarding claim 4, Bolea discloses the reference respiratory pattern comprises a reference respiratory cycle and where a duration of each respective stimulation period is greater than a duration of an inspiratory phase of the reference respiratory cycle (eg. Para. 472-474).

11. Regarding claim 5, Bolea discloses the reference respiration-related parameter is based on stable respiration (eg. 498-500, 639).

12. Regarding claim 6, Bolea discloses the reference respiratory-related parameter comprises a reference respiratory cycle and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is less than a duration of the reference respiratory cycle (eg. Para. 129, 420, period 514-516).

13. Regarding claim 7, Bolea discloses reference respiratory-related parameter comprises a reference respiratory cycle (eg. Para. 315-319) and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is no greater than a duration of a reference respiratory cycle (eg. Para. 420 multiple pulses within a respiration cycle).

14. Regarding claim 8, Bolea discloses the duration of the respective stimulation periods remain uniform (eg. Para. 501, can choose uniform or non-uniform pulses).

15. Regarding claim 9, Bolea discloses the reference respiratory-related parameter comprises a reference respiratory cycle, and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 30 percent of duration of a reference respiratory cycle (eg. Para. 420).

16. Regarding claim 10, Bolea discloses the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 20 percent of duration of the reference respiratory cycle (eg. Para. 420).

17. Regarding claim 11, Bolea discloses a respective one of the stimulation periods and a respective one of the non-stimulation periods are in a proportion of at least 1.5 to 1 (eg. Para. 474 and 481).

18. Regarding claim 12, Bolea discloses a duration of a respective one of the stimulation periods exceeds the duration of a respective one of the non-stimulation periods by a factor of 3 (eg. Para. 474 and 481, prior art lists the 69% duty cycle as a non-limiting example). The Examiner believes increasing the duty cycle to 75% would be obvious to one of ordinary skill in the art as it is a very similar range to the non-limiting example disclosed in Bolea. The Examiner asserts that it would also be obvious to try under routine optimization since there is a finite number of solutions due to a duty cycle being between 0 and 100% (See MPEP 2144.05 I-II).

19. Regarding claim 13, Bolea discloses a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein a duration of the respective one of the stimulation periods comprises at least 80 percent of a duration of the stimulation cycle (same reason as Claim 13 rejection).

20. Regarding claim 14, Bolea discloses each respective stimulation period comprises continuous pulsed stimulation (eg. Para. 302, 354).

21. Regarding claim 15, Bolea discloses the non-cardiac stimulation element comprises an implantable electrode and the device comprises an implantable pulse generator electrically connectable to the implantable electrode (eg. Fig. 1, Para. 127).

22. Regarding claim 16, Bolea discloses a processor; and a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation protocol (eg. Para. 136).

23. Regarding claim 17, Bolea discloses a device for treating obstructive sleep apnea (eg. Abstract, Para. 2-4), comprising: a non-cardiac stimulation element to stimulate an upper airway patency-related nerve (Eg. Abstract, Para. 361), according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing (eg. Para. 473 and 514, asynchronous stimulation), wherein a duration of

each respective stimulation period is greater than a duration of each respective non-stimulation period (eg. Para. 460, 473-474), duty cycle values are non-limiting examples), wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle (eg. Para. 420 multiple pulses within a respiration cycle).

24. Regarding claim 18, Bolea discloses the duration of each respective non-stimulation period is at least less than half of the duration of each respective stimulation period (eg. Para. 474 and 481).

25. Regarding claim 20, Bolea discloses the stimulation protocol is to deliver at least some of the multiple stimulation periods within a duration of an inspiratory phase of the reference respiratory cycle (eg. Para. 420).

26. Regarding claim 21, Bolea discloses the duration of each respective stimulation period is at least less than 30 percent of a duration of the reference respiratory cycle (eg. Para. 420).

27. Regarding claim 22, Bolea discloses a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein the first stimulation protocol is to deliver more than one stimulation cycle within a duration of the reference respiratory cycle (eg. Para. 420).

28. Regarding claim 23, Bolea discloses a device for treating obstructive sleep apnea (eg. Abstract, Para. 2-4), comprising: a non-cardiac stimulation element to stimulate an upper airway patency-related nerve (Eg. Abstract, Para. 361), according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing (eg. Para. 473 and 514, asynchronous stimulation), wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period (eg. Para. 460, 473-474), and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle (eg. Para. 474, 499, 636).

29. Regarding claim 24, Bolea discloses the duration of a respective one of the stimulation periods is greater than the duration of the reference respiratory cycle (eg. Para. 474, 499, 636).

30. Claim 19 is rejected under 35 U.S.C. 103 as being unpatentable over multiple embodiments of Bolea (US 2014/0228905 A1) in view of Nakata (US 2014/0194793 A1).

31. Regarding claim 19, Bolea discloses the invention of claim 17 and the reference respiratory cycle comprises at least one of: a historical patient-specific reference respiratory cycle (eg. Para. 266, 298); but does not disclose a multiple patient reference respiratory cycle.

32. Nakata teaches a sleep apnea monitor that analyzes normal ranges of respiratory rates based on population averages (eg. Para. 345).

33. It would have been obvious to one of ordinary skill to have combined the invention of Bolea to adjust the reference cycles to be based on a population average as taught by Nakata to better tune a fixed/asynchronous signal if the patient does not have enough historical data for a stable breathing pattern.

Conclusion

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL J LAU whose telephone number is (571)272-2317. The examiner can normally be reached 8-5:30 PM.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carl Layno can be reached on (571) 272-4949. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of published or unpublished applications may be obtained from Patent Center. Unpublished application information in Patent Center is available to registered users. To file and manage patent submissions in Patent Center, visit: https://patentcenter.uspto.gov. Visit https://www.uspto.gov/patents/apply/patent-center for more information about Patent Center and https://www.uspto.gov/patents/docx for information about filing in DOCX format. For additional questions, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MICHAEL J LAU/
Examiner, Art Unit 3792

/CARL H LAYNO/
Supervisory Patent Examiner, Art Unit 3792

Notice of References Cited	Application/Control No. 17/012,481	Applicant(s)/Patent Under Reexamination Wagner et al.	
	Examiner MICHAEL J LAU	Art Unit 3792	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	CPC Classification	US Classification
*	A	US-20200147376-A1	05-2020	Dieken; David	A61N1/36139	1/1
*	B	US-5146918-A	09-1992	Kallok; Michael J.	A61N1/3601	607/42
*	C	US-20150039045-A1	02-2015	Ni; Quan	A61N1/36139	607/42
*	D	US-20140228905-A1	08-2014	BOLEA; Stephen L.	A61N1/3601	607/42
*	E	US-20140194793-A1	07-2014	Nakata; Robert Haruo	G01S13/825	601/48
	F					
	G					
	H					
	I					
	J					
	K					
	L					
	M					

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	CPC Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
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	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00164

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	Art Unit
	MICHAEL J LAU	3792

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/27/2022								
	1	✓								
	2	✓								
	3	✓								
	4	✓								
	5	✓								
	6	✓								
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	22	✓								
	23	✓								
	24	✓								

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00165

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	17/012,481	Wagner et al.
	Examiner	Art Unit
	MICHAEL J LAU	3792

CPC - Searched*		
Symbol	**Date**	**Examiner**
A61N1/3601,36146,3611,36171	10/27/2022	ML
A61B5/0826,0816,113,4818,4848,686,0205	10/27/2022	ML
G16H20/40	10/27/2022	ML

CPC Combination Sets - Searched*		
Symbol	**Date**	**Examiner**

US Classification - Searched*			
Class	**Subclass**	**Date**	**Examiner**
607	42	10/27/2022	ML

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	**Date**	**Examiner**
inventor and prior art search on pe2e search	10/27/2022	ML

Interference Search			
US Class/CPC Symbol	**US Subclass/CPC Group**	**Date**	**Examiner**

/MICHAEL J LAU/ Examiner, Art Unit 3792	

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00166

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3700
Examiner Name	Fristoe Jr., John K.
Attorney Docket Number	I618.118.104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5277193		1994-01-11	Takishima et al.	
	2	9737708	B2	2017-08-22	Kobayashi	

If you wish to add additional U.S. Patent citation information please click the Add button. Add

U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20120232611	A1	2012-09-13	Sasaki et al.	
	2	20140188185	A1	2014-07-03	Tesfayesus et al.	

If you wish to add additional U.S. Published Application citation information please click the Add button. Add

FOREIGN PATENT DOCUMENTS Remove

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2] i	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	H0323870	JP	A	1991-01-31	CHEST CORP	[English Equivalent US 5277193]	

EFS Web 2.1.17

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	2	2015217108	JP	A	2015-12-07	TECHNO LINK CO LTD	[English Equivalent US 9737708]	

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NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

If you wish to add additional non-patent literature document citation information please click the Add button Add

EXAMINER SIGNATURE

Examiner Signature	/MICHAEL J LAU/	Date Considered	10/27/2022

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2022-06-28
Name/Print	Paul S. Grunzweig	Registration Number	37143

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Doc description: Information Disclosure Statement (IDS) Filed

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3700
Examiner Name	Fristoe Jr., John K.
Attorney Docket Number	I618.118.104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4379462		1983-04-12	Borkan et al.	
	2	4567892		1986-02-04	Plicchi et al.	
	3	4630614		1986-12-23	Atlas	
	4	4813431		1989-03-21	Brown	
	5	4830008		1989-05-16	Meer	
	6	5133354		1992-07-28	Kallok	
	7	5134995		1992-08-04	Gruenke et al.	
	8	5148802		1992-09-22	Sanders et al.	

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	9	5158080		1992-10-27	Kallok	
	10	5167229		1992-12-01	Peckham et al.	
	11	5174287		1992-12-29	Kallok et al.	
	12	5178156		1993-01-12	Takishima et al.	
	13	5203343		1993-04-20	Axe et al.	
	14	5211173		1993-05-18	Kallok et al.	
	15	5215082		1993-06-01	Kallok et al.	
	16	5233983		1993-08-10	Markowitz	
	17	5239995		1993-08-31	Estes et al.	
	18	5245995		1993-09-21	Sullivan et al.	
	19	5265624		1993-11-30	Bowman	

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	20	5281219		1994-01-25	Kallok	
	21	5300094		1994-04-05	Kallok et al.	
	22	5335657		1994-08-09	Terry, Jr. et al.	
	23	5344438		1994-09-06	Testerman et al.	
	24	5351394		1994-10-04	Weinberg	
	25	5385144		1995-01-31	Yamanishi et al.	
	26	5388578		1995-02-14	Yomtov et al.	
	27	5398682		1995-03-21	Lynn	
	28	5458137		1995-10-17	Axe et al.	
	29	5483969		1996-01-16	Testerman et al.	
	30	5485851		1996-01-26	Erickson	

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	31	5522862		1996-06-04	Testerman et al.	
	32	5524632		1996-06-11	Stein et al.	
	33	5540731		1996-07-30	Testerman	
	34	5540732		1996-07-30	Testerman	
	35	5540733		1996-07-30	Testerman et al.	
	36	5540734		1996-07-30	Zabara	
	37	5546952		1996-08-20	Erickson	
	38	5549655		1996-08-27	Erickson	
	39	5588439		1996-12-31	Hollub	
	40	5591216		1997-01-07	Testerman et al.	
	41	5605151		1997-02-25	Lynn	

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	42	5645053		1997-07-08	Remmers et al.	
	43	5671733		1997-09-30	Raviv et al.	
	44	5797852		1998-08-25	Karakasoglu et al.	
	45	5823187		1998-10-20	Estes et al.	
	46	5843135		1998-12-01	Weijand et al.	
	47	5895360		1999-04-20	Christopherson et al.	
	48	5904141		1999-05-18	Estes et al.	
	49	5919221		1999-07-06	Miesel	
	50	5944680		1999-08-31	Christopherson et al.	
	51	5999846		1999-12-07	Pardey et al.	
	52	6015389		2000-01-18	Brown	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

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	53	6021352		2000-02-01	Christopherson et al.	
	54	6025624		2000-02-15	Figura	
	55	6041780		2000-03-28	Richard et al.	
	56	6099479		2000-08-08	Christopherson et al.	
	57	6120441		2000-09-19	Griebel	
	58	6125290		2000-09-26	Miesel	
	59	6125291		2000-09-26	Miesel et al.	
	60	6126611		2000-10-03	Bourgeouis et al.	
	61	6132384		2000-10-17	Christopherson et al.	
	62	6134459		2000-10-17	Roberts et al.	
	63	6144866		2000-11-07	Miesel et al.	

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	64	6175767		2001-01-16	Doyle, Sr.	
	65	6181961		2001-01-30	Prass	
	66	6198952		2001-03-06	Miesel	
	67	6223064		2001-04-24	Lynn et al.	
	68	6240316		2001-05-29	Richmond et al.	
	69	6248080		2001-06-19	Miesel et al.	
	70	6249703		2001-06-19	Stanton et al.	
	71	6251126		2001-06-26	Ottenhoff et al.	
	72	6269269		2001-07-31	Ottenhoff et al.	
	73	6307481		2001-10-23	Lehrman et al.	
	74	6309350		2001-10-30	Van Tassel et al.	

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	Art Unit	3700
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	75	6314324		2001-11-06	Lattner et al.	
	76	6342039		2002-01-29	Lynn et al.	
	77	6345202		2002-02-05	Richmond et al.	
	78	6361494		2002-03-26	Lindenthaler	
	79	6393325		2002-05-21	Mann et al.	
	80	6449507		2002-09-10	Hill et al.	
	81	6450957		2002-09-17	Yoshimi et al.	
	82	6456866		2002-09-24	Tyler et al.	
	83	6522928		2003-02-18	Whitehurst et al.	
	84	6532388		2003-03-11	Hill et al.	
	85	6572543		2003-06-03	Christopherson et al.	

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	86	6574507		2003-06-03	Bonnet	
	87	6587725		2003-07-01	Durand et al.	
	88	6609016		2003-08-19	Lynn	
	89	6609032		2003-08-19	Woods et al.	
	90	6629527		2003-10-07	Estes et al.	
	91	6641542		2003-11-04	Cho et al.	
	92	6645143		2003-11-03	Van Tassel et al.	
	93	6647289		2003-11-11	Prutchi	
	94	6651652		2003-11-25	Ward	
	95	6654634		2003-11-25	Prass	
	96	6665560		2003-12-16	Becker et al.	

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	97	6666830		2003-12-23	Lehrman et al.	
	98	6689068		2004-02-10	Hale et al.	
	99	6703939		2004-03-09	Lehrman et al.	
	100	6718208		2004-04-06	Hill et al.	
	101	6719708		2004-04-13	Jansen	
	102	6731976		2004-05-04	Penn et al.	
	103	6731984		2004-05-04	Cho et al.	
	104	6735471		2004-05-11	Hill et al.	
	105	6752765		2004-06-22	Jensen et al.	
	106	6770022		2004-08-03	Mechlenburg et al.	
	107	6773404		2004-08-10	Poezevera et al.	

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	108	6805667		2004-10-29	Christopherson et al.	
	109	6811538		2004-11-02	Westbrook et al.	
	110	6842647		2005-01-11	Griffith et al.	
	111	6881192		2005-04-19	Park	
	112	6890306		2005-05-10	Poezevera	
	113	6893405		2005-05-17	Kumar et al.	
	114	6904320		2005-06-07	Park et al.	
	115	6907293		2005-06-14	Grill et al.	
	116	6928324		2005-08-09	Park et al.	
	117	6935335		2005-08-30	Lehrman et al.	
	118	6936011		2005-08-30	Sheldon	

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	119	6964641		2005-11-15	Cho et al.	
	120	6978171		2005-12-20	Goetz et al.	
	121	6988498		2006-01-24	Berthon-Jones et al.	
	122	7025730		2006-04-11	Cho et al.	
	123	7041049		2006-05-09	Raniere	
	124	7054692		2006-05-30	Whitehurst et al.	
	125	7077810		2006-07-18	Lange et al.	
	126	7081095		2006-07-25	Lynn et al.	
	127	7082331		2006-07-25	Park et al.	
	128	7082336		2006-07-25	Ransbury et al.	
	129	7087053		2006-08-08	Vanney	

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	130	7117036		2006-10-03	Florio	
	131	7128717		2006-10-31	Thach et al.	
	132	7145461		2006-12-05	Lehrman et al.	
	133	7149573		2006-12-12	Wang	
	134	7155278		2006-12-26	King et al.	
	135	7160252		2007-01-09	Cho et al.	
	136	7160255		2007-01-09	Saadat	
	137	7167743		2007-01-23	Heruth et al.	
	138	7174215		2007-02-06	Bradley	
	139	7186220		2007-03-06	Stahmann et al.	
	140	7187978		2007-03-06	Malek et al.	

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	141	7189204		2007-03-13	Ni et al.	
	142	7195594		2007-03-27	Eigler et al.	
	143	7200440		2007-04-03	Kim et al.	
	144	7206635		2007-04-17	Cho et al.	
	145	7212862		2007-05-01	Park et al.	
	146	7214197		2007-05-08	Prass	
	147	7252640		2007-08-07	Ni et al.	
	148	7269457		2007-09-11	Shafer et al.	
	149	7269459		2007-09-11	Koh	
	150	7277749		2007-10-02	Gordon et al.	
	151	7330760		2008-02-12	Heruth et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

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	152	7336996		2008-02-26	Hartley et al.	
	153	7340302		2008-03-04	Falkenberg	
	154	7351208		2008-04-01	Brodnick et al.	
	155	7366572		2008-04-29	Heruth et al.	
	156	7371220		2008-05-13	Koh et al.	
	157	7387608		2008-06-17	Dunlop et al.	
	158	7395113		2008-07-01	Heruth et al.	
	159	7396333		2008-07-08	Stahmann et al.	
	160	7398115		2008-07-08	Lynn	
	161	7422015		2008-09-09	Delisle et al.	
	162	7438686		2008-10-21	Cho et al.	

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	163	7447545		2008-11-04	Heruth et al.	
	164	7454250		2008-11-18	Bjorling et al.	
	165	7453928		2008-12-09	Lee et al.	
	166	7468040		2008-12-23	Hartley et al.	
	167	7469697		2008-12-30	Lee et al.	
	168	7473227		2009-01-06	Hsu et al.	
	169	7491181		2009-02-17	Heruth et al.	
	170	6509164		2009-03-24	Jensen et al.	
	171	7510531		2009-03-31	Lee et al.	
	172	7526341		2009-04-29	Goetz et al.	
	173	7542803		2009-06-02	Heruth et al.	

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	174	7572225		2009-08-11	Stahmann et al.	
	175	7590455		2009-09-15	Heruth et al.	
	176	7591265		2009-09-22	Lee et al.	
	177	7596413		2009-09-29	Libbus et al.	
	178	7603170		2009-10-13	Hatlestad et al.	
	179	7610094		2009-10-27	Stahmann et al.	
	180	7634315		2009-12-15	Cholette	
	181	7644714		2010-01-12	Atkinson et al.	
	182	7662105		2010-02-16	Hatlestad	
	183	7672728		2010-03-02	Libbus et al.	
	184	7678061		2010-03-16	Lee et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

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	185	7680538		2010-03-16	Durand et al.	
	186	7702385		2010-04-20	Moffitt et al.	
	187	7717848		2010-05-18	Heruth et al.	
	188	7720541		2010-05-18	Stahmann et al.	
	189	7725195		2010-05-25	Lima et al.	
	190	7734340		2010-06-08	De Ridder	
	191	7734350		2010-06-08	Dubnov et al.	
	192	7742819		2010-06-22	Moffitt	
	193	7747323		2010-06-29	Libbus et al.	
	194	7751880		2010-07-06	Cholette	
	195	7775993		2010-08-17	Heruth et al.	

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	196	7783353		2010-08-24	Libbus et al.	
	197	7792583		2010-09-07	Miesel et al.	
	198	7809442		2010-10-05	Bolea et al.	
	199	7818063		2010-10-19	Wallace et al.	
	200	7853322		2010-12-14	Bourget et al.	
	201	7881798		2011-02-01	Miesel et al.	
	202	7908013		2011-03-15	Miesel et al.	
	203	7917230		2011-03-29	Bly	
	204	7942822		2011-05-17	Koh	
	205	7957809		2011-06-07	Bourget et al.	
	206	7957797		2011-06-07	Bourget et al.	

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	207	7979128		2011-07-12	Tehrani et al.	
	208	8016776		2011-09-13	Bourget et al.	
	209	8021299		2011-09-20	Miesel et al.	
	210	8150531		2012-04-03	Skelton	
	211	8160711		2012-04-17	Tehrani et al.	
	212	8175720		2012-05-08	Skelton et al.	

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U.S.PATENT APPLICATION PUBLICATIONS Remove

Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20010010010		2001-07-26	Richmond et al.	
	2	20020010495		2002-01-24	Freed et al.	
	3	20020049479		2002-04-25	Pitts	

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	4	20020156507		2002-10-24	Lindenthaler	
	5	20030093128		2005-05-15	Freed et al.	
	6	20030224895		2003-06-19	Gordon et al.	
	7	20030114905		2003-06-19	Kuzma	
	8	20030163059		2003-08-28	Poezevera et al.	
	9	20030195571		2003-10-16	Burnes et al.	
	10	20030216789		2003-11-20	Deem et al.	
	11	20040015204		2004-01-22	Whitehurst et al.	
	12	20040073272		2004-04-15	Knudson et al.	
	13	20040111139		2004-06-10	McCreery	
	14	20040215288		2004-10-28	Lee et al.	

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	15	20040230278		2004-11-18	Dahl et al.	
	16	20040254612		2004-12-16	Ezra	
	17	20050004628		2005-01-06	Goetz et al.	
	18	20050010265		2005-01-13	Baru Fassio et al.	
	19	20050042589		2005-02-24	Hatlestad et al.	
	20	20050043765		2005-02-24	Williams et al.	
	21	20050043772		2005-02-24	Stahmann et al.	
	22	20050074741		2005-04-07	Lee et al.	
	23	20050076908		2005-04-14	Lee et al.	
	24	20050080348		2005-04-14	Stahmann et al.	
	25	20050080461		2005-04-14	Stahmann et al.	

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	26	20050081847		2005-04-21	Lee et al.	
	27	20050085865		2005-04-21	Tehrani	
	28	20050085866		2005-04-21	Tehrani	
	29	20050085868		2005-04-21	Tehrani et al.	
	30	20050085869		2005-04-21	Tehrani et al.	
	31	20050085874		2005-04-21	Davis et al.	
	32	20050101833		2005-05-12	Hsu et al.	
	33	20050113710		2005-05-26	Stahmann et al.	
	34	20050115561		2005-06-02	Stahmann et al.	
	35	20050145246		2005-07-07	Hartley et al.	
	36	20050165457		2005-07-28	Benser et al.	

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	37	20050182457		2005-08-18	Thrope et al.	
	38	20050209513		2005-09-22	Heruth et al.	
	39	20050209643		2005-09-22	Heruth et al.	
	40	20050222503		2005-10-06	Dunlop et al.	
	41	20050234523		2005-10-20	Levin et al.	
	42	20050251216		2005-11-10	Hill et al.	
	43	20050261747		2005-11-24	Schuler et al.	
	44	20050267380		2005-12-01	Poezevera	
	45	20050277844		2005-12-15	Strother et al.	
	46	20050277999		2005-12-15	Strother et al.	
	47	20050278000		2005-12-15	Strother et al.	

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	48	20060052836		2006-03-09	Kim et al.	
	49	20060058852		2006-03-16	Koh et al.	
	50	20060064029		2006-03-23	Arad (Abboud)	
	51	20060079802		2006-04-13	Jensen et al.	
	52	20060095088		2006-05-04	De Ridder	
	53	20060103407		2006-05-18	Kakizawa et al.	
	54	20060135886		2006-06-22	Lippert et al.	
	55	20060142815		2006-09-29	Tehrani et al.	
	56	20060212096		2006-09-21	Stevenson	
	57	20060224209		2006-10-05	Meyer	
	58	20060241708		2006-10-26	Boute	

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	59	20060247729		2006-11-02	Tehrani et al.	
	60	20060259079		2006-11-16	King	
	61	20060264777		2006-11-23	Drew	
	62	20060266369		2006-11-30	Atkinson et al.	
	63	20060271137		2006-11-30	Stanton-Hicks	
	64	20060276701		2006-12-07	Ray	
	65	20060293720		2006-12-28	DiLorenzo	
	66	20060293723		2006-12-28	Whitehurst et al.	
	67	20070021785		2007-01-25	Inman et al.	
	68	20070027482		2007-02-01	Parnis et al.	
	69	20070038265		2007-02-15	Tcheng et al.	

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	70	20070150022		2007-06-28	Ujhazy et al.	
	71	20070233204		2007-10-04	Lima et al.	
	72	20070255379		2007-11-01	Williams et al.	
	73	20080009685		2008-01-10	Kim et al.	
	74	20080039904		2008-02-14	Bulkes et al.	
	75	20080046055		2008-02-21	Durand et al.	
	76	20080064977		2008-03-13	Kelleher et al.	
	77	20080103545		2008-05-01	Bolea et al.	
	78	20080103570		2008-05-01	Gerber	
	79	20080109046		2008-05-08	Lima et al.	
	80	20080109048		2008-05-08	Moffitt	

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	First Named Inventor	Darrell Wagner et al.
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	Attorney Docket Number	I618.118.104

	81	20080132802		2008-06-05	Ni et al.	
	82	20080294060		2008-11-27	Haro et al.	
	83	20090024047		2009-01-22	Shipley et al.	
	84	20090062882		2009-03-05	Zhang et al.	
	85	20090112116		2009-04-30	Lee et al.	
	86	20090118787		2009-05-07	Moffitt et al.	
	87	20090234427		2009-09-17	Chinn et al.	
	88	20090287279		2009-11-19	Parramon et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1							

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Application Number	17012481
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Attorney Docket Number	I618.118.104

NON-PATENT LITERATURE DOCUMENTS Remove

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

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EXAMINER SIGNATURE

Examiner Signature	/MICHAEL J LAU/	Date Considered	10/27/2022

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2020-10-29
Name/Print	Paul S. Grunzweig	Registration Number	37143

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

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Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00201

PE2E SEARCH - Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
L1	57	((("INSPIRE") near3 ("MEDICAL") near3 ("SYSTEMS") near3 ("INC"))).AS,AANM.	(USPAT)	OR	ON	ON	2022/10/25 03:54 PM
L2	558	((("WAGNER") near3 ("Darrell")) OR (("NI") near3 ("Quan")) OR (("RONDONI") near3 ("John")) OR (("DIEKEN") near3 ("Dave"))).INV.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 03:57 PM
L3	0	607/042.ccls.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:15 PM
L4	1065	607/42.ccls.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:15 PM
L5	6479	A61N1/3601,36146,3611,36171.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:27 PM
L6	44916	A61B5/0826,0816,113,4818,4848,686,0205.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:28 PM
L7	13477	G16H20/40.cpc.	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 04:28 PM
L8	59691030	@pd<"20150319"	(US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT)	OR	ON	ON	2022/10/25 05:17 PM
L9	42	(Artificial Intelligence) Similar to: 17/012,481 with 0 CPC Selections and 0 Text Selections Text: (US-20200398051-A1 OR US-10898709-B2 OR US-20200147376-A1 OR AU-2016233377-B2 OR AU-2020210249-A1 OR CN-113908438-A OR US-20210308454-A1 OR AU-2020210249-B2 OR US-20180117316-A1 OR EP-3881892-A1 OR AU-2016233377-A1 OR EP-3271008-A1 OR WO-2016149344-A1 OR CA-3004583-A1 OR	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN))	OR	ON	ON	2022/10/25 05:34 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00202

		AU-2021232791-A1 OR US-20170128002-A1 OR JP-6759227-B2 OR JP-2020203110-A OR CN-107864617-B OR US-20200146620-A9 OR US-10888267-B2 OR EP-2358268-B1 OR EP-0505195-A2 OR US-20200238084-A1 OR US-5146918-A OR US-7680538-B2 OR US-20180015281-A1 OR US-20160354603-A1 OR AU-649145-B2 OR CA-2084312-A1 OR WO-2016149176-A1 OR US-20150283383-A1 OR EP-0541763-A1 OR US-5174287-A OR WO-9221407-A1 OR JP-H05103839-A OR US-20160354602-A1 OR EP-0541763-B1 OR CA-2744269-C OR JP-2018508299-A OR US-9370657-B2 OR WO-2020102193-A1 OR US-10946195-B2 OR US-20020049479-A1 OR CN-107864617-A OR CA-2062171-A1 OR US-20220160295-A1 OR EP-3714771-A1 OR US-5215082-A OR US-20100131029-A1).did.					
L10	43	(Artificial Intelligence) Similar to: 17/012,481 with 0 CPC Selections and 1 Text Selection Text: (US-20200147376-A1 OR US-10888267-B2 OR US-5146918-A OR EP-0505195-A2 OR EP-2358268-B1 OR CA-2084312-A1 OR AU-649145-B2 OR EP-0541763-A1 OR WO-9221407-A1 OR EP-0541763-B1 OR US-5174287-A OR JP-H05103839-A OR US-20200238084-A1 OR CA-2744269-C OR US-7680538-B2 OR US-	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN))	OR	ON	ON	2022/10/25 05:34 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00203

		20200146620-A9 OR US-20170128002-A1 OR US-20020049479-A1 OR US-5215082-A OR CA-2062171-A1 OR US-20160354603-A1 OR US-20060167523-A1 OR US-8498712-B2 OR US-20150283383-A1 OR US-20080103407-A1 OR US-20160354602-A1 OR EP-0507580-A2 OR US-20120234332-A1 OR US-8626304-B2 OR US-5540733-A OR US-7225021-B1 OR US-20100125310-A1 OR US-8644939-B2 OR CA-2744269-A1 OR WO-2010057286-A1 OR EP-2358268-A1 OR US-5275159-A OR US-20170188940-A9 OR US-20140051938-A1 OR US-9370657-B2 OR US-20170119306-A1 OR EP-0702978-A3 OR AR-030368-A1 OR US-20200398051-A1 OR WO-2019088582-A1 OR US-20060149334-A1 OR US-7004908-B2 OR US-6770037-B2 OR US-10368800-B2 OR US-9402563-B2).did.					
L11	168300	L4 OR L5 OR L6 OR L7	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:07 PM
L12	51493	L8 AND L11	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA,	OR	ON	ON	2022/10/26 02:07 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00204

			EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L13	564	L12 AND upper ADJ air$1way WITH nerve	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:17 PM
L14	77	L12 AND upper ADJ air$1way WITH nerve WITH puls$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:17 PM
L15	72	L12 AND upper ADJ air$1way WITH nerve WITH puls$ AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO;	OR	ON	ON	2022/10/26 02:18 PM

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			JPO; DERWENT; IBM_TDB)				
L16	53	L12 AND upper ADJ air$1way WITH nerve WITH puls$ AND duration$ AND (independent$ OR a$1synchron$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:22 PM
L17	7	L12 AND upper ADJ air$1way WITH nerve WITH puls$ SAME (independent$ OR a$1synchron$) AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:23 PM
L18	11	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ SAME (independent$ OR a$1synchron$) AND duration$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:26 PM
L19	100	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS,	OR	ON	ON	2022/10/26 02:27 PM

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			IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L20	98	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$ SAME (signal$ OR stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:27 PM
L21	46	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND duration SAME inspirat$ SAME (signal$ OR stimulat$) AND (a$synchron$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:48 PM
L22	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (signal$ OR stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM

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L23	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM
L24	10	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ SAME (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:50 PM
L25	71	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (fixed OR regular OR a$synchron$) AND duration SAME inspirat$	(US-PGPUB; USPAT; USOCR; FIT (AU, AP, AT, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, OA, RU, SU, WO, MC, MD, MY, NL, NO, NZ, PH, PL, PT, RO, RS, SE, SG, SI, SK, TH, TN, TR, TW, UA, VN); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:53 PM
L26	71	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL,	OR	ON	ON	2022/10/26 02:55 PM

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		(inspirat$)	NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L27	59	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (inspirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:56 PM
L28	19	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) WITH (fixed OR regular OR a$synchron$) AND duration SAME inspirat$ SAME (inspirat$) AND duty ADJ cycle	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 02:58 PM
L29	1	"20140228905".pn. AND duration SAME (respirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/26 04:40 PM
L30	1	"20140228905".pn. AND duration SAME	(US-PGPUB; USPAT; USOCR; FIT (AP, AT,	OR	ON	ON	2022/10/27 12:35 PM

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		(respirat$) SAME (stimulat$ OR puls$ OR therap$ OR wave$form)	AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L31	1	"20140228905".pn. AND duration SAME (respirat$) SAME (stimulat$ OR puls$ OR therap$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:21 PM
L32	1	"20140228905".pn. AND duration SAME (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:23 PM
L33	1	"20140228905".pn. AND duration WITH (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE,	OR	ON	ON	2022/10/27 01:23 PM

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00210

			SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L34	1	"20140228905".pn. AND (duration OR length$ OR period$ OR time$) WITH (respirat$ OR breath$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 01:40 PM
L35	1	"20140228905".pn. AND duty ADJ cycle	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 02:14 PM
L36	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (signal$ OR stimulat$ OR pulse$) AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$) WITH populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:37 PM
L37	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU,	OR	ON	ON	2022/10/27 03:37 PM

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		puls$ AND (signal$ OR stimulat$ OR pulse$) AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$)	CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L38	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period) SAME (histor$ OR templat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:37 PM
L39	38	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:51 PM
L40	0	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve WITH puls$ AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN,	OR	ON	ON	2022/10/27 03:59 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00212

			WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L41	4	L12 AND (hypo$1glossal OR upper ADJ air$1way) WITH nerve AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 03:59 PM
L42	155	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:00 PM
L43	5	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) SAME populat$ SAME (stimulat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:00 PM
L44	162	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB,	OR	ON	ON	2022/10/27 04:08 PM

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		templat$) SAME (populat$ OR multipl$ near2 patient$)	HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L45	10	L12 AND (sleep ADJ apn$1ea) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:08 PM
L46	10	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) AND (duration OR width OR duty ADJ cycle OR period OR reference) SAME (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:23 PM
L47	30	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) AND (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT;	OR	ON	ON	2022/10/27 04:26 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00214

			IBM_TDB)				
L48	3	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:26 PM
L49	1	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$) WITH (populat$ OR multipl$ near2 patient$) SAME (duration OR period OR width OR length)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:30 PM
L50	11	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$) WITH (populat$ OR multipl$ near2 patient$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 04:31 PM
L51	27	L12 AND (sleep ADJ (apn$1ea OR disorder$1)) SAME implant$ AND (histor$ OR templat$ average$ OR respirat$ OR inspirat$) WITH (populat$ OR multipl$	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV,	OR	ON	ON	2022/10/27 04:32 PM

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00215

		near2 patient$)	MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)				
L52	1	"20140228905".pn. AND (duration OR length OR time OR width) SAME (breath$ OR respirat$)	(US-PGPUB; USPAT; USOCR; FIT (AP, AT, AU, BE, BG, BR, BY, CA, CH, CN, CS, CU, CZ, DD, DE, DK, EA, EE, EP, ES, FI, FR, GB, HR, HU, ID, IE, IL, IS, IT, JP, KR, LT, LU, LV, MA, MC, MD, MY, NL, NO, NZ, OA, PH, PL, PT, RO, RS, RU, SE, SG, SI, SK, SU, TH, TN, TR, TW, UA, VN, WO); FPRS; EPO; JPO; DERWENT; IBM_TDB)	OR	ON	ON	2022/10/27 05:11 PM

PE2E SEARCH - Search History (Interference)

There are no Interference searches to show.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00216

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3700
Examiner Name	Fristoe Jr., John K.
Attorney Docket Number	I618.118.104

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Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	8280513		2012-10-02	Tehrani	
	2	8265759		2012-09-11	Tehrani	
	3	8233987		2012-07-31	Gelfand	
	4	8781587		2014-07-15	Alt et al.	
	5	5123425		1992-06-23	Shannon, Jr. et al.	
	6	5190053		1993-03-02	Meer	
	7	8160712		2012-04-17	Freed	
	8	5591216		1997-01-07	Testerman et al.	

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	Attorney Docket Number	I618.118.104

	9	8718776		2014-05-06	Mashiach et al.	
	10	9895540		2018-02-20	Mashiach	
	11	8731678		2014-05-20	DeRidder	

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	1	20090308395		2009-12-17	Lee et al.	
	2	20090326408		2009-12-31	Moon	
	3	20100010566		2010-01-14	Thacker et al.	
	4	20100016749		2010-01-21	Atsma et al.	
	5	20100094379		2010-04-15	Meadows	
	6	20100125310		2010-05-20	Wilson et al.	

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	Attorney Docket Number	I618.118.104

	7	20100125314		2010-05-20	Bradley et al.	
	8	20100125315		2010-05-20	Parramon et al.	
	9	20100137931		2010-06-03	Hopper et al.	
	10	20100152553		2010-06-17	Ujhazy et al.	
	11	20100174341		2010-07-08	Bolea et al.	
	12	20100198103		2010-08-05	Meadows et al.	
	13	20100198289		2010-08-05	Kameli et al.	
	14	20100228133		2010-09-09	Averina et al.	
	15	20100228317		2010-09-09	Libbus et al.	
	16	20100241195		2010-09-23	Meadows et al.	
	17	20100262210		2010-10-14	Parramon et al.	

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	18	20100174341		2010-07-08	Bolea et al.	
	19	20110093036		2011-04-21	Mashiach	
	20	20110112601		2011-05-12	Meadows et al.	
	21	20110152706		2011-06-23	Christopherson et al.	
	22	20110152965		2011-06-23	Mashiach et al.	
	23	20110160794		2011-06-30	Bolea et al.	
	24	20110264164		2011-10-27	Christopherson et al.	
	25	20120290036		2012-11-15	Karamanoglu	
	26	20140364919		2014-12-11	Doan	
	27	20110093032		2011-04-21	Boggs	
	28	20140135868		2014-05-15	Bashyam	

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	29	20110288609		2011-11-24	Tehrani	
	30	20120192874		2012-08-02	Bolea	
	31	20120253249		2014-10-04	Wilson	
	32	20080161878		2008-07-03	Tehrani	
	33	20080154330		2008-06-26	Tehrani	
	34	20150039045		2015-02-05	Ni et al.	
	35	20160193468		2016-07-07	Rondoni et al.	
	36	20160022204		2016-01-28	Mostov	
	37	20160354602		2016-12-08	Keenan	
	38	20160354603		2016-12-08	Keenan	
	39	20160354608		2016-12-08	Keenan	

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	40	20060155341		2006-07-13	Tehrani et al.	
	41	20110172733		2011-07-14	Lima et al.	
	42	20100228310		2010-09-09	Shuros et al.	
	43	20050148897		2005-07-07	Cho et al.	
	44	20110060380		2011-03-10	Gelfand et al.	
	45	20170368337		2017-12-28	Steier	
	46	20080154330		2008-06-26	Tehrani et al.	
	47	20090216293		2009-08-27	Sasaki et al.	
	48	20150328451		2015-11-19	Kobayashi	
	49	20140228905		2014-08-14	Bolea	
	50	20130253627		2013-09-26	Meadows et al.	

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	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	51	20060167523		2006-07-27	Tehrani et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	2010502276	JP		2010-01-28	Cardiac Pacemaker, Inc.	[English Equivalent WO2008027297]	
	2	2011520526	JP		2011-07-21	Inspire Medical Systems, Inc.	[English Equivalent WO2009140636]	
	3	2009140636	WO		2010-03-11	Inspire Medical Systems, Inc.		
	4	2006047264	WO		2006-05-04	Advanced Neuromodulation Systems, Inc.		
	5	2006057734	WO		2006-06-01	Advanced Neuromodulation Systems, Inc.		
	6	2006102591	WO		2006-09-28	Vanderbilt University		
	7	2007068284	WO		2007-06-27	Synergio AG		
	8	2008048471	WO		2008-04-24	Apnex Medical, Inc.		

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	Attorney Docket Number	I618.118.104

	9	2009048580	WO		2009-04-16	Imthera Medical, INc.		
	10	2009048581	WO		2009-04-16	Imthera Medical, Inc.		
	11	2009135138	WO		2009-11-05	Medtronic, Inc.		
	12	2009135140	WO		2009-11-05	Medtronic, Inc.		
	13	2009140636	WO		2009-11-19	Inspire Medical Systems, Inc.		
	14	2010039853	WO		2010-04-08	Inspire medical Systems, Inc.		
	15	2010057286	WO		2010-05-27	Victhom Human Bionics Inc.		
	16	2010059839	WO		2010-05-27	Inspire Medical Systems, Inc.		
	17	2010117810	WO		2010-10-14	Inspire Medical Systems, Inc.		
	18	H11514557	JP		1999-12-14		[English Equivalent WO9749455]	
	19	9749455	WO		1997-12-31	Medtronic, Inc.		

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	Attorney Docket Number	I618.118.104

	20	2013023218	WO		2013-02-14	Inspire Medical Systems, Inc.		
	21	102548610	CN		2012-07-04	CARDIAC CONCEPTS INC	[Equivalent to US20110060380]	
	22	2013509943	JP		2013-03-21	Imthera Medical, Inc.	[Equivalent US20130253627]	
	23	4960704	JP		2008-08-07		[Equivalent US20090216293]	
	24	5636129	JP		2015-12-07	TECHNO LINK CO LTD	[Equivalent US20150328451]	
	25	2008027297	WO		2008-06-05	CARDIAC PACEMAKERS INC		
	26	9750049	WO		1997-12-31	MEDTRONIC INC		

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	Naples Article – Gregory G. Naples et al., "A Spiral Nerve Cuff Electrode for Peripheral Nerve Stimulation," 8088 IEEE Transactions on Biomedical Engineering, 35. November 1988, No. 11, New York, NY, pages 905-915.	
	2	Eisele Article – David W. Eisele, MD et al., "Tongue neuromuscular and direct hypoglossal nerve stimulation for obstructive sleep apnea," Otolaryngologic Clinics of North America, Otolaryngol Clin N Am 36 (2003) 501-510 (10 pages).	

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	Attorney Docket Number	I618.118.104

	3	Goodall Article – Eleanor V. Goodhall et al., "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode," IEEE Transaction on Biomedical Engineering, Vol. 43, No. 8, August 1996, pages 851-856.	
	4	Oliven Article – Arie Oliven et al., "Upper airway response to electrical stimulation of the genioglossus in obstructive sleep apnea," Journal of Applied Physiology, Volume 95, pages 2023-2029, November 2003, www.jap.physiology.org on September 18, 2006. (8 pages)	
	5	Schwartz Article – Alan R. Schwartz MD et al., "Theraputic Electrical Stimulation of the Hypoglossal Nerve in Obstructive Sleep Apnea, Arch Otolaryngol HeadAnd Neck Surg., Vol. 127, Oct. 2001, pages 1216-1223. Copyright 2001 American Medical Association. (8 pages)	
	6	PARK, "Preoperative Percutaneous Cranial Nerve Mapping in Head and Neck Surgery," ARCH FACIAL PLAST SURG/VOL 5, Jan/Feb 2003, www.archfacial.compages 86-91.	
	7	Stanescu, "Expiratory flow limitation during sleep in heavy snorers" European Respiratory Journal, 1996, 9, 2116-2121.	
	8	J Sleep Res., "Hypoglossal nerve stimulation improves obstructive sleep apnea: 12-month outcomes" Journal, 2014, 23, 77-83.	
	9	The Laryngoscope, "Implanted Upper Airway Stimulation Device for Obstructive Sleep Apnea" Journal, 2012, 122, 1626-1633.	

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EXAMINER SIGNATURE

Examiner Signature	/MICHAEL J LAU/	Date Considered	10/27/2022

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

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	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2020-10-29
Name/Print	Paul S. Grunzweig	Registration Number	37143

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /M.L./

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00228

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United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
www.uspto.gov

BIB DATA SHEET

CONFIRMATION NO. 3270

SERIAL NUMBER	FILING or 371(c) DATE RULE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
17/012,481	09/04/2020	607	3792	I618.118.104

APPLICANTS

INSPIRE MEDICAL SYSTEMS, INC., Golden Valley, MN;

INVENTORS

Darrell Wagner, Ham Lake, MN;
Quan Ni, Shoreview, MN;
John Rondoni, Plymouth, MN;
Dave Dieken, Minneapolis, MN;

**** CONTINUING DATA ***************************

This application is a CON of 15/562,714 09/28/2017 PAT 10898709
which is a 371 of PCT/US2016/022611 03/16/2016
which claims benefit of 62/135,305 03/19/2015

**** FOREIGN APPLICATIONS ***************************

**** IF REQUIRED, FOREIGN FILING LICENSE GRANTED ****

09/15/2020

Foreign Priority claimed ❑ Yes ☑ No 35 USC 119(a-d) conditions met ❑ Yes ☑ No Verified and Acknowledged /MICHAEL J LAU/ Examiner's Signature	❑ Met after Allowance Initials	STATE OR COUNTRY	SHEETS DRAWINGS	TOTAL CLAIMS	INDEPENDENT CLAIMS
		MN	13	24	3

ADDRESS

DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402
UNITED STATES

TITLE

STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

FILING FEE RECEIVED		
2280	FEES: Authority has been given in Paper No._____ to charge/credit DEPOSIT ACCOUNT No._____ for following:	❑ All Fees ❑ 1.16 Fees (Filing) ❑ 1.17 Fees (Processing Ext. of time) ❑ 1.18 Fees (Issue) ❑ Other _____ ❑ Credit

BIB (Rev. 05/07).

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Not for submission under 37 CFR 1.99)

Application Number	17012481
Filing Date	2020-09-04
First Named Inventor	Darrell Wagner et al.
Art Unit	3700
Examiner Name	Fristoe Jr., John K.
Attorney Docket Number	I618.118.104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	5277193		1994-01-11	Takishima et al.	
	2	9737708	B2	2017-08-22	Kobayashi	

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Examiner Initial*	Cite No	Publication Number	Kind Code[1]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	20120232611	A1	2012-09-13	Sasaki et al.	
	2	20140188185	A1	2014-07-03	Tesfayesus et al.	

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Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
	1	H0323870	JP	A	1991-01-31	CHEST CORP	[English Equivalent US 5277193]	

EFS Web 2.1.17

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	2	2015217108	JP	A	2015-12-07	TECHNO LINK CO LTD	[English Equivalent US 9737708]	

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
	1		

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EXAMINER SIGNATURE

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1] See Kind Codes of USPTO Patent Documents at www.USPTO.GOV or MPEP 901.04. [2] Enter office that issued the document, by the two-letter code (WIPO Standard ST.3). [3] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [4] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [5] Applicant is to place a check mark here if English language translation is attached.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00231

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2022-06-28
Name/Print	Paul S. Grunzweig	Registration Number	37143

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these record s.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

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Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00233

Electronic Acknowledgement Receipt

EFS ID:	46067797
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	28-JUN-2022
Filing Date:	04-SEP-2020
Time Stamp:	17:01:08
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	2022-06-28SIDS.pdf	612362 131c3803ba6b3e4a9c5f4085d9cb822f6a4a36ca	no	4
Warnings:					

Information:	
Total Files Size (in bytes):	612362

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Docket I618.118.103

PTO/AIA/01 (09-12)
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DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN APPLICATION DATA SHEET (37 CFR 1.76)

Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

As the below named inventor, I hereby declare that:

This declaration is directed to:

☐ The attached application, or

☒ United States application or PCT international application number 15/562,714 filed on September 28, 2017.

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTOR

Inventor: Darrell Wagner Date (Optional): 7 Feb 2018

Signature: Darrell Wagner

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

This collection of information is required by 35 U.S.C. 115 and 37 CFR 1.63. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 1 minute to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Docket I618.118.103

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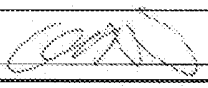
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LEGAL NAME OF INVENTOR

Inventor: Quan Ni Date (Optional): 15 Feb 2018

Signature: 

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Docket I618.118.103

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The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

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LEGAL NAME OF INVENTOR

Inventor: John Rondoni Date (Optional): 26 Feb 2018

Signature:

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

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LEGAL NAME OF INVENTOR

Inventor: David Dieken Date (Optional): 7 Feb 2018

Signature: _____

Note: An application data sheet (PTO/SB/14 or equivalent), including naming the entire inventive entity, must accompany this form or must have been previously filed. Use an additional PTO/AIA/01 form for each additional inventor.

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EFS ID:	44100153
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	22-OCT-2021
Filing Date:	04-SEP-2020
Time Stamp:	13:22:14
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/012,481	09/04/2020	Darrell Wagner	I618.118.104

CONFIRMATION NO. 3270

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PUBLICATION NOTICE



Title:STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

Publication No.US-2020-0398051-A1
Publication Date:12/24/2020

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00243

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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61N 1/36, 1/372	A1	(11) International Publication Number: WO 97/49455
		(43) International Publication Date: 31 December 1997 (31.12.97)

(21) International Application Number: PCT/US97/11618

(22) International Filing Date: 25 June 1997 (25.06.97)

(30) Priority Data:
08/673,717 26 June 1996 (26.06.96) US

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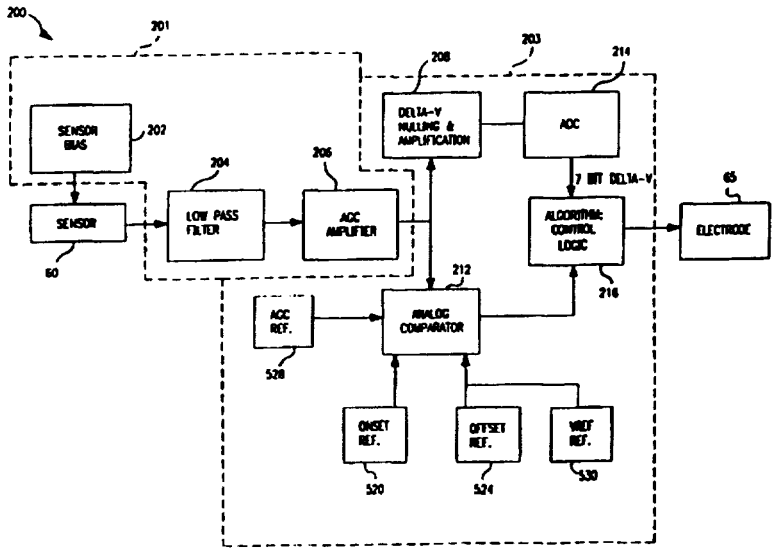
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(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: DIAGNOSTIC TESTING METHODS AND APPARATUS FOR THERAPY DEVICES



(57) Abstract

A testing method for use with a patient stimulation system includes providing a stimulation system including a patient control unit. The patient control unit initiates and terminates treatment periods. At least one period of stimulation to stimulate the patient is automatically provided upon initiating a treatment period. Another method includes a system test method for use with a therapy system. The method includes providing a therapy system having a plurality of components; the therapy system physiologically interacting with a patient. A diagnostic self test of a component of the therapy system is performed internally to the system to determine if the component is functioning properly at a time when the therapy system is not interacting physiologically with the patient. Apparatus for using such methods are also provided.

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DIAGNOSTIC TESTING METHODS AND APPARATUS FOR THERAPY DEVICES

Field of the Invention

The present invention relates generally to medical devices and methods of testing such devices. More particularly, the present inv

ention pertains to self diagnostic testing methods for use with therapy devices and systems.

Background of the Invention

Sleep apnea, an airway disorder, has been known for some time as a medical syndrome in two generally recognized forms. The first is central sleep apnea, which is associated with the failure of the body to automatically generate the neuromuscular stimulation necessary to initiate and control a respiratory cycle at the proper time. Work associated with employing electrical stimulation to treat this condition is discussed in Glenn, ADiaphragm Pacing: Present Status@, Pace, V.I, pp 357-370 (July-September 1978).

The second sleep apnea syndrome is known as obstructive sleep apnea. Ordinarily, the contraction of the dilator muscles of the upper airways (nose and pharynx) allows their patency at the time of inspiration. In obstructive sleep apnea, the obstruction of the airways results in a disequilibrium between the forces which tend to collapse airways (negative inspiratory transpharyngeal pressure gradient) and those which contribute to their opening (muscle contraction). The mechanisms which underlie the triggering of obstructive apnea include a reduction in the size of the superior airways, an increase in their compliance, and a reduction in the activity of the muscle dilator. The muscle dilators are intimately linked to the respiratory muscles and these muscles respond in a similar manner to a stimulation or a depression of the respiratory center. The ventilatory fluctuations observed during sleep (alternately hyper and hypo ventilation of periodic respiration) thus favors an instability of the superior airways and the occurrence of oropharyngeal obstruction. In sleep apnea the respiratory activation of the genioglossus muscle has been particularly noted to be ineffective during sleep. The cardiovascular

consequences of apnea include disorders of cardiac rhythm (bradycardia, auriculoventricular block, ventricular extrasystoles) and hemodynamic (pulmonary and systemic hypertension). This results in a stimulatory metabolic and mechanical effect on the autonomic nervous system. The syndrome is therefore associated with an increased morbidity (the consequence of diurnal hypersomnolence and cardiovascular complications).

A method for treatment of sleep-apnea syndrome is to generate electrical signals to stimulate those nerves which activate the patient=s upper airway muscles in order to maintain upper airway patency. For example, in U.S. Patent 4,830,008 to Meer, inspiratory effort is monitored and electrical signals are directed to upper airway muscles in response to the monitored inspiratory effort. Or, for example, in U.S. Patent 5,123,425 to Shannon, Jr. et al., a collar contains a sensor to monitor respiratory functioning to detect an apnea episode and an electronics module which generates electrical bursts to electrodes located on the collar. The electrical bursts are transferred transcutaneously from the electrodes to the nerves innervating the upper airway muscles. Or, for example, in U.S. Patent 5,174,287 issued to Kallok, sensors monitor the electrical activity associated with contractions of the diaphragm and also the pressure within the thorax and the upper airway. Whenever electrical activity of the diaphragm suggests that an inspiration cycle is in progress and the pressure sensors show an abnormal pressure differential across the airway, the presence of sleep apnea is assumed and electrical stimulation is applied to the musculature of the upper airway. Or, for example, in U.S. Patent 5,178,156 issued to Wataru et al., respiration sensing includes sensors for sensing breathing through left and right nostrils and through the mouth which identifies an apnea event and thereby triggers electrical stimulation of genioglossus muscle. Or, for example, in U.S. Patent 5,190,053 issued to Meer, an intra-oral, sublingual electrode is used for the electrical stimulation of the genioglossus muscle to maintain the patency of an upper airway. Or, for example, in U.S. Patent 5,211,173 issued to Kallok et al., sensors are used to determine the effectiveness of the stimulation of the upper airway and the amplitude and pulse width of the stimulation are modified in response to the measurements from the sensors. Or, for

example, in U.S. Patent 5,215,082 issued to Kallok et al., upon sensing of the onset of an apnea event, a stimulation generator provides a signal for stimulating the muscles of the upper airway at a varying intensity such that the intensity is gradually increased during the course of the stimulation. Or, for example, in U.S. Patent 5,483,969 issued to Testerman et al., stimulation of an upper airway muscle is synchronized with the inspiratory phase of a patient=s respiratory cycle using a digitized respiratory effort waveform. A fully implantable stimulation system is described in Testerman et al. with a sensor implanted in a position which has pressure continuity with the intrapleural space such as the suprasternal notch, the space between the trachea and esophagus or an intercostal placement.

However, even with these modes of respiratory disorder treatment, there remain many practical difficulties for implementing them and other therapy treatments in medically useful systems. In particular, it is important that therapy systems, for example, systems including neuromuscular stimulators such as used in treating respiratory disorders, and other systems used for various therapy applications, be reliably operated. Various testing devices for medical devices, such as stimulators, and various fault indicating devices are available. However, such devices typically do not provide for diagnostic or operability testing on a regular basis. For example, if an implantable stimulator for treatment of respiratory disorders is utilized, particularly when such a system is operated when a patient is asleep, operability of the device should be tested regularly to determine if the system is performing its desired function. For example, it should be regularly verified and the patient given feedback that appropriate sensing upon which treatment is based is being performed. Further, for example, with respect to a patient undergoing respiratory disorder treatment, the patient should be comfortable that the amplitude of stimulation is adequate for performing the treatment associated with such stimulation. Thus, there is a need in the art for providing such diagnostic self testing for various therapy systems, including systems for treating respiratory disorders.

Summary of the Invention

A testing method for use with a patient stimulation system in accordance with the present invention includes providing a stimulation system including a patient control unit. The patient control unit initiates and terminates treatment periods. The method further includes automatically providing at least one period of stimulation to stimulate the patient upon initiating a treatment period.

In one embodiment, the stimulation system is for providing stimulation to treat respiratory disorders. Further, after the automatic provision of the period of stimulation, the system does not permit patient stimulation for a predetermined period of time. In another embodiment, the stimulation system is an implantable system and the patient control unit uses telemetry to initiate the system.

A stimulation system in accordance with the present invention includes stimulation means for providing stimulation of a patient during a treatment period. A patient control unit initiates and terminates treatment periods and the stimulation means automatically provides at least one period of stimulation to stimulate the patient upon initiation of a treatment period.

A system test method for use with a therapy system in accordance with the present invention includes providing a therapy system having a plurality of components; the therapy system physiologically interacting with a patient. The method further includes performing, internally to the system, a diagnostic self test of a component of the therapy system to determine if the component is functioning properly at a time when the therapy system is not interacting physiologically with the patient.

In one embodiment of this method, the therapy system includes a patient control unit for initiating therapy to the patient during a treatment period. Further, the diagnostic self test of the component is automatically performed upon initiation of the treatment period by the patient.

In another embodiment of this method, the therapy system includes an input circuit for receiving a sensed signal characteristic of a physiological parameter of the patient and an output circuit for generating a therapy output for

physiological treatment of the patient. A feedback signal from the output to the input is used to perform the self test of the component.

In another embodiment of this method, the therapy system includes an input circuit for receiving a sensed signal characteristic of a physiological parameter of the patient and an output circuit for generating a therapy output for providing therapy to the patient. A therapy output is generated for providing therapy to the patient. An effect of the therapy on the patient due to the therapy output is measured using the sensed signal and the effect resulting from the therapy output is verified.

A system for use in testing a therapy system in accordance with the present invention is also provided. The system includes a therapy system having a plurality of components; the therapy system for physiologically interacting with a patient. The system further includes means for performing, internally to the system, a diagnostic self test of a component of the therapy system to determine if the component is functioning properly at a time when the therapy system is not interacting physiologically with the patient.

Brief Description of the Drawings

Fig. 1 is a side sectional diagram of a patient having normal respiratory activity.

Figs. 2a-c are graphs of normal respiratory waveforms (shown with full normal inspiration at the peak). Fig. 2a shows a respiratory effort waveform and indicated phases of the respiratory effort waveform. Fig. 2b shows a graph of a respiratory airflow waveform with Fig. 2c showing the corresponding respiratory effort waveform.

Fig. 3 is a side sectional diagram of the patient of Fig. 1 at the onset of obstructive apnea.

Figs. 4a and 4b are respiratory waveforms of inspiratory effort showing normal inspiratory effort (Fig. 4a) and the change in normal inspiratory effort at the onset of an apnea event (Fig. 4b). Fig. 4c is a respiratory waveform showing respiratory airflow (as opposed to the respiratory effort waveform shown in Figs. 4a and 4b) in a patient during an apnea event.

Fig. 5 is a front sectional diagram of a patient showing the implantable components of the stimulation system in accordance with the present invention.

Fig. 6 is a block diagram of the stimulation system shown in Fig. 5 further including physician and patient programming units.

Fig. 7 is a diagram of one embodiment of the physician programming unit shown in block form in Fig. 6.

Fig. 8 is a diagram of one embodiment of the patient programming unit shown in block form in Fig. 6.

Fig. 9 is a diagram showing one embodiment of the IPG/stimulator shown in block form in Fig. 6.

Figs. 10a-10e are illustrations showing various positions or configurations for mounting the sensor shown in block form in Fig. 6 for sensing respiratory effort at a position in proximity to the posterior surface of the manubrium.

Figs. 11a-11d are various views of one embodiment of the sensor shown in block form in Fig. 6. Fig. 11a is a side view of the sensor, Fig. 11b is a cutaway view showing the sensing element portion of the sensor with the sleeve subassembly of the sensor cut partially away, Fig. 11c is a cross-section view of the sensing element portion of the sensor, and Fig. 11d is a cross-section view of the connector portion of the sensor.

Fig. 12a is a first embodiment of a block diagram of the signal processing circuitry of the IPG/stimulator shown in block form in Fig. 6, implemented in logic, for receiving the respiratory effort signal from the sensor and providing an inspiration synchronized stimulation signal to the electrode in accordance with the present invention.

Fig. 12b is a second embodiment of a block diagram of the signal processing circuitry of the IPG/stimulator shown in block form in Fig. 6, implemented with a microprocessor, for receiving the respiratory effort signal from the sensor and providing an inspiration synchronized stimulation signal to the electrode in accordance with the present invention.

Fig. 13a is a top level flow diagram of the algorithm/control logic shown in block form in Fig. 12a and 12b in accordance with the present invention.

Fig. 13b is a flow diagram of the IPG-ON block of the flow diagram of Fig. 13a.

Fig. 13c is a flow diagram of the Onset Detection block of the flow diagram of Fig. 13a.

Fig. 13d is a flow diagram of the Offset Detection During Stimulation block of the flow diagram of Fig. 13a.

Fig. 13e is a flow diagram of the Offset Detection block of the flow diagram of Fig. 13a when stimulation is not occurring.

Fig. 13f is a flow diagram of the Suspension, Artifact, Therapy Delay block of the flow diagram of Fig. 13a.

Fig. 13g is a flow diagram of the AGC Adjust block of the flow diagram of Fig. 13a.

Fig. 14 is a graph showing a normal respiratory effort waveform indicating various critical points detected in accordance with the present invention, various thresholds used in such detection, a normal differential pressure signal, a stimulus signal synchronously applied based on the critical points detected with respect to the respiratory effort waveform, and an illustration showing the definition of a refractory period, all in accordance with the present invention.

Fig. 15 is a graph showing a respiratory effort waveform having an artifact therein, a stimulus signal applied according to the present invention, and an illustration of the refractory period utilized to reject the artifact as an inspiration onset, all in accordance with the present invention.

Fig. 16a shows a normal respiratory effort waveform and stimulus applied according to the present invention. Fig. 16b shows a respiratory effort waveform of a patient with central sleep apnea and a stimulus applied according to the present invention utilizing a maximum stimulation time limit in accordance with the present invention. Fig. 16c shows a central sleep apnea occurring between cycles of respiratory effort. Fig. 16d illustrates stimulation periods for treatment of

the central sleep apnea occurring in Fig. 16c. Fig. 16e shows AGC gain for the respiratory signal shown in Fig. 16c during the central sleep apnea.

Figs. 17a-c are graphs of one embodiment of a stimulation burst used for stimulating the patient according to the present invention.

Fig. 18 is a block diagram of one embodiment of a microprocessor based stimulation system.

Fig. 19 is a block diagram illustration of one diagnostic self test strategy for a therapy system.

Figs. 20a-d are block diagrams of various internal diagnostic self tests for the system shown in Fig. 18.

Detailed Description of the Embodiments

The following description relates generally to therapy systems including implantable therapy and stimulation systems. Although many portions of this description are particularly applicable to the treatment of respiratory disorders, such as sleep apnea, by administering stimulation of musculature in synchrony with detected periodic events of the respiratory cycle, many portions of the system are equally applicable to other therapy systems. For example, automatic gain control, diagnostic testing, and methods for conserving energy are applicable to one or more other therapy systems such as, for example, drug delivery systems, blink stimulation systems, and cardiac related systems.

With respect to the synchronization of stimulation to the respiratory cycle of a patient to treat respiratory disorders, such synchronized stimulation requires a suitable respiratory sensor, proper placement of the respiratory sensor, and signal processing capability for converting the sensed respiratory effort signal from the sensor to a stimulation signal for use in stimulating the patient. In Fig. 1 and Figs. 2a-c, normal respiratory activity is depicted. In Fig. 1, a patient 10 has an airway 15 which remains patent during inspiration of air 20. Fig. 2a shows a typical respiratory effort waveform for two complete respiratory cycles. This analog waveform can be generated by various transducers such as, for example, a belt transducer worn snugly about the chest of the patient as used for detection and analysis of sleep apnea in sleep laboratories, an implanted pressure sensor such as

that described in detail below, or any other transducer that provides a respiratory effort signal adequate for analysis to detect critical points thereof for use in the treatment of respiratory disorders, such as sleep apnea. Each wave of the waveform is characterized by a negative peak 30 on completion of expiration, a positive peak 35 on completion of inspiration (i.e. inspiration offset) and a turning point 40 which indicates the onset of inspiration (i.e. inspiration onset). Each wave of the waveform can therefore be separated into a period of respiratory pause 32, an inspiratory phase 33 and an expiratory phase 34. Respiratory effort waveforms having similar identifiable characteristics can be provided by monitoring other physiological signals such as intrathoracic pressure, intrathoracic impedance or electromyographic potentials. Other characteristics of the waveform could also be identified in connection with tracking and analyzing the respiratory waveform to monitor respiratory activity in sleep apnea treatment. In normal respiration, the respiratory effort waveform is related to airflow as set forth in Figs. 2b and 2c. In Fig. 2b a trace of normal respiratory airflow from a flow transducer is shown while Fig. 2c shows the corresponding trace of the normal respiratory effort which produces the airflow.

In Figs. 3 and 4b, respiration in the same patient at the onset of an obstructive sleep apnea event is depicted. Fig. 3 shows the patient 10 and airway 15 with an airway obstruction 17 that is characteristic of an obstructive apnea event. Fig. 4a shows that in a normal respiratory effort waveform 43, the inspiratory peaks 45a-d are of approximately the same amplitude. By comparison in Fig. 4b, in a waveform 47, the inspiratory peaks 48a-d become significantly greater in amplitude at the onset of obstructive apnea than the immediately preceding inspiratory peak 49. This is reflective of the increased inspiratory effort undertaken by the patient in response to the difficulty of breathing through the obstructed airway.

In treatment of sleep apnea, the increased respiratory effort is avoided by synchronized stimulation of a muscle which holds the airway open during the inspiratory phase. Preferably, the muscle stimulated is an upper airway muscle, such as the genioglossus muscle stimulated by a cuff electrode placed

around the hypoglossal nerve. However, there may be other upper airway muscles or nerves which can be used for stimulation to perform the same function and also other nerves or muscles apart from the upper airway which may be stimulated, such as the diaphragm, to treat respiratory disorders, such as, for example, sleep apnea. The effect of this stimulation on obstructive sleep apnea can be seen in the airflow trace of Fig. 4c. During a first period indicated as 46a, stimulation is enabled producing a normal respiratory airflow. During a second period indicated as 46b, stimulation is disabled causing obstruction of the airway and reduction in airflow volume (apnea). During a third period indicated as 46c, stimulation is resumed, restoring patency to the airway and increasing airflow volume.

Components, and one implantable configuration, of an implantable stimulation system 50 for providing inspiration synchronous stimulation treatment of sleep apnea are shown in Fig. 5. A block diagram of these components and other associated programming components of the system 50 for treating sleep apnea is shown in Fig. 6. As shown in Fig. 5, inspiration synchronous stimulation is controlled by the implantable pulse generator (IPG)/stimulator 55. IPG 55, also shown in Fig. 9, provides inspiration synchronized stimulation, e.g. one or more stimulation pulses, through stimulation lead 52 to an electrode or electrode system 65 placed around the hypoglossal nerve 53 for stimulation of the genioglossus muscle of the upper airway. The electrode or electrode system 65 may be positioned with respect to any other respiratory nerve, or other nerve or muscle that provides the desired stimulation result for the respiratory disorder treated. The IPG 55, i.e. stimulator/controller, receives respiratory effort waveform information via a sensor lead 57 from a respiratory sensor or transducer 60 sensing the respiratory effort of a patient 10.

One associated component of system 50 includes a physician programmer 80, such as a laptop computer having programming software and communication capabilities for communicating with the IPG 55, and which is capable of programming the IPG 55 with various parameters in order to adapt the system for treatment of a particular patient. The system 50 of Fig. 5, is therefore adapted to be programmed using the physician programmer 80 as shown in Figure 7

by telemetry via transmitting/receiving element 81 electrically coupled to the processor based programmer 80. Thereafter, the system 50 is used each night by the patient to prevent the closure of the upper airway during the inspiratory phase of the respiration cycle.

It will be apparent to those skilled in the art that such a system must be made to be easy to use by the patient and since it is used without constant medical supervision, it must be able to adapt to many different operating conditions. Therefore, the system 50 includes another associated component, i.e. patient programmer 70, as shown in Fig. 8. The patient programmer 70 gives the patient the capability to turn the stimulator ON/OFF, adjust the stimulation amplitude within preset limits programmed by the physician and adjust any other stimulation parameters or parameters of the IPG 55 as may be allowed by the physician, such as, for example, stimulation pulse rate, pulse width, dose time, therapy delay time. The patient programmer 70 provides both a visual and audio confirmation of communication with the stimulator and further may include other patient control elements for controlling parameters of the treatment of sleep apnea. In addition, as described further below, the patient turning the power on for initiation of the treatment using the patient programmer 70 starts an automatic self stimulation test and/or an automatic diagnostic self test of the components of the system 50. Such a diagnostic self test may be performed at any time, in addition to the initiation of the treatment period by the patient. Further, such self stimulation test and diagnostic tests are equally applicable to other therapy systems in addition to the treatment of respiratory disorders, such as sleep apnea.

The pressure sensor or respiratory transducer 60, may be a dynamic relative pressure sensor such as that disclosed in U.S. Patent 4,407,296 to Anderson or U.S. Patent 4,485,813 issued to Anderson et al which are incorporated herein by reference in their entirety. The pressure sensor 60 is surgically implanted in a region that has pressure continuity with the intrapleural space such as the suprasternal notch, the space between the trachea and esophagus or attached to either of the trachea or esophagus, an intercostal placement, or secured as shown in Figs. 10a-10e in a position for sensing pressure at the posterior side of the

manubrium as described in further detail below. The suprasternal notch 62 and manubrium 63 of sternum 64 as shown in Figure 5, are well known structures on the upper chest that are in anatomical continuity with the intrapleural space. It is also well known that changes in intrapleural pressure provide a characteristic respiratory effort waveform. The location for placement of the sensor is, at least in part, chosen as a function of delay, i.e. propagation time of a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position and as a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. filtering necessary to remove waveforms other than the waveform of the sensed characteristic, such as cardiac waveform activity.

Preferably, the pressure sensor 60 utilized is a pressure sensor assembly or sensor lead 115 similar to the sensor lead sold under the trade designation of Medtronic Model 4321, available from Medtronic, Inc., Mpls., MN as modified and represented in Figs. 11a-11d. The pressure sensor assembly 115 includes a sensing section 120, a lead anchoring section 122, and a connector section 124. A flexible lead body 121 forms a part of each section. The sensing section 120 includes, as shown in the detail views of Figs. 11b and 11c, a relative pressure sensing element 126 which is mounted at an open distal end 123 of assembly 115 opposite the connector section 124. The relative pressure sensing element 126 senses respiration pressures through the use of piezo-electric crystals attached to a sensor diaphragm lying perpendicular to a longitudinal axis 125 extending through assembly 115. Pressures are transmitted to the diaphragm through the portholes 128 on both sides of the sensing element 126. Pressure transmits from the portholes 128 to the diaphragm via a medical adhesive 132, such as silicone rubber, which fills the nose cavity of the pressure sensing element 126. The sensor is driven, for example, with a fixed bias current on which the AC pressure signal is coupled onto. Such a fixed sensor bias can range from about 8FA to about 100FA. Such a sensor has a nominal output of about 3mV/mmHg over the usable bandwidth of about 0.1 to about 100Hz.

The sensing element 126 has coil leads 136 electrically connected thereto. The coil leads 136 are provided within bilumen tubing 138. The bilumen tubing 138 at the sensor section end and the sensing element 126 are positioned in a flexible tube 130 by medical adhesive 132 which also fills the cone of the sensing element 126 and covers the outer portions of the sensing element 126. There is no exposed metal surface of the sensing element 126 and the sensor is electrically isolated from the patient.

As shown in Fig. 11d, a connector assembly 168, such as, for example, a bipolar IS-1 compatible connector assembly, is electrically connected to the lead body 121, such as by crimping, to coil leads 136 in connector section 124 of the sensor assembly 115. Any connector assembly may be utilized that is compatible with a connector port of the IPG 55. The connector includes sealing rings 167 to ensure that body fluids do not disrupt the sensor assembly 115 and IPG 55 connection.

A sleeve attachment subassembly 140 has the sensing element 126 and a portion of the lead body 121 positioned therein. The sleeve subassembly extends from a distal surface 174 of the sensing element 126 at the open distal end 123 to beyond the interface between the lead body 121 and sensing element 126. The sleeve attachment subassembly 140 includes an outer threaded sleeve 142, an inner threaded sleeve 144, and a soft umbrella ring 146. The sleeve attachment subassembly 140 is mounted on the outer surface of the flexible tube 130 with medical adhesive 132. The inner surface of the inner threaded sleeve 144 is abraded to provide adhesion with the medical adhesive 132 to stably mount the sensing element 126 in the subassembly 140. The inner threaded sleeve 144 has holes 148 about the longitudinal axis therethrough for molding a flexible element, i.e. soft umbrella ring 146, about the distal open end of the inner threaded sleeve 144.

The soft umbrella ring 146 may be formed of silicone rubber and includes a flexible outer umbrella portion 152 that extends outward relative to the longitudinal axis and rearwardly relative to the distal open end of the inner threaded sleeve 144 and a fixed portion 154 of the umbrella ring 146. The flexible outer

umbrella ring 152 performs the function of preventing tissue and bone growth over the distal open end 123 of the sensor assembly 115 when implanted. The soft umbrella ring 146 is preferably formed of a radio opaque material so that it can be seen in imaging processes throughout implantation and explanation. Further, the umbrella ring 146 may include a treatment to prevent tissue and bone overgrowth of the sensor 126. Such treatment may include treatment with a steroid, such as heparin, chemical coatings, surface roughening, or any other treatment that reduces such tissue and bone overgrowth.

The flexible element, i.e. umbrella ring 146, may be of any configuration that prevents bone and tissue overgrowth. Further, if the sensor is implanted into a drill hole in the manubrium as described below, the flexible element must be capable of being inserted and removed through the drilled hole. For example, the flexible element may be a donut shape or a simple flange extending outward relative to the longitudinal axis 125 at the distal open end of inner threaded sleeve 144.

The outer threaded sleeve 142 includes a threaded portion 156 and an unthreaded flange portion 158 extending substantially perpendicular to and outward relative to the longitudinal axis 125 of the sensor assembly 115. The outer and inner threaded sleeves 142 and 144 are utilized for adjusting the length of the subassembly 140 along the longitudinal axis 125. Further, they provide for anchoring the sleeve subassembly, i.e. securing the sensor, in the manubrium as described further below with the unthreaded flange portion 158 of the outer threaded sleeve 142 providing means for direct or indirect contact at the anterior side of the manubrium and with the flexible element 146 providing for direct or indirect contact at the posterior side of the manubrium. The adjustability is important as the thickness of the manubrium varies from patient to patient. One or more holes 160 in the flange portion 158 are available for anchoring the sensor section 120 by suture to tissue or by bone screw to the anterior side of the manubrium. The outer threaded sleeve 142 and the inner threaded sleeve 144 are preferably formed of stainless steel, but can be any biocompatible material, preferably a rigid biocompatible material.

In alternative configurations, the flange portion 158 may include a soft cover thereabout or may be formed of a different shape as long as it still performs the function of direct or indirect contact with the manubrium to hold the sensing element 126 in position and/or includes means for attachment by a bone screw, suture, or other securing means. For example, the flange portion 158 may be a tab structure or multiple tabs extending away from and substantially perpendicular to the longitudinal axis 125 from the end 159 of threaded portion 156.

Further, the adjustability function of the inner and outer sleeves 142 and 144 may be provided by any structure that allows a length of the sleeve to be adjusted and then capable of being fixed at a particular length. For example, two telescoping members or sliding members may be used with, for example, a ratchet technique coupling the two and providing fixation at a particular length.

The anchoring section 122 includes lead body anchoring sleeve 164 slidably mounted on the lead body 121 and having suture grooves 165 for the anchoring of the lead body 121 when implanted. The lead body 121 is flexible such that it can make a sharp right angle from the sleeve subassembly 140 at the anterior region of the manubrium when the sensor assembly 115 is implanted to avoid skin erosion and bulge thereat. For example, the lead body 121 may include pentifilar conductor coils 136 in a bilumen silicon tubing. Alternatively, the lead body 121 may include a right angle attachment at the anterior region of the manubrium 63 for providing direction to the lead body as it extends from the drilled hole at the anterior of the manubrium 63.

One skilled in the art will recognize that various connection techniques for connecting the sensing element 26 to the IPG 55 may be utilized. For example, fiber optic connection may be used, RF techniques may be used, and also techniques using the body mass itself to propagate a signal between components may be used. With use of at least some of these connection techniques, a lead extending from the anterior of the manubrium would not be present. Without the need for a lead, the sleeve subassembly 140 for positioning and anchoring the sensor in the drilled hole of the manubrium 63 could take the form of any mounting element having an adjustable length. The mounting element would no longer need

to have an opening therethrough, such as a sleeve, but could take the form of, for example, a spring loaded elongated member with one open end for holding the sensor. In other words, the mounting elements used to mount the sensing element may take any elongated form with an adjustable length and elements for securing it in the manubrium hole by direct or indirect contact with the anterior and posterior surfaces of the manubrium.

The pressure sensor 60, such as pressure sensor assembly 115, or any other suitable sensor for providing a signal characteristic of respiratory effort, may be implanted in various positions, such as those previously mentioned and further including attachment to the esophagus or trachea or in a position therebetween, or to any other soft tissue in the suprasternal notch. Various positions for the sensor are described in U.S. Patent Serial No. 08/310,177 entitled AMethod and Apparatus For Detecting and Treating Obstructive Airway Disorders@ incorporated herein by reference in its entirety. Further, the sensor 60 may be positioned as shown in the Figs.10a-10e. Preferably, the pressure sensor assembly 115 is implanted through a drilled hole in the manubrium 63 as shown in Figs. 10a and 10b. However, the sensor assembly 115 could be implanted through the sternum 64 at any location thereof or through any other bone such that the sensing element 126 is in communication with the intrathoracic region or a region with pressure changes characteristic of respiratory effort.

As shown in Fig. 10b, the brachiocephalic vein 195, also known as the inominant vein, is located in a region on the posterior side of the manubrium 63 and erosion of the vein is to be avoided. The present invention is configured to allow sensing in the region where this vein is located. The pressure sensor 60 is positioned in proximity to the vein, however, the term in proximity to the vein means that the sensing element is positioned in the region of the vein but is configured and/or positioned such that erosion of the vein is avoided.

To implant the pressure sensor assembly 115, a small pocket posterior to the manubrium 63 via the suprasternal notch 62 is created, such as by blunt dissection. A hole 185 is drilled perpendicularly through the superior aspect of the manubrium 63 and at the midline of the manubrium 63. It is desired that the

sensor element 126, be placed near the top 187 of the manubrium 63 so that the pocket created on the posterior side of the manubrium 63 is minimized lessening surgical excavation risk and lessening the effects of cardiac signals which are stronger at lower portions. Further, by implanting the sensor assembly 115 toward the top of the manubrium 63, the implanter can see the position of the umbrella ring 146 easily, especially with mirrors. During drilling, a retractor is placed on the posterior side of the manubrium 63 to protect intrathoracic structures. Although placement of the sensing element 126 near the top 187 of the manubrium is preferred, the sensing element may be positioned anywhere along the length of the sternum 64, although the manubrium is preferred. More preferably, the sensing element is positioned about 0.5 cm to about 3 cm from the top 187 of the manubrium.

When implanting the sensor, the length of the sensor section 120 of the pressure sensor assembly 115 (i.e. length of subassembly 140) is maximized by turning the outer threaded sleeve 142 with respect to the inner threaded sleeve 144 of the sleeve attachment subassembly 140. The sleeve attachment subassembly 140 of the sensing section 120 is then inserted in the drilled hole 185 and the sensor section length is adjusted such that the soft umbrella ring 146 is in direct or indirect contact with the posterior surface of the manubrium 63. When the sensor section 120 is inserted into the drilled hole 185, the umbrella ring 146 collapses or is compressed against the side of the sleeve subassembly 140 and will spring outward upon protruding into the posterior side of the manubrium 63. The umbrella ring portion 152 will act as an anchor and will prevent bone and tissue growth over the sensor opening. The implanter can utilize a finger to make sure the umbrella ring 146 is flush with the posterior surface and to stabilize the sensor while the outer threaded sleeve 142 is turned to adjust the length of the sleeve attachment subassembly 140 of the sensor section 120 to the thickness of the patient=s manubrium 63. The distal tip 174 of the sensing element 126 should protrude in the range of about 1 mm to about 3mm posteriorly from the manubrium 63. A position less than 1 mm results in a greater chance of tissue or bone overgrowth of the sensing element 126. The distal tip 174 of the sensing element 126 is flush with the

open end of the inner threaded sleeve 144. The sensor assembly 115 can then be anchored on the anterior side of the manubrium by a suture or bone screw through the hole 160 of the unthreaded flange 158 of the outer threaded sleeve 142. The lead body 121 can be anchored with use of suture grooves 165 on the anchoring sleeve 164.

With the IPG 55 implanted in a position on the upper chest, such as just below the clavicle 61 as shown in Fig. 5, the lead body 121 of the pressure sensor assembly 115 is inserted in a tunnel created from the manubrium 63 to a pocket created for implanting the IPG 55. When the IPG 55 is implanted, the connector section 124 of the pressure sensor assembly 115 is connected to sensor port 58 of the IPG 55.

Figs. 10c-10e show alternative configurations for implanting the pressure sensor 60 of the implantable stimulation system 50. As shown in Fig. 10c, a pressure sensor 60 has a sensing element 197 positioned posterior to the manubrium 63 with the lead body extending over the top 187 of the manubrium 63. The lead is then brought down the anterior portion of the manubrium 63. Various anchors 178 are utilized to hold the sensing element 197 in place behind the manubrium 63.

As shown in Fig. 10d, the sensor 60 is positioned in a manner similar to that shown with respect to the drill through technique described with reference to Figs. 10a and 10b. However, in this configuration, the drill hole 180 is made at an angle through the manubrium 63.

As shown in Fig. 10e, the sensor 60 is positioned substantially as described in Fig. 10c. However, in order to protect against erosion of fragile veins posterior of the manubrium, the sensing element 197 and a portion of the lead body extending therefrom are covered with a soft guard 182. The guard 182 may serve the function of anchoring the sensor 60 as well as preventing any erosion of the brachiocephalic vein 195. The distal end 196 of the guard is open.

As demonstrated by the various configurations shown, many various positions for implant of the sensor 60 are possible behind the manubrium yet while avoiding the fragile veins. The present invention contemplates the positioning and

securing of various sensing elements with respect to the manubrium 63 to sense pressure or any other characteristic for obtaining a respiratory effort waveform at a region posterior of the manubrium 63. The sensing elements are preferably placed in close proximity to the posterior surface of the manubrium 63.

The electrode or electrode system 65 of the implantable stimulation system 50 may be any conventional electrode system for stimulation of muscles to treat respiratory disorders, such as sleep apnea. As previously described, although various respiratory muscles may be stimulated, stimulation of the genioglossus muscle is utilized herein for treatment of sleep apnea. For example, the electrode system 65 utilized may be a Model 3990B Half Cuff Nerve Electrode available from Medtronic, Inc., Mpls., MN. This electrode and other suitable electrode configurations are described in U.S. Patent 5,344,438 to Testerman et al., entitled ACuff Electrode@ and incorporated entirely by reference herein. This electrode is utilized for placement around a respiratory motor nerve, such as the hypoglossal nerve 53, with the stimulation lead 52 for connection to the stimulation port 59 of IPG 55 as shown in Figs. 5 and 9. One or more stimulation pulses are delivered to the electrode 65 by the IPG 55 and transferred to the nerve resulting in opening of the airway during respiration. It should be readily apparent to one skilled in the art that any suitable electrode for stimulating the desired muscle may be utilized with the stimulation system 50 according to the present invention. For example, the electrode may be a full cuff electrode or any other electrode configuration for capturing a respiratory motor nerve, such as the hypoglossal nerve. Further, with respect to any other neuromuscular stimulation systems which may benefit from the present inventions described herein, the electrode(s) may include any electrode(s) that provide the desired stimulation for such systems.

The IPG 55 includes signal processing circuitry 200, including detection algorithm or control logic 216, as shown in block diagram form in Fig. 12a, respectively, and functionally shown in the flow diagrams of Figs. 13a-13g. The signal processing circuitry 200 processes the respiratory effort signal provided by the pressure sensor 60, such as pressure sensor assembly 115, and provides

inspiration synchronized stimulation via electrode or electrode system 65 for the treatment of respiratory disorders.

To achieve adequate treatment of sleep apnea, the stimulation is initiated by detection of inspiration onset, for example, within a predetermined time of the actual physiological onset, for example 200 ms. Sensing onset 200 ms early (i.e. >predictive=) is desired. Stimulation is terminated as a function of a detected inspiration offset. Slight errors of approximately 300 ms or less in timing causing early offsets, late offsets, or early onsets are typically permitted by the treatment system. Late onsets, however, are preferably no later than, for example, 200 ms. The requirement that detection of onsets be no later than, for example, 200 ms, is necessary to avoid airway obstruction prior to stimulation. The timing to recruit a muscle to overcome obstructions which occur prior to stimulation force such a requirement. The present invention provides means for predictively detecting onsets to meet this requirement. In addition to rigid timing requirements, the detection algorithm operates reliably in the presence of cardiac artifacts and motion artifacts.

The description herein is set forth in a manner such that stimulation for treatment of sleep apnea occurs substantially continuously and synchronous with inspiration throughout the treatment period, except for time of nonstimulation such as suspension, dose, therapy delay, etc. as determined by the algorithm described below. The treatment period is the time period from when the treatment is turned on to when the treatment is turned off. However, many of the concepts described herein are equally applicable to sleep apnea treatment systems wherein the onset of apnea is detected in some manner and stimulation only performed after such detection of apnea. For example, waveform analysis could be performed to determine when an apnea is about to occur and then treatment by stimulation could be initiated using concepts described herein. Such detection of the onset of sleep apnea is described in U.S. Patent 5,483,969 to Testerman et al. which is incorporated herein by reference in its entirety.

The detection algorithm or control logic 216 of the signal processing circuitry 200, which will be described in detail below, makes significant reference to Fig. 14. Therefore, a brief description of Fig. 14 is appropriate at this point to introduce the elements thereof and provide a brief description of some of the functionality of the control logic 216. Fig. 14 includes a normal respiratory effort waveform 500 characteristic of the signal sensed by the pressure sensor 60, a differential pressure signal 300, an illustrative stimulus window 400 during which one or more pulses are generated for treatment of airway disorders synchronized with inspiration onset 501a and inspiration offset 502a, and a refractory period illustration wherein a refractory period (R) is defined during at least a part of the expiratory and pause periods 34 and 32 (Fig. 2a) of the respiratory cycle.

Further, Fig. 14 shows the respiratory period (T) which is represented as the period from inspiration offset 502a to inspiration offset 502b, the time of inspiration (TI) which is shown as the time from inspiration onset 501b to inspiration offset 502b, and a variety of thresholds which are utilized by the detection algorithm/control logic 216 to control and provide inspiration synchronous stimulation. Such thresholds include analog onset threshold 520 and)V (i.e. slope) onset threshold 522 used for detection of inspiration onset, analog offset threshold 524 and)V offset threshold 526 used for detection of inspiration offset (i.e. latched offset), Vref threshold 530 or zero crossing threshold used for validating or declaring a detected latched inspiration offset, and AGC amplitude threshold 528 used in updating gain of the respiratory signal from the sensor 60.

)V is representative of the slope of the respiratory effort waveform 500. For illustration, the)V values can be generated by sampling the sensor output during a sample period, such as for example every 10 to 70 ms. The sampled value is then compared to the previously sampled value to obtain the net change in voltage (i.e. change in intrathoracic pressure) over the sample period. The net change,)V, is thus the pressure signal slope and therefore, representative of slope of the respiratory effort waveform.

The normal respiratory effort waveform 500 shows the amplitudes and slopes which are characteristic of inspiration onset and offset. The polarity of the voltage respiratory effort waveform 500 in Figure 14 is inverted with respect to the polarity of the actual physiologic pressure measured by sensor 60. Inspiration is represented as a positive going voltage which indicates a negative inspiration pressure. Expiration is shown as a negative going voltage which indicates a positive expiration pressure. The stimulation system 50 includes automatic gain control (AGC) that references or normalizes the respiratory effort signal. For example, the signal may be normalized such that the positive signal peak is 1.2 volts, baseline (Vref) is 0 volts (DC), and the negative signal peak is at approximately -1.2 volts. In other words, a 2.4 peak to peak signal is provided. The AGC is described in further detail below and is applicable to any variable input signal characteristic of a periodic physiological parameter and is not limited to only the respiratory effort pressure signal described herein. The normalization of such signals is particularly advantageous when used in systems where timing detection is based on comparison to signal thresholds.

Inspiration onset 501 is characterized as a rapid change in slope at an amplitude above a predetermined level, i.e. analog onset threshold 520 (Figure 14), and is detected by the control logic of the present invention as a function of such characterization. Inspiration offset 502 is characterized by a negative change in slope above a predetermined amplitude, i.e. analog offset threshold 524 (Figure 14). A sustained non-positive slope and an amplitude above the predetermined amplitude typically indicate an offset 502 and an offset is detected and latched by the control logic of the present invention as a function of such characterization.

Physiological artifacts caused by cardiac pressures and body motions add complexity to the respiratory effort waveform. Cardiac artifacts produce slope changes very similar to onset and offset slope changes. However, the slope is not typically sustained for the same duration. The respiratory amplitude level is typically not altered by the cardiac artifacts. Therefore, the combination of sustained slope and amplitude provides information to differentiate between inspiration events (onsets and offsets) and cardiac artifacts to avoid stimulation at

the improper time. The control logic, for example, by using consecutive)V samples to detect offsets and onsets, utilizes such characteristics to prevent misdetection of valid onsets and offsets, i.e. offsets and onsets that are not artifact onsets and offsets.

Motion artifacts are similar to inspiration in both sustained slope and amplitude. Figure 15 displays a motion artifact 542 on a respiratory waveform 540. Depending on the source of the artifact (slow or fast body movement, etc.) the slope and amplitude may be sufficient to satisfy the characteristics of either an inspiration onset and/or offset and stimulation based on such an artifact is to be avoided. As illustrated in Fig. 15, the control algorithm in accordance with the present invention utilizing a defined refractory period minimizes stimulation from occurring based on artifacts like artifact 542. Such distinguishing of the artifact from normal respiration will become apparent from the detail description of the control logic 216 below.

The techniques used by the algorithm or control logic 216 to distinguish motion artifacts are based on known physiological parameters of breathing during sleep. First, respiratory rate is known to be very stable and consistent during sleep. For example, a typical breath-to-breath rate variation of 15 % has been established, with maximum variations as high as 35 %. Periods of wakefulness will have more breath-to-breath variations, coughs, sighs, etc., but stimulation is not necessary nor desirable while the patient is awake. The detection algorithm establishes the presence of a stable respiratory rate or respiratory period in order for stimulation to occur when signal onset characteristics are present, i.e. stimulation is suspended if a stable respiratory rate or respiratory period is not detected. Second, as the ratio between time of inspiration / total respiratory period (TI/T) is generally known, such as for example, between 0.30 and 0.40, a refractory period (i.e. blanking period after inspiration has occurred), that includes both hard and soft refractory periods, is utilized to detect or predict onset at a time just prior to the next expected onset. These two ideologies, along with others as will become apparent from the further detail below, are utilized by the algorithm to reject motion artifacts.

The IPG 55, shown in Fig. 9, is any IPG or stimulator capable of being configured for control of stimulation as required herein for treatment of sleep apnea. The IPG 55 may be, for example, a Medtronic nerve stimulator sold under the trade designation ITREL II Model 7424 or a Medtronic nerve stimulator sold under the trade designation ITREL III Model 7425, both available from Medtronic Inc., Mpls., MN., modified to include an input from the respiratory sensor 60 and modified to include all the signal processing capabilities as shown in Fig. 12a for control of stimulation as required herein. Each of these nerve stimulators include circuitry for providing a wide range of stimulation therapies which can be used with the present invention. The stimulator utilized should be capable of implementing the signal processing with minimum power consumption. Many various hardware configurations may be utilized to implement the described signal processing circuitry. For example, various designs incorporating hardware, software, processors, analog circuits, digital circuits, combinations of the aforementioned, etc. may be used to perform the necessary signal processing and the present invention is not limited to any particular configuration. Any IPG 55 utilized requires an energy source.

The IPG 55 is implanted in the patient at a location such as shown in Figure 5. However, any location normally utilized for implanting an IPG can be used for the location of IPG 55 as would be readily apparent to one skilled in the art. A suitable implantable neurostimulator has advanced programmable features permitting mode changes by transcutaneous RF telemetry. The patient-controllable parameters of the IPG=s operation, such as the amplitude of stimulation, can therefore be controlled by the patient through a small hand-held telemetry device, i.e. patient programmer 70, shown in Figure 8. Likewise, the physician can preset additional operational parameters of the IPG 55 through a handheld telemetry device 81 of the physician programmer 80, as shown in Fig. 7, held over the implanted IPG 55.

As shown in Fig. 9, the IPG 55 includes two connector ports 58 and 59. The connector port 58 is for insertion of the sensor lead 57 and the connector port 59 is for insertion of the stimulator lead 52.

Fig. 12a is a first embodiment of a block diagram of the processing circuitry 200 that includes sensor input circuitry 201 necessary to acquire a respiratory signal from the pressure sensor 60 including means for biasing the sensor, filtering the sensor output and providing a normalized sensor signal. Processing circuitry 200 further includes monitoring circuitry 203 for monitoring the sensed signal to synchronize stimulation with respiration.

In this first embodiment, as shown in Fig. 12a, a combination of analog and digital circuits is used. Logic functions are provided without use of a microprocessor, i.e. purely analog and digital circuits. The analog front end or sensor input circuitry 201 for obtaining a respiratory effort signal includes sensor bias 202 required for biasing the pressure sensor 60. The pressure sensor 60, for example, the sensing element 126, requires a stable bias current in the range of 8.8 :A to 100 :A. One method of sensor bias 202 includes providing a static bias current in the range of, for example, 15 :A to 25 :A. Currents of this magnitude provide the best trade-off in terms of battery life and adequate immunity from noise. Alternatively, a second manner of sensor bias 202 includes providing a duty-cycled bias current. In this manner of operation, for example, a 80 :A to 100 :A bias is applied to the sensor just prior to the sampling the respiratory signal. Such duty cycling provides lower power operation, i.e. saves battery life, and provides noise immunity benefits.

The pressure induced AC voltage from the sensor 60 is AC coupled with a high pass filter pole at 0.1 Hz from the sensor bias current to a filter 204, for example, a 2 pole, 3 Hz RC low pass filter. The filter 204 is for anti-aliasing the signal prior to providing the signal to the AGC amplifier 206 and to remove the higher frequency edges of non-respiratory artifacts, such as cardiac artifacts, and also motion artifacts.

The AGC amplifier 206 (Fig. 12a) may operate at a sampling frequency using switched capacitor techniques or may be operated continuously. The AGC amplifier 206 is responsible for normalizing the sensor output, such as, for example, to a consistent 2.4 volt peak-to-peak signal. The amplitude of this signal is then sampled and used by the analog threshold comparator 212 for comparison to various thresholds and is presented to the ADC 214 for conversion into digital delta voltage measurements ()V's) via the)V nulling amplifier 208 for providing an indication of the slope of the waveform. The outputs from the analog comparator 212 and ADC 214 are then utilized by algorithm/control logic 216 to provide inspiratory synchronous stimulation as further described below.

The AGC amplifier 206 compensates for patient-to-patient and inter-patient respiration amplitude variabilities. For example, pressure amplitudes will vary as a patient changes sleeping positions. The AGC amplifier 206 provides adaptivity to the variable amplitudes and thus the physician is not required to program a gain setting. The AGC amplifier 206 also makes the detection algorithm much easier to implement as the thresholds, as described above and also further below, become relative to the normalized peak-to-peak signal and will operate the same even as the true pressure varies throughout the night.

In the first embodiment of processing circuitry 200, the measurement of the pressure sensor signal amplitude is implemented in analog circuitry. The analog amplitude of the pressure signal is measured by comparison to various thresholds and digital outputs are provided to the detection algorithm 216 as a function of such comparisons. Because of the fixed nature of the AGC amplitude threshold 528, the signal amplitude is easily determined and readily comparable to the various analog thresholds in the analog domain. The one comparator 212 can be multiplexed between the onset analog reference 520, offset analog reference 524, Vref threshold 530, and AGC analog reference 528. As mention above, digital outputs are provided by the comparator 212 to the algorithm/control logic 216 to indicate the crossing of such amplitude thresholds.

The sampled signal amplitudes of the signal from AGC amplifier 206 are used by the)V nulling amplifier 208 and ADC 214 to generate)V values of a desired bit size, for example, a 7 bit or 8 bit)V value. Configuring the amplifier prior to the ADC 214 and nulling the present amplitude sample value with the previous sample amplitude value allows for digitally converting a change in voltage (i.e. slope) to)V=s. The nulling amplifier 208 has a gain, for example, of 16, to restore amplitude to the differenced value. The ADC 214 sampling period is synchronized (non-overlapping) to the stimulus to avoid degrading the ADC sensitivity with stimulus circuitry noise. The stimulator frequencies of the IPG 55 may be, for example, and thus the sampling frequencies may be, for example, 20, 30, 33, and 40 Hz. One skilled in the art will readily recognize that the ADC 214 and)V nulling and amplification block 208 could be switched, with the ADC 214 digitally converting the sampled amplitude to a digital value and the digital values from the present sample and previous sample used to determine a digital)V value.

The)V values represent the change in amplitude over the sampling period. Several consecutive)V values can be evaluated to confirm the sustained slope characteristic of inspiration onset or offset as described further below with reference to the detection algorithm. By using several, for example, two or more, consecutive)V samples, short duration (higher frequency) noise or cardiac artifacts can be rejected and thus misdetection of a valid onset or offset is avoided. The tradeoff for considering more than one sample is that delay is added by waiting to use multiple samples for detection of an onset or offset.

As an alternative to using digital)Vs for representation of slope of the respiratory waveform to the detection algorithm 216, an analog differentiator and peak detector could be utilized for slope measurement. However, the availability of the)V's in the digital domain allows for precise threshold settings and variation in bandwidth by choosing the number of samples to evaluate.

A second embodiment of signal processing circuitry 400 for performing the signal processing with substantially equivalent results to signal processing circuitry 200 is shown in Fig. 12b. The sensor input circuitry, including the sensor bias 402, low pass filter 404, and AGC amplifier 406, is substantially the

same as previously described with respect to the first embodiment. However, the monitoring circuitry 203, as indicated by the dashed line in Figure 12a, is performed with the use of a microprocessor 410 and associated code. The microprocessor 400 includes an internal analog to digital convertor (ADC) 414 which presents a converted sampled amplitude to the algorithm/control logic 416 and comparator 412, i.e. the logic and comparison are implemented in software. In this embodiment,)V=s are still determined based on the sampled signal from the AGC amplifier representative of slope of the respiratory effort waveform, and sampled amplitude comparisons are still made with the various thresholds. However, the sampled amplitude of the respiratory effort signal is immediately converted to the digital domain by the ADC 414 and processed digitally by the algorithm to obtain the)V=s. Further, the digitally converted sampled amplitude is digitally compared to digital thresholds 420, 424, 430, and 428 as necessary to carry out the functions as described further below. The algorithm 416 then processes the)V, i.e. slope, information which it generated, and the amplitude comparison information generated by digital comparison 412, as described further below. Also as described further below, the processor 400 can be powered down at certain times when it is not required; conserving energy. Although both the first and second embodiment may be utilized in accordance with the present invention, along with various other configurations of digital or analog circuits, whether with the use of a processor or without, the remainder of the description shall be made with reference to Fig. 12a for simplification, except as otherwise noted and for specific features which are particularly beneficial to the processor based configuration, such as processor power down.

The detection algorithm as shown in the flow diagrams of Figs. 13a-13h shall now be described with reference thereto and with reference to other figures herein as required. The detection algorithm or algorithm logic 216 as shown in Fig. 12a resides in the IPG 55 of the implantable system 50 shown in Fig. 5. The detection algorithm 216 detects inspiration onset and offset using comparisons of sampled amplitude to multiple thresholds and)V values representative of the slope of the respiratory effort signal. As described previously

with reference to Fig. 12a, in the first embodiment, the digital outputs used by detection algorithm 216 to track the respiratory effort waveform, are the onset and offset amplitude threshold comparison outputs from the analog comparator 212 and the digital)V slope value output from the ADC 214 (Fig. 12a). With respect to the second embodiment utilizing the microprocessor and associated code, the digital comparison of the digitally converted sampled amplitude to the various digital thresholds along with the)V values generated using the digitally converted sampled amplitude, all generated inside the microprocessor, are utilized by the processor control logic algorithm 416. This respiratory effort signal information concerning amplitude and slope and the knowledge of respiratory timing parameters during sleep are used by the algorithm to reject cardiac and motion artifacts and control stimulus of muscle in the treatment of sleep apnea.

A top level flow diagram of the detection algorithm/control logic 216 is shown in Fig. 13a. Generally, the detection algorithm is initiated at IPG-ON (block 600). The sensor signal is then sampled (block 610) at a programmed sample rate and the appropriate outputs (i.e.)V=s and analog threshold outputs) are generated by the associated components of the system. Offset detection (block 620) and onset detection (block 700) are then performed, with offset detection taking precedence over onset detection. If neither offset nor onset is detected then the sensor signal is further sampled and offset and onset detection repeated. If offset is detected, then various functions are performed such as determining whether suspension mode is to be entered, therapy delayed, or AGC updated (blocks 640, 680). If onset is detected (block 700), then stimulation is initiated (block 720). The stimulation is continued and the sensor sampled during stimulation (blocks 730) until an offset is detected (block 740) and stimulation is terminated (block 760). The various functions performed after an offset is detected (blocks 640, 680) are then performed.

The IPG ON command block 600 is a patient or physician controlled function, where he/she turns the IPG "ON" via the patient programmer 70 or physician programmer 80. The IPG 55 recognizes the IPG ON command (block 602) and begins a start-up sequence including dose control timer (block 603), a

dose delay (block 604), a setting of initial conditions 606, and the entrance of suspension mode until a regular breathing pattern is recognized. The IPG ON command may also initiate a patient self stimulation test and/or a diagnostic self test, as described further below.

Dose control timer (block 603) is immediately started by the on command, i.e., IPG-ON state. Dose is considered the treatment time over which the IPG 55 is on and stimulation synchronous with inspiration can occur as the patient sleeps. A patient typically uses the system 50 during a regular night=s sleep. A patient may sleep anywhere from, for example, 1 to 15 hours. The dose period is initiated by the patient programmer 70 or a physician programmer 80 transmitting an IPG-ON command to the IPG. Dose is terminated or dose timer timeout occurs by either reaching a maximum programmed dose time or the patient programmer 70 transmits an IPG-OFF command, i.e. IPG-OFF state. The dose time-out provides an automated method for turning off stimulation in the morning after a night=s sleep. The maximum dose time is physician programmable and may be for example, from 1 hour to 15 hours in 1 hour increments.

The initial IPG-ON command also initiates the dose delay period (block 604). The delay waits a sufficient amount of time before starting stimulation to allow the patient time to fall asleep. Dose delay 604 is physician programmable from, for example, 0 to 75 minutes, in 5 minute increments. If stimulation were to start too soon, the patient may be disturbed and may have difficulty sleeping. The detection algorithm does not operate during dose delay 604 and minimal battery power is consumed during this delay period, for example, in a microprocessor based design, the microprocessor could be powered down.

At the end of the dose delay (block 604), the detection algorithm parameters are initialized (or reset). The initial conditions include: Onset Count = 0, Offset Count = 0, Artifact Count = 0, Average Respiratory Period Weighted Sum (TWS) = 1 second, Max Stimulation On Timer = OFF. In addition, the start AGC watchdog timeout timer as described further below is initialized to 1 second and AGC gain is initialized to a mid-gain setting as described further below. After initialization of the conditions (block 606), as indicated above, stimulus is

indefinitely suspended, i.e. suspension mode is entered, until a regular breathing pattern is recognized (block 608).

Generally as will be explained further below, in suspension mode, stimulation is disabled in the presence of artifacts or non-periodic respiration. Suspension is defined as a state where stimulation is suspended due to the lack of a stable respiratory pattern. If the present measured respiratory period (T) is not within a specified minimum and maximum time or if it is not relatively equivalent, i.e. within a certain tolerance (Tvar) of, a stored weighted sum respiratory period (TWS), then stimulus is suspended or suspension mode is entered. The detection algorithm does not exit suspension mode until a measured respiratory period (T) is within the allowed variability from the weighted sum respiratory period (TWS).

As shown in Fig. 13a, during the sampling of the sensor 60 (block 610), the detection algorithm looks for a valid onset so that stimulation can be initiated (block 720). The onset of inspiration is characterized as a sustained increase in slope greater than a physician programmable)V onset threshold value and an amplitude greater than a physician programmable analog onset threshold as shown in Figure 14. An offset detection takes precedence over onset detection, as reflected by Offset Latched & Analog Vref block 622 (Fig. 13c).

As shown in block 700 of Fig. 13c, two consecutive)V's greater than the physician programmed)V onset threshold value are required to indicate a sustained increase in slope. The comparison of sampled)V=s to the)V onset threshold is shown as block 704. The time required to obtain the two samples, for example, may be between 40 ms and 80 ms, depending on the sampling rate; the stimulus rate and sampling rate being the same. The stimulus rate is programmed or fixed by the physician and the)V onset threshold can be adjusted at the same time to compensate for shorter or longer sampling rates. For example, a faster stimulus/sampling rate would result in smaller)V's since less change is seen over the shorter sampling period. Thus, a lower)V onset threshold may be appropriate.

As shown in block 704, if a)V does not exceed the)V onset threshold, the onset counter for counting the number of times the)V onset threshold is exceeded is reset. If the)V onset threshold is exceeded, it is determined whether the stimulation has been suspended (block 706). Although a valid)V onset threshold level was detected, if the IPG 55 is in suspension mode, the onset counter is not incremented. Further sampling and comparisons are then performed to detect offsets. The offsets are detected to determine if a stable respiratory signal is present. If the IPG is not in suspension mode then it is checked to see whether the IPG is in refractory, i.e., a period of time between offset declaration and onset as described further below. Refractory (R), as shown in Fig. 14, includes both a hard refractory (HR) and a soft refractory (SR), i.e. a final portion of refractory (R). Refractory (R) is a processed time, based on a preprogrammed percentage of measured patient respiratory periods (T), during which time the patient is typically denied access to stimulation, except possibly in soft refractory.

As shown in block 708, if the IPG is in refractory (R), then it is checked to see whether it is in hard refractory (HR) or soft refractory (SR) (block 710). If the IPG 55 is in hard refractory (HR), the onset counter is not incremented and more)V comparisons are made. If the respiratory effort signal is in soft refractory (SR), then the amplitude of the signal is compared to the programmed analog amplitude onset threshold (block 714). If the signal does not exceed the analog onset threshold, the onset counter is not incremented but rather reset to zero and sampling is continued. If the signal exceeds the analog onset threshold, then the onset counter is incremented (block 716). Also as shown by blocks 708 and 712, if the)V onset threshold is exceeded and the IPG is not in the refractory period, then the onset counter is also incremented (block 712). If the onset counter is equal to a count of two, a valid onset is declared (block 716), the counter is reset to zero, a stimulation timer is initiated for controlling the maximum stimulation length (block 718) as described further below, and stimulation is initiated (block 720).

The illustrative 200 ms onset previously described is obtainable, particularly by adjusting the programmable)V and analog amplitude onset thresholds along with refractory (R) and soft refractory (SR) discussed further

below. By such adjustment, the algorithm can be made to be >trigger happy= or predictive such that onset detection is not late and the refractory (R) is maximized to save battery life. For example, with use of the soft refractory period, the analog threshold may be set lower to allow a lower signal to exceed the threshold and increment the onset counter. This still, however, blocks motion artifacts from being detected as an onset is detected only if both slope and amplitude thresholds are exceeded during soft refractory, as opposed to just slope out of refractory (R).

Generally, to declare an onset and thus start stimulation, in addition to the)V onset threshold being exceeded by two consecutive samples, the algorithm must be out of refractory (R) during the two consecutive)V samples above threshold or the pressure signal amplitude must be greater than the analog amplitude onset threshold and the algorithm must be in soft refractory (SR). Further, the algorithm must be out of dose delay, therapy delay, and suspension for stimulation to occur.

It should be apparent to one skilled in the art, that variations of onset detection may provide suitable detection. For example, the number of counts may vary, the sampling rate may vary, more)V values may be used alone to detect onset in soft refractory as opposed to the use of both)V and amplitude information in soft refractory and other variation as would be readily apparent to one skilled in the art.

During stimulation, the sensor signal is still being sampled (block 730). Offset detection (block 740) is being performed using the sampled signal during stimulation (block 740). If an offset is detected and latched while stimulation is on, stimulation is terminated (block 760) when the latched offset is validated or declared a valid offset. If offset is not detected, stimulation proceeds until a maximum stimulation period is reached as timed by max-stimulation on timer (block 718), at which time an offset is automatically declared.

Therefore, maximum stimulation time is used in the event that an offset of the inspiratory phase is not detected. A maximum stimulation time shall terminate the stimulation and algorithm functions which typically occur at a regularly detected and validated offset are initiated. In other words, if maximum stimulation time is reached, an offset is declared and functions such as calculating

weighted sum, starting refractory, etc. are initiated. When an offset is detected and latched (block 740) and stimulation is terminated (block 760) after the latched offset is validated, the algorithm proceeds to suspension, artifact, therapy delay block 640 as will be described further below.

The detection and declaration of an offset during stimulation (block 740) and when stimulation is off (block 620) shall be described together, as the flow of both blocks is substantially similar with the exceptions as noted. Such description shall be set forth with reference to Figs. 13d and 13e.

Inspiration offset is the most reliable and repeatable signal characteristic to detect as the respiratory waveform slope changes from a positive slope to a sharp negative slope and the amplitude of the respiratory waveform signal reaches a peak value which is controlled by the AGC, for example, the 1.2 volts. Therefore, detection algorithm operation and timing is centered around the detection of offsets, although other periodic events in the respiratory signal may also be used

Respiration timing, AGC control, and the accuracy, for example, of the prediction of the next onset are all dependent on offset detection. Generally, the detection of offset requires three consecutive)V samples below the physician programmed)V offset threshold 526 (Figure 14) and the first of the three)V samples is required to have an amplitude greater than the analog amplitude offset threshold 524 (Figure 14). Once these requirements are achieved, an offset is detected and latched. The algorithm then waits for the respiratory effort signal level to fall below the Vref or zero crossing threshold 530 before validating the latched offset, i.e. declaring a valid offset and terminating stimulation. Waiting for the signal to fall below the Vref threshold 530 discriminates against cardiac artifacts riding on the signal, which may cause another offset to be prematurely detected. Alternatively, the offset could also be validated at any amplitude after the offset requirements are met, such as for example, onset threshold or even immediately upon latching the offset.

With reference to the flow diagram of Fig. 13d, as the sensor signal is sampled during stimulation (block 730), if an offset has not been declared or validated (block 742) and the maximum stimulation on time for stimulation has not

been reached (block 744), a comparison of)V samples to the programmed)V offset threshold 526 is performed (block 746). If the programmed)V offset threshold is not met, then the algorithm resets the offset counter to zero and sample and comparison continues. If the programmed)V offset threshold is met, then the state of the offset counter is queried (block 748). If the offset count is at zero and the analog respiratory effort signal is not greater than the analog offset threshold to produce a first offset count (block 750), then the offset counter is reset to zero, the offset counter is not incremented and sampling and comparison is continued to detect an offset. If the offset count is equal to zero and the analog respiratory signal is greater than the analog offset threshold, then a first count is made (block 752). If the offset count is not equal to zero (i.e., a first offset count has been made), then such consecutive)V samples that meet the)V offset threshold increment the offset counter (block 752). If the counter registers three consecutive counts during three consecutive sample periods (block 754) with the first offset crossing the analog offset threshold 524, an offset is detected and latched. Once the amplitude falls below Vref (block 742) the latched offset is validated and stimulus is terminated. If the three consecutive offset count requirement is not met, then the offset counter is reset, and sampling and comparison is continued for detecting offsets.

The offset declared or validated is then processed further by Suspension, Artifact, Therapy Delay block 640 and an offset hysteresis timer is started (block 758). Offset hysteresis is utilized to prevent artifacts from declaring two offsets in a very short period of time. For example, if the offset slope was too shallow, multiple offsets could be triggered by artifacts in the signal waveform (e.g., if 6 consecutive)V=s satisfied the)V offset threshold and the analog offset threshold was met for at least the first of each set of three, then two offsets could be declared). Therefore, offset hysteresis provides a blanking period, for example, about 475 ms, after an offset has been declared during which no other offset can be declared. The blanking period is to provide a form of hysteresis such that the algorithm will only >see= one offset per respiratory cycle. The offset hysteresis should be sufficiently short to resume the detection of possible artifact signals for proper suspension mode and artifact counting operation.

Various alternatives to the offset detection portion of the algorithm can be made. For example, the number of counts necessary for an offset to be detected may be modified, the analog threshold may be required to be satisfied for all three)V samples as opposed to just one, the sampling rate may be different, different levels of analog thresholds may be used for declaration or validation of an offset to terminate stimulus and any other variation may be made that would be apparent to one skilled in the art.

The offset detection when stimulation is off (block 620) is substantially the same as described above with the exception that maximum stimulation on time does not need to be checked (block 744) as stimulation is off.

As mentioned previously, the detection algorithm/control logic 216 uses at least two ideologies including that the respiratory period (T) of respiration is known to be stable and consistent during sleep and that the ratio of the time of inspiration (TI) to the respiratory period (T) is typically known or can be evaluated with statistical measures. The detection algorithm 216 uses at least these two ideologies and also respiratory timing statistics of sleeping humans to make the algorithm robust and exclusionary of misdetecting artifacts for onset and offset. As part of implementing the ideologies, the weighted sum respiratory period (TWS) is used to build a running average of measured patient respiration periods (T) and is utilized in connection with various algorithm functions to control stimulation and reject artifacts. The various functions which employ the use of TWS include refractory (R)/soft refractory (SR) function, suspension function, AGC control, and the artifact counter function. After a general discussion of the these functions, the suspension function, AGC control and artifact counter function will be described further with reference to the flow diagram of Fig. 13f and 13g. The use of refractory (R)/soft refractory (SR) function has been previously described with reference to the flow diagram for onset detection (Fig. 13c).

The detection algorithm 216 evaluates the equivalence of every patient respiration period (T) by comparison of measured periods (T) to the continuously calculated weighted sum respiratory period (TWS) and to bounds for a respiratory period to evaluate whether respiration is stable. The detection algorithm

having knowledge of the weighted sum respiratory period (TWS) and a substantially constant inspiration time (TI), also approximates the time between each offset and onset such that onsets can be predicted.

The geometric-series weighted sum used to generate the weighted sum respiratory average (T) is weighted more heavily by the most current measured T periods. The algorithm adds the present weighted sum to the present T period and then divides by 2. The result is expressed in the following equation: T Weighted Sum (n) = [T Weighted Sum (n-1) + T Interval (n)] / 2. The maximum number of T periods contained in one sum is ten, but the T periods beyond the fifth have an insignificant contribution to the sum. Not all measured T periods are utilized in determining TWS. The algorithm measures the patient respiratory period (T) at each offset. If T falls out of the predetermined bounds set for T, i.e. Tmin and Tmax, for example, in the range of 1 second to 16 seconds, indicating nonperiodic respiration, then the algorithm will consider the T period invalid. The invalid T periods are not added to the weighted sum (TWS).

With the weighted sum average respiratory period (TWS) calculated, the refractory period (R) can be approximated as described below. Onsets (and thus stimulation) can be kept from occurring for a period of time in the refractory period (R) following the declaration of offset of inspiration. This time frame is in the expiration phase of respiration. Any physiologic or sensor disturbances (artifacts, noise, etc.) during this time period can be rejected as onsets. Stimulation is thus inhibited during at least a portion of refractory (R), but sampling continues in order to detect the presence of artifacts and enter suspension mode, if necessary.

The refractory period (R) begins at the offset of inspiration (i.e. the end of stimulus) and continues almost until when the next inspiration onset is expected. A percentage of the weighted sum (TWS) is used to calculate the refractory (R) duration. For example, with TI/T ranges known from, for example, statistical analysis, the expiration portion of respiration and thus the refractory period (R) can be calculated as a fraction of the weighted sum (TWS). For example, the calculated refractory period (R) may be implemented based on the weighted sum by multiplying a physician programmable refractory multiplier of

0.375, 0.50, 62.5, or 0.75 times the weighted sum: refractory (R) = (Refractory Multiplier x Respiratory Period Weighted Sum (TWS)). Such particular refractory multipliers are for illustration only and any portion of T may be designated as refractory, such as from 0.1 to 0.75, particularly depending upon the individual patient=s respiratory cycle.

The weighted sum respiratory period (TWS) is initialized upon the on command for the IPG 55 to be 1 second. The algorithm remains in suspension mode as described further below until the TWS is equivalent to the present measured T, i.e. periodic respiration is determined. The algorithm does not use refractory (R) to blank onsets until suspension mode is exited. This insures that the weighted sum (TWS) will have established a valid value and thus the refractory (R) will also be a valid duration for predicting onsets and blanking artifacts.

Refractory (R) is limited to a minimum time. This is achieved by only updating the weighted sum (TWS) for T periods greater than 1 second and therefore the weighted sum (TWS) has a minimum of 1 second. As such the refractory (R) minimum time is given by: Minimum Refractory = (Refractory Multiplier x 1 second). The establishment of a minimum refractory time is a safety guard against over stimulation by establishing some minimum of blanking time.

Soft refractory (SR) is implemented in the final portion of the refractory period (R). The other portion of refractory (R) is referred to as hard refractory (HR) and is shown in Fig. 14. In hard refractory (HR), stimulation is not allowed, i.e. onsets are not responded to. In the soft refractory (SR) period of refractory (R), as shown in Fig. 14, an onset (i.e. stimulation) is allowed if the analog onset threshold and the)V comparison as described with reference to Fig. 13c both indicate an onset. The soft refractory (SR) portion of refractory period (R) may be a fraction of, for example, 12.5 % of the weighted sum (TWS). Therefore, for illustration, if refractory (R) is 75% of the weighted sum, then the soft refractory (SR) is during the 62.5% to 75% portion of refractory (R).

Alternatively, the soft refractory (SR) could be a function or percentage of refractory (R). Further, the refractory functions may be based on stimulus duration as opposed to respiratory rate. With this alternative, the

algorithm would measure the duration of the previous stimulus interval and multiply the interval by a predetermined value. A further alternative for refractory could be based on both stimulus duration and the respiratory period (T) or any other alternative respiratory timing parameter that would be suitable for defining a refractory, hard refractory, and/or soft refractory period following offset detection, such as TI.

Suspension mode, which also utilizes TWS, provides several benefits. For example, the suspension function keeps the patient from being overly stimulated, i.e. patient comfort. Further, this technique also conserves energy to increase battery life. In suspension mode, stimulation is disabled in the presence of artifacts or non-periodic respiration. Suspension is defined as a state where stimulation is suspended due to the lack of a stable respiratory pattern. If the present measured patient respiratory period (T) is not within a specified minimum and maximum time or if it is not relatively equivalent to, i.e. within an allowed variability of, a stored weighted sum respiratory period (TWS), then stimulus is suspended, i.e. suspension mode is entered. The detection algorithm does not exit suspension mode until a measured patient respiratory period (T) is within the allowed variability from the weighted sum respiratory period (TWS) . The programmable values of allowed T variability (hereafter referred to as Tvar) may be for example, 25 %, 33 %, 50 %, and infinite. Each and every offset is considered as a measure of the respiratory period (T) and/or the presence of artifacts. While in suspension mode, the algorithm continues all other signal processing tasks such as threshold comparisons, AGC adjustments, and weighted sum calculations.

Generally, suspension is entered by the algorithm under the following conditions indicative of nonperiodic respiration. First, upon initialization of the IPG 55, the algorithm is in the suspension state, as shown in Fig. 13b, block 608, after the IPG 55 is turned ON and dose delay (block 604) is completed. Second, if the presently measured respiratory period (T) is less than the minimum or greater than the maximum bounds programmed for T, suspension mode is entered, i.e. the bounds of 1 second and 16 seconds as previously mentioned. Third, if the present respiratory period (T) is not within a programmed allowed variability, i.e. Tvar,

suspension mode is entered. And last, suspension is entered after the completion of a therapy delay initiated with use of the artifact counter as described below. It should be readily apparent to one skilled in the art that the number of respiratory violations of, for example, Tmin, Tmax or Tvar, which are required for suspension mode to be entered may vary. For example, more than one violation may be required to enter suspension.

The above described suspension mode technique disables stimulus in the presence of physiologic artifacts such as arm movements and head movements. Such movements occur only when the patient is in shallow sleep or awake. An example of the benefit of suspension mode is the case of a sleeping patient awakening to a phone call. Suspension mode will be entered as the patient moves about and stimulation will be inhibited while the patient speaks on the phone. Suspension mode is also intended to disable stimulus in the presence of non-physiologic and environmental noise sources. During suspension mode, the algorithm continues to evaluate the signal and will exit suspension mode and return to stimulus as soon as a periodic respiratory signal is re-established. Therefore, only the prevention of stimulus conserves energy as the sensor must still be operated.

As mentioned above, an artifact counter is used to initiate a therapy delay during which time stimulation is disabled. This is technique also conserves energy, lengthens battery life, and rejects artifacts. If the respiratory waveform continues to be too variable or multiple motion artifacts are occurring while in suspension mode, then the artifact counter will cause the algorithm to enter therapy delay. While in suspension mode, the number of offsets are counted by the artifact counter, in which case an offset is defined as the falling peak of either a respiratory or artifact event. If a maximum number of offsets are counted during suspension mode, then the algorithm enters a therapy delay period. The maximum artifact count is physician programmable, for example, to 10, 20, 40, or 80. During therapy delay, initiated by the artifact counter, the algorithm does not process the respiratory waveform signal and therefore, energy is conserved by turning the pressure sensor off and by preventing stimulation. Upon completion of the therapy

delay period, the algorithm resets to an initial state (AGC gain and weighted sum reset, etc.) like when the IPG 55 was first turned on. Sampling the signal in the suspension mode is then resumed.

The counting of offsets during suspension mode is a simple method for determining the extent of non-respiratory activity. If frequent offsets are occurring, then this indicates that extensive movement exists and the algorithm shall transition quickly into therapy delay. If suspension mode occurs due to a short duration event, the offset artifact count will not reach the maximum, and stimulus will resume after the steady respiration rate has been re-established. If suspension mode is maintained by a variable respiratory rate, the offset artifact count will eventually lead to a maximum artifact count and therapy delay from counting of offsets. It should be noted that the artifact count is reset to zero upon exiting suspension mode.

The artifact counter function also provides the patient a method to quickly terminate stimulation without the use of the patient programmer 70. This is accomplished by tapping in the proximity of the pressure sensor to induce artifact counts. Such tapping allows the patient to terminate stimulus for the duration of therapy delay in the event that the patient programmer 70 is lost or fails during the night. Such termination could also be accomplished by use of a magnet being passed over a reedswitch built into the IPG 55.

Offset hysteresis, as previously described, is also used to conserve energy, as during this period of time the sensor can be shut down. Further, although some functions described herein may depend on the sensor functioning during refractory, with some modifications to the algorithm, the sensor may also be shut down during refractory, particularly hard refractory, as stimulation is prohibited. Thus, energy can also be conserved by shutting down the sensor whenever the respiratory waveform is not needed by the remainder of the system.

With reference to Fig. 13f, the flow of the suspension and artifact counting techniques in the detection algorithm shall be described. If offset is detected while stimulation is off (block 620), then it is determined whether the algorithm is in suspension as described above. If the unit is in suspension mode,

artifacts (i.e. offsets, both inspiratory and artifact) are counted to determine if the algorithm should go into therapy delay (block 644). If the count exceeds some predetermined number, such as, for example, 16 counts, then the artifact counter is reset to zero, suspension mode is exited and activation of programmed therapy delay is entered (block 666). The therapy delay time is also started upon receiving the IPG on command during either an already occurring therapy delay (block 666) or dose delay (block 604) (Fig. 13b). After the therapy delay is exited, the initial conditions are set, substantially the same as when the IPG is turned on with the patient programmer (Fig. 13b).

If an offset has been detected either during stimulation or when stimulation is off, respiratory period (T) is measured (i.e. offset-to-offset or the time from the last offset to the current offset) (block 648). The current measured respiratory period (T) is then compared to Tmin and Tmax (block 650). If the current respiratory period (T) is not greater than Tmin and less than Tmax, then refractory (R) is started (block 652) based on a percentage of the previous weighted sum respiratory period (TWS). Further, if three consecutive current respiratory periods (T) measured do not meet these requirements, then the algorithm goes into suspension mode and stimulation is not allowed, otherwise, artifact counter is reset to zero and suspension mode is exited.

If the current respiratory period (T) is greater than Tmin and less than Tmax, then the current measured respiratory period (T) is added to the weighted sum average respiratory period and a weighted sum (TWS) of the previous breaths is calculated to determine a new average weighted sum respiratory period (block 654). Refractory is started (block 652) based on a percentage of the new average weighted sum, as updated. Further, the current respiratory period (T) measured is compared to the weighted sum from the previous offsets (i.e. the old weighted sum prior to the addition of the current T) (block 656). If the current T is equivalent, i.e. meets Tvar, indicating periodic respiration, then the artifact counter is reset to zero and suspension mode is exited. Otherwise, it is once again determined if three current respiratory periods (T) measured do not meet the Tmin, Tmax and Tvar requirements (block 658). As before, if three consecutive T=s do

not meet the Tmin, Tmax, and Tvar requirements, then the algorithm goes into the suspension mode or suspension mode is continued (block 670) and stimulation is not allowed, otherwise, artifact counter is reset to zero and suspension mode is exited (block 662).

The number of consecutive out of tolerance T=s necessary to enter suspension mode is programmable. For example, the number can be set at one or other suitable values. Further, Tvar can be set to infinity which overrides the suspension feature and suspension is never entered.

In either case, whether suspension mode is entered or exited, the automatic gain control (AGC) is continually utilized or adjusted (block 680) as shall be described with reference to Fig. 13g. However AGC is not operational during treatment delays, i.e. dose delay or therapy delay, as the pressure sensor need not be operated during this delay time, conserving battery life. The AGC control described herein is applicable to the provision of any signal characteristic of a periodic physiological parameter for use in a therapy system. For example, the normalization provided by the AGC control is particularly applicable to systems which perform functions based on comparing the signal to the thresholds.

The AGC amplifier 206 (Fig. 12a), as described previously, is required to normalize the pressure sensor output to a consistent peak to peak signal, for example, 2.4 volt peak-to-peak signal. The operation of the AGC for the system 50 is dependent on the detection algorithm for synchronizing gain increment and decrements. The AGC consists of a plurality of gain steps, for example, 64 gains steps. Gain is incremented exponentially such that each gain step increases by the same percentage, for example, about 5.3 %. However, gain may be performed by other than exponential techniques, such as, for example, techniques that produce equivalent increases as opposed to equivalent percentage increases.

Generally, the AGC functions in the following manner. The gain is incremented or decremented once per respiratory period (T). The AGC gain is changed immediately following detection of a periodic event in the waveform, i.e. a >true= offset. True offset is defined here so as to indicate those offsets which are likely to be from an actual, stable inspiration offset and not a motion artifact or

irregular breathing. The algorithm determines an offset is true if it does not occur during refractory (R) (including both soft refractory and hard refractory), as during refractory (R) it is assumed that the offset is an artifact offset. Offsets resulting in a respiratory period (T) outside of the predetermined bounds set for the periods, such as, for example, less than 1 second or greater than 16 seconds, are also considered invalid.

It is desirable to not change gain during refractory as the offsets which occur in this period may be of large amplitude, due to a motion artifact, and gain may be unnecessarily updated. Also, the refractory sets a limit on how fast the gain can be changed. Thus, if a rapid burst of artifacts occurs during refractory (R) then there will be no rapid change in gain. If a burst of artifacts occurs while the algorithm is not in refractory (R), then the first artifact will be considered an offset and subsequent artifacts will not change the gain as they will be in refractory (R). Thus, rapid offsets can only change the gain once during a respiratory cycle, i.e. increment or decrement once. AGC control is performed during suspension mode, along with offset detection and refractory, as only stimulus is inhibited and an exceeding of the artifact counter results in a therapy delay while in suspension mode.

An AGC watchdog timer also forms a part of AGC control. The AGC watchdog timer is reset each time a valid offset occurs resulting in the AGC gain being updated. The watchdog timer will otherwise time-out at, for example, 1.5 times the respiratory period weighted sum (TWS) or in other words, the watchdog timer time-outs at 50 % beyond the point where an offset is expected. At time-out an AGC threshold is used to determine if the AGC gain should be incremented or decremented by one step. The watchdog timer will continue to time-out and increment or decrement until offsets begin occurring. The offsets then take control of the AGC operation. Therefore, the watchdog timer gets the gain to a level such that offsets can be detected and normal AGC control via offsets can be established, particularly when the IPG 55 is first turned on.

The AGC is initialized to a mid-range setting. If this initial gain is too low, the watchdog timer may have to cycle several times before offsets begin to occur and equilibrium is reached. The watchdog timer is loaded with a predetermined time, for example, 1 second at the initialization of the algorithm. Thus, the gain will increment one step per second until offsets are achieved, unless the initialized gain is too high, in which case each offset and/or the watchdog timer will decrement the gain until equilibrium is reached. The AGC is reset or reinitialized at each exit of therapy delay or dose delay.

Generally, therefore, gain is updated when an offset is detected following onset, even while in suspension mode or gain is updated when a watchdog time out occurs if an offset is not detected within a predetermined period of time. However, offsets detected while in refractory (R), whether or not in suspension mode, do not initiate gain update. Further, since offsets are not even looked for in dose delay or therapy delay, AGC is not updated during this time period. Typically, after initialization, the gain is incremented with use of the watchdog timer until valid offsets can be detected. Thereafter, the AGC typically controls the gain by toggling between increments and decrements to keep the gain at a particular level, i.e. the AGC threshold 528 (Fig. 14) and the waveform is normalized.

The flow of AGC control 680 is shown in Fig. 13g. AGC is run virtually simultaneously with the determination after an offset is detected of whether the algorithm should be in suspension or not as described previously with reference to Fig. 13f. As such, block 650 (Figs. 13f and 13g) appears in both flow diagrams. AGC is not performed until the current measured respiratory period (T) meets the requirements of being greater than Tmin and less than Tmax (block 650), i.e. a somewhat stable periodic signal is sensed. Further, AGC update is performed if Tvar is set to infinity (block 650), regardless of the Tmin and Tmax requirements, i.e. if Tvar is set to infinity then all requirements for T are disabled for suspension and AGC functions. If the gain is not updated the sensor is continued to be sampled (block 610) and offset and onset detection is performed (blocks 620 and 700). If such requirements are met, then it is determined whether the algorithm is in refractory (R). If the algorithm is in refractory (R), then the gain is not updated

(block 684). If the algorithm is not in refractory, then gain is either incremented or decremented based on a comparison with a predetermined AGC amplitude threshold (Fig. 14) (blocks 686 and 690). If the amplitude of the respiratory effort signal is less than the AGC threshold at any time since the previous update, then gain is incremented at, for example, offset, watchdog timeout or any other periodic event in the respiratory cycle. If the amplitude of the signal is greater than the threshold at any time since the previous update, then the gain is decremented at offset, watchdog timeout or any other defined periodic event in the cycle. The watch dog timer is reset at each and every AGC increment or decrement. However, at any time when no offsets are detected in a specified period of time, then the gain is incremented or decremented using the watchdog timer, i.e. a time based on the weighted sum respiratory period (block 692).

Generally, therefore, for a signal characteristic of a periodic physiological parameter, such as respiration, which include multiple periodic cycles, gain is updated when a periodic event is detected. The gain, however, is updated only once during a periodic cycle. Further, a watchdog timeout occurs if the periodic event is not detected and gain is updated even though a periodic event is not detected. Thus, the gain will be adjusted once per periodic cycle upon detection of a periodic event or at a watchdog timeout.

Other alternative methods of AGC implementation may be utilized with the present invention. For example, the AGC may adjust the amplifier gain after each amplitude sample has been taken. The magnitude of the sample would then be processed digitally to adjust the gain such that the amplifiers operate in mid-dynamic range. This technique has the advantage of quick gain adjustments and continuous digital knowledge of the signal amplitude. However, the AGC would not provide normalization and thus relative threshold measurements are not possible.

In general, the algorithm must be in the following state for stimulation to occur. A valid onset consisting of a certain number of)V=s, for example, two)V=s, above)V onset threshold must be detected. The refractory period (R) must be complete or the analog onset threshold must be crossed if the

algorithm is in soft refractory (SR). The algorithm must not be in suspension mode and the algorithm must not be in either dose delay or therapy delay.

Further, any one of the following events will terminate stimulation: a predetermined consecutive number of)V=s, for example, three consecutive)V=s, below)V offset threshold with the first)V sample below the)V offset threshold satisfying the analog offset threshold (the offset must also be validated by comparison to another threshold level such as zero crossing); maximum stimulation time is reached; a patient initiates therapy delay by giving another IPG on command when treatment is on; end of the dose timer period after a night=s sleep; and an IPG-OFF command.

Moreover, in general, implantable stimulation system 50, operates in the following manner. At some point following the IPG 55 implant, the patient will undergo a sleep laboratory evaluation where algorithm parameters, such as those programmable parameters described herein (onset and offset thresholds, refractory, dose times, etc.) are optimized to achieve proper stimulation for the individual patient. The stimulation parameters (amplitude, rate, and pulse width) are also adjusted to achieve the muscle stimulation necessary to overcome respiratory obstructions. After being programmed by the physician, the patient is provided with a hand-held patient programmer 70 which is primarily used to turn the IPG ON and OFF each evening and morning, respectively. The patient programmer 70 also may provide the patient with display indications regarding system information such as battery life warnings, failed stimulus components, etc., and further may be used to automatically initiate other diagnostic and stimulation testing as described further below. The implanted stimulation system 50, upon initialization of treatment, then utilizes the sensed respiration effort waveform to detect critical points in the waveform to provide inspiration synchronous stimulation for treating respiratory disorder in accordance with the algorithm as described above.

The system 50 can also be used for patients with central apnea, or patients whose central nervous system provides no drive to breath. Central apneas often occur in obstructive sleep apnea patients in what are call mixed apneas. To ensure effective therapy, the patient must be stimulated over the first breaths

following the central apnea, in order to prevent obstructive apneas. Patients with such conditions generate a respiratory effort waveform somewhat as shown in Fig. 16b or Fig. 16c as compared to a normal respiratory waveform (Fig. 16a). Because of the relative flatness of the waveform, offset and onset detection is difficult and almost unusable for providing stimulation to treat the upper airway condition. However, the detection algorithm can be adjusted to continue stimulation asynchronously when the signal amplitude becomes small. By making the)V and analog onset thresholds sensitive to flat sensor signals, stimulation can be maintained for such a patient. Although offsets are not detected, the maximum stimulation time can be used to terminate stimulation. Further, stimulation occurs, i.e., turns on, either at the end of hard refractory (HR) or refractory (R). The average respiratory period weighted sum (TWS) is approximately maintained by the repetitive stimulation occurring based on the maximum stimulation time and asynchronous stimulation will continue until the patient=s periodic respiration returns. Further, the maximum stimulation time can be adjusted to forego overstimulation.

A central sleep apnea is shown in Fig. 16c. For example, the central sleep apnea 802 may occur over a time period of 5 seconds to 30 seconds. As shown in Fig. 16d, stimulation is synchronized to inspiration during the first and second cycles of respiration prior to central apnea occurring. Stimulation, in accordance with the present invention, then occurs for the maximum stimulation time 804 as offset is not detected during central apnea. The offset is then due to maximum stimulation time being reached. Refractory then occurs after the maximum stimulation time, during which time no stimulation is allowed. This particular refractory period 806 is shown by the time period between the two maximum stimulation times during the central sleep apnea. During this time, i.e. central sleep apnea, the AGC is operating by means of the watchdog timer and/or the maximum stimulation time offsets which update gain when no inspiration offsets are detected for a particular period of time. This operation of the AGC, increases the signal amplitude, and allows the algorithm to detect an onset with use of a smaller amplitude respiratory signal. Once a first onset is detected (or offset) then

stimulation can be continued synchronous with inspiration as opposed to stimulating based on maximum period of stimulation and refractory. This ability to increase gain to detect offsets or onsets of a smaller respiratory signal is important because the first breaths 800, Fig. 16c after central apnea are typically shallow (low effort) and thus the algorithm compensates for the low effort by increasing the gain of the signal using the watchdog timer. The increase in gain 810 during the central apnea is shown in Fig 16e.

The stimulation control using the detection algorithm described above and synchronized to the respiratory effort waveform allows for the provision of a preprogrammed train of pulses, i.e., voltage, current, power, to the electrode 65 (Fig. 5) as shown in Fig. 17a. This train of pulses, also referred to as a burst, stimulate the nerve/muscle, such as a muscle in the upper airway, the diaphragm, or any other muscles which are suitable for use in treatment.

Fig. 17b shows characteristics of a typical train of pulses that is initiated upon onset detection as previously described. The train of pulses is shown to begin upon onset at an amplitude of about 75% of the programmed value. The amplitude is then ramped to 100% of the programmed value. This ramped function provides added comfort during the nerve stimulation. However, alternatively, the train of pulses may be started at any percentage of the programmed value or any percentage of the programmed value, i.e. 100%, 110%, 150%. The train of pulses ends upon the declaration of an offset, when maximum stimulation time is reached or the IPG off command is entered as described previously.

Fig. 17c shows the characteristics of the individual pulses within the train of pulses. Amplitude, the rate at which the pulses are delivered and the width of the individual pulses all impact the stimulation of the muscle. Minimizing the programmable amplitude, pulse width and rate of stimulation increases the longevity of the system. As one of ordinary skill in the art will recognize there are various manners of providing the train of pulses or a single pulse, and the present invention is not limited to any particular manner of generating such pulses. Any suitable circuit configuration for providing such pulses may be utilized, such as those available with the ITREL platforms.

Fig. 18 shows the system 50, as shown in Fig. 5, including the IPG 55 which is a processor based IPG such as shown in Fig. 12b, sensor 60, and lead/electrode 65. The microprocessor 410 as previously described internally includes ADC 414. The IPG also includes the other components previously discussed including sensor bias 402, low pass filter 404, and AGC amplifier 406. Further included in the IPG 55 are telemetry components 440 coupled to antenna 442, stimulus output circuit 434 and digital to analog convertor (DAC) 432 which is used to produce the correct stimulus output amplitude for the system. The microprocessor 410, in addition to controlling stimulation, also controls the sensor bias 402, AGC amplifier 406 and diagnostic self test functions as described further below.

With reference to the system of Fig. 18, an energy conserving technique shall be described which is not only applicable to this particular system, but also to other implantable therapy systems, such as, for example, drug delivery systems, other stimulation systems, and any other systems which could benefit from such an energy conservation technique. The processor based IPG 55 enters an off state, i.e. a treatment period is not occurring, as a result of various events. For example, the off state in the system 50 is entered when the patient programmer 70 is used to send an IPG off command via telemetry using the telemetry circuitry and antenna 442. Further, the treatment period may end as a result of a dose timer timing out at the end of a dose period, such as in the morning after a nighttime treatment period, or the treatment period may end as a result of some other event. In such cases, the microprocessor 410 goes through a shut-down sequence and enters an off or >sleep= mode during which it is not required to function.

The shut down sequence includes turning off power to all non-essential circuits of the system 50. Such non-essential circuits during the sleep mode include the amplifier 406, sensor bias 402, ADC 414, DAC 432, and stimulus output circuits 434. In the microprocessor based system, the microprocessor can also enter the sleep mode or stop mode where very little current is consumed, but the microprocessor will awake when an interrupt line is toggled. The telemetry

block 440 remains on to listen for telemetry communication, such as from the patient programmer 70, and then wakes the microprocessor 410 when the external communication, i.e. telemetry command, is received. During operation of the sleep mode, energy is conserved.

This sleep mode can also be used with the IPG having processing circuitry that is not microprocessor based. For example, the logic circuits could be shut down or powered down. Further, methods other than telemetry could be used to wake up the processor. For example, a patient held magnet and a reedswitch trigger located in the IPG could be used, or a background timer in the IPG could be used to automatically turn the IPG on at a certain time. Further, as previously indicated above, this sleep mode could be used with other implantable therapy systems. For example, a blink stimulation system could enter sleep mode at night when essential circuits are not used or a drug delivery system could use sleep mode when there is a period of time that the essential components are not needed.

The patient programmer 70, Fig. 8, and the physician programmer 80, Fig. 7, communicate with the IPG 55 via telemetry. The physician programmer 80 allows the programmable parameters of the system to be adjusted by the physician to conform to the needs of the patient. Such programming devices are readily known to those skilled in the art. Examples of such devices are described in U.S. 4,236,524 to Powell et al., U.S. Patent 4,250,884 to Hartlaub et al., U.S. Patent 4,305,397 to Weisbrod et al., U.S. Patent 4,323,074 to Nelms, U.S. Patent 4,432,360 to Mumford et al., and U.S. Statutory Invention Registration No. H1347 to Greeninger et al., all incorporated herein by reference in their entirety. For example, all the programmable parameters mentioned with respect to the detection algorithm and also the stimulus pulse amplitude, stimulus pulse duration, stimulus pulse frequency, and stimulus ramp on/off times can be adjusted through the physician programmer 80. In addition, the physician programmer 80 can be used to access any stored data and retrieve such data stored in the implanted system. For example, the patient=s name, the code number of the hospital or clinic, the prescription date, and the last follow-up date could be stored in hardware of the system. Further, patient compliance data, system performance data, diagnostic

testing data could be accumulated by the system and read out through use of the programmer 80. For example, the total time the power is on, total stimulation time for the patient, the number of power cycles or reset cycles, the average battery voltage and fault detection could be stored and retrieved through the physician programmer 80.

Fig. 8 shows the patient programmer 70 for patient control of the system 50. The control panel of programmer 70 includes on and off switches 71, 75 which allow the patient to turn the system on or off. Turning switch 71 on initializes the treatment period using the above described control logic. The buttons 73 allow the patient to adjust the amplitude of stimulation for comfort level and other controls could be added to allow the patient to control other parameters such as, for example, pulse rate, pulse width, delay times.

The power on switch 71 also may be utilized to initiate various self test functions as well as initiating a dose delay (block 604) if the device is already operating. One self test function initiated by the power on switch is a patient stimulation self test function, wherein when the patient turns the stimulation system on with the patient programmer 70 for a treatment period, i.e. before going to bed, the stimulator immediately thereafter automatically provides stimulation to the patient, such as to the hypoglossal nerve. This stimulation may be based on the maximum stimulation time or any other predetermined time period. Such power on stimulation, gives the patient the ability to verify that the system is capable of stimulating properly. For example, the stimulation verifies that the nerve/muscle was captured, that the lead placement is correct, that the lead from the IPG 55 to the electrode 65 is operative, and also that the IPG stimulator output circuits for providing the pulse are functioning properly. At any time during the treatment, if the patient did not think that the system 50 was functioning properly, the patient could, by pushing the power on switch, provide a stimulus to check the device. Further, the stimulation self test could be performed at IPG-OFF.

The patient stimulation self test is not only applicable to respiratory treatment systems as described herein, but is equally applicable to any stimulation systems that provide patient treatment. For example, such a self test could be used

with a muscle therapy or conditioning system, a blink electrode stimulation system, or any other neuromuscular stimulation system. With respect to the respiratory disorder treatment system described herein which, for example, stimulates the hypoglossal nerve, the stimulation automatically provided provides stimulation sufficient to evoke tongue protrusion, which the patient senses and thus can verify that the stimulator is on and stimulation is functional.

Any faults detected by the stimulator using the stimulation self test or by any of the other tests described herein, such as the diagnostic self tests, can be reported to the patient via the patient programmer 70. Further, since the patient by the power on stimulus has tested the adequacy of the stimulation, the patient can adjust the amplitude of stimulation by buttons 73, for example, within certain bounds set by the physician. This adjustment would allow the patient to increase stimulation amplitude if capture of the nerve was not occurring or decrease amplitude of stimulation if adequate capture was occurring, in order to increase battery longevity. Such patient adjustment may be used for any other physician programmable parameters that the physician would want the patient to be able to control. For example, stimulus rate, pulse width, therapy delay periods, etc. Moreover, if the system is not functioning properly, a visit to the physician can be made for evaluation of the system, i.e. such as by accessing test data or fault data stored in the system.

The power on switch 71 may also be utilized to initiate an internal diagnostic self test for testing the system to determine whether the components and circuit functions, along with the detection algorithm are operating properly. However such diagnostic self test can also be run whenever the system is not interactive with the patient. For example, a diagnostic self test of the system described with reference to Fig. 18 could be run during a dose delay, a sleep mode, a therapy delay, at IPG-OFF or anytime during the day when the patient is awake. During the diagnostic self test, components and functions of the system can be tested, for example, with reference to the system of Fig. 18, the amplifier 406, the filter 404, and all the rest of the components can be tested as described further below. Typically, such testing is performed at the physicians office using the

physician programmer 80. However, since this treatment is performed during the sleep period of a patient=s day, it may not be known whether the system is functioning properly or not as the patient is asleep when it is operating. Therefore, a diagnostic self test during a period of time when the system is not interacting with the patient, i.e. stimulation or sensing, or in other words when the patient is not dependent on the treatment, is beneficial. With, for example, a fault indication sent to the patient programmer 70 when faults are detected, the patient has some assurance that the system is functioning properly.

The diagnostic self test strategy as shown in Fig. 19, is applicable to many different therapy systems. For example, as shown therein, a typical therapy system 900 includes a therapy device 901, i.e. IPG 55, having an input circuit 908 for receiving an input such as a sensed signal 904 of a patient 10. The device 901 further includes a microprocessor or some other logic circuitry 912 for processing the sensed signal and generating an output 906 via output circuit 910. Further, the device may include telemetry circuitry 914 for receiving and transmitting information from and to an external source.

The general diagnostic test strategy for such a generally described therapy system, includes applying the generated output 906 from the output circuit 910 to the patient 10. The result of the therapy due to the generated output 906 is sensed via the input circuit 908 to verify operation of the system. For example, a stimulus output, i.e. a cardiac pace, could be applied to the patient and the input circuit could sense whether the cardiac pace resulted in a physiological response in the patient. Further, for example, the stimulus output could be a train of pulses to the genioglossus muscle to treat sleep apnea. The input circuit would then provide the sensed signal characteristic of respiratory effort to the microprocessor to verify that a correct respiratory response was achieved with the stimulus of the genioglossus muscle, i.e. open airway and proper respiratory action. If a correct response is not indicated, the system could be further tested. An internal attenuated feedback output 916 (shown as a thicker line than the lines of system normal configuration) from the output to the input can be used to determine if the input or output circuits are operating properly. This general test strategy will detect faults

internal and external to the device 601. For example, a broken stimulus or sense lead could be detected or a faulty output circuit could be detected.

Figs. 20a-d show various block diagrams of other more specific internal diagnostic self tests for testing various components of the system shown in Fig. 18. Fig. 20a shows the blocks of Fig. 18 involved in a front end amplifier self test. The DAC 432 sends a voltage or voltage pulse to the input of filter 404, amplifier 406, or ADC 414. The microprocessor 410 then verifies the correct response. The DAC 432 is also verified by its participation in these loops.

Fig. 20b shows the blocks involved in a sensor bias self test. A bias signal from sensor bias 402 is directed to the ADC 414 and measured and compared to set references by the microprocessor 410. A sensor signal from sensor 60, for example, a DC static voltage resulting from sensor bias, can also be directed to the ADC 414, measured and compared to set references by the microprocessor 410 for verification.

Fig. 20c shows the blocks involved in a stimulus output self test. The output from the stimulus output 434 with its amplitude under control of DAC 432 is directed to the ADC 414 and verified by the microprocessor 410. The output can be ramped to its maximum stimulus and then attenuated for input to ADC 414 for measurement.

Fig. 20d shows the blocks involved in a telemetry self test. The telemetry circuitry 440 can be tested in a couple of ways. First, known voltage pulses are applied to the telemetry circuit 440 via the DAC 432 to drive the circuit, i.e. simulate a received ping, and telemetry reception is verified via the microprocessor 410 and a demodulated voltage measured on the ADC 414. Likewise, the microprocessor 410 could initiate a telemetry uplink, i.e. ping on antenna, and the ADC 414 will verify the signal on the antenna 442. Second, a telemetry uplink can be initiated with the microprocessor 410, i.e. ping the antenna, and then immediately enable the telemetry demodulator of circuitry 440 to detect the ringing of the antenna 442 with verification of the detection performed by the microprocessor 410. This second test would not use the ADC 414 or the DAC 432.

Further tests could be performed to verify other components and functions. For example, the AGC could be calibrated by switching in a known signal, analog offset and onset detection could be verified by a DAC generated signal, and lead and battery measurements could be made. Further, diagnostic self test results can be stored and uplinked to allow quick fault identification at either a patient or a physician programmer.

It will be appreciated by those skilled in the art that while the invention has been described above in connection with particular embodiments and examples, the invention is not necessarily so limited and that numerous other embodiments, examples, uses, modifications and departures from the embodiments, examples and uses may be made without departing from the inventive concepts.

What is claimed is:

1. A testing method for use with a patient stimulation system, comprising the steps of :

providing a stimulation system including a patient control unit, the patient control unit for initiating and terminating treatment periods; and

automatically providing at least one period of stimulation to stimulate the patient upon initiating a treatment period.

2. The method according to claim 1, wherein the length of the at least one period of stimulation is based upon a maximum stimulation time defined for the system.

3. The method according to claim 1, wherein the patient control unit further allows the patient to adjust one or more characteristics of stimulation.

4. The method according to claim 3, wherein the one or more characteristics include one or more of amplitude, rate, pulse width.

5. The method according to claim 1, wherein the stimulation system is for providing stimulation to treat respiratory disorders, and further wherein after the automatic provision of the at least one period of stimulation, the system does not permit patient stimulation for a predetermined period of time.

6. The method according to claim 5, wherein the stimulation system is an implantable system and the patient control unit uses telemetry to initiate the system.

7. A stimulation system, comprising:

stimulation means for providing stimulation of a patient during a treatment period; and

a patient control unit for initiating and terminating treatment periods, the stimulation means including means for automatically providing at least one period of stimulation to stimulate the patient upon initiation of a treatment period.

8. The system according to claim 7, wherein the length of the at least one period of stimulation is based upon a maximum stimulation time defined for the system.

9. The system according to claim 7, wherein the control unit further includes means for allowing the patient to adjust one or more characteristics of the stimulation.

10. The system according to claim 9, wherein the one or more characteristics include one or more of amplitude, rate, and pulse width.

11. The system according to claim 7, wherein the stimulation means includes a stimulation control device for generating the at least one period of stimulation and at least one electrode connected thereto for providing the stimulus to the patient, whereby the at least one period of stimulation provides an indication that at least the placement of the electrode is adequate and functional.

12. The system according to claim 7, wherein the stimulation means provides stimulation to treat respiratory disorders, the stimulation means including delay means for prohibiting stimulation after the automatic provision of the at least one period of stimulation for a predetermined period of time.

13. The system according to claim 7, wherein the stimulation system is an implantable stimulation system and the patient control unit uses telemetry to initiate treatment periods.

14. A system test method for use with a therapy system, the method comprising the steps of:

providing a therapy system having a plurality of components, the therapy system for physiologically interacting with a patient; and

performing, internally to the system, a diagnostic self test of a component of the therapy system to determine if the component is functioning properly at a time when the therapy system is not interacting physiologically with the patient.

15. The method according to claim 14, wherein the therapy system includes a patient control unit for at least initiating therapy to the patient during a treatment period, and further wherein the performing step includes automatically performing the diagnostic self test of the component upon initiation of the treatment period by the patient.

16. The method according to claim 15, wherein the therapy system is an implantable stimulation system for providing stimulation to treat respiratory disorders of the patient, and further wherein the stimulation system is programmed to provide stimulation of the patient substantially only during periods when the patient is asleep.

17. The method according to claim 14, wherein the therapy system is an implantable system.

18. The method according to claim 14, further including the step of communicating a fault to the patient if a failure of the component is determined.

19. The method according to claim 14, wherein the therapy system includes an input circuit for receiving a sensed signal characteristic of a physiological parameter of the patient and an output circuit for generating a therapy output for physiological treatment of the patient, and further wherein the performing step includes the step of using a feedback signal from the output to the input to perform the self test of the component.

20. The method according to claim 14, wherein the therapy system includes an input circuit for receiving a sensed signal characteristic of a physiological parameter of the patient and an output circuit for generating a therapy output for providing therapy to the patient, and further wherein the performing step includes the steps of:

generating a therapy output for providing therapy to the patient;

measuring an effect of the therapy on the patient due to the therapy output using the sensed signal; and

verifying that the effect resulting from the therapy output was correct.

21. The method according to claim 14, wherein the performing step includes the steps of:

applying a known signal to an input of the component and measuring an output generated as a function of the component; and

verifying the accuracy of the output.

22. A system for use in testing a therapy system, comprising:

a therapy system having a plurality of components, the therapy system for physiologically interacting with a patient; and

means for performing, internally to the system, a diagnostic self test of a component of the therapy system to determine if the component is functioning properly at a time when the therapy system is not interacting physiologically with the patient.

23. The system according to claim 22, wherein the therapy system includes a patient control unit for initiating therapy to the patient during a treatment period, and further wherein the means for performing includes means for automatically performing the diagnostic self test of the component upon initiation of the treatment period by the patient.

24. The system according to claim 23, wherein the therapy system is an implantable stimulation system for providing stimulation to treat respiratory disorders of the patient, and further wherein the stimulation system is programmed to provide stimulation of the patient substantially only during periods when the patient is asleep.

25. The system according to claim 22, wherein the therapy system is an implantable system.

26. The system according to claim 22, further including means for communicating a fault to the patient if a failure of the at least one component is determined.

27. The system according to claim 22, wherein the therapy system includes an input circuit for receiving a sensed signal characteristic of a physiological parameter of the patient and an output circuit for generating a therapy output for physiological treatment of the patient, and further wherein the means for performing includes the means for generating a feedback signal from the output circuit to an input of the input circuit for use in performing the self test of the component.

28. The method according to claim 27, wherein the output circuit generates a therapy output resulting in a physiological effect on the patient, wherein the input circuit receives the sensed signal characteristic of the physiological effect, and further wherein the performance means includes means for verifying that the

physiological effect resulting from a particular therapy output is a correct physiological effect.

29. The system according to claim 22, wherein the means for performing includes:

means for applying a known signal to an input of the component;

means for measuring an output generated as a function of the component acting on the known signal; and

means for verifying the measured output to determine correct performance of the component.

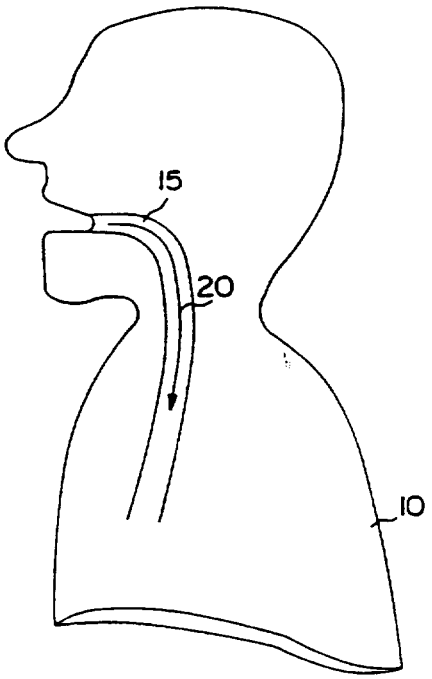


FIG. 1

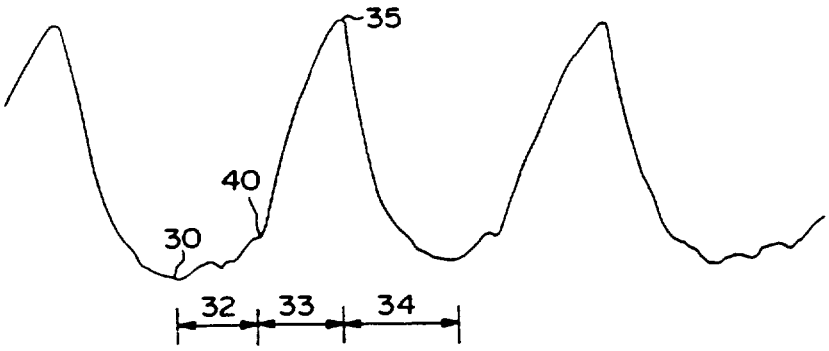


FIG. 2A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00307

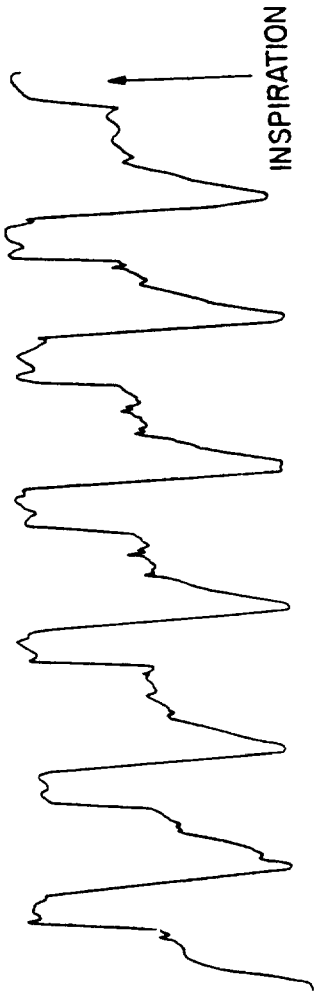


FIG. 2B



FIG. 2C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00308

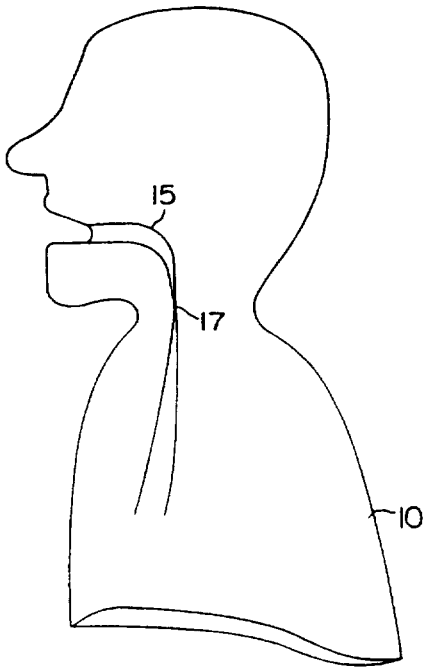


FIG. 3

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00309

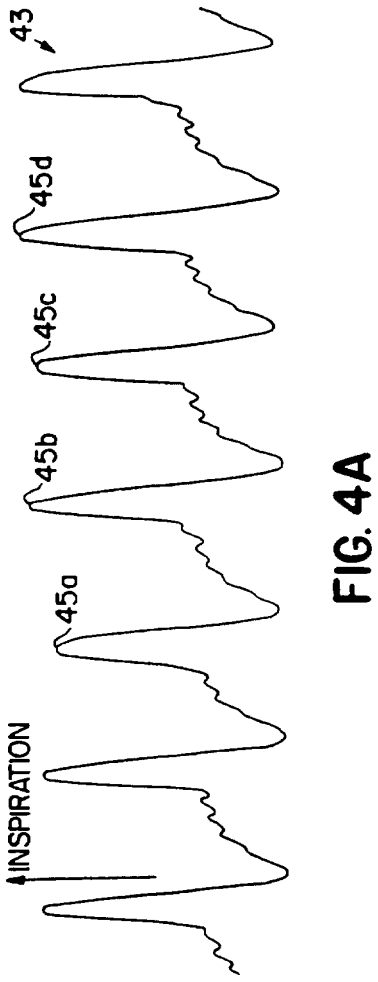


FIG. 4A

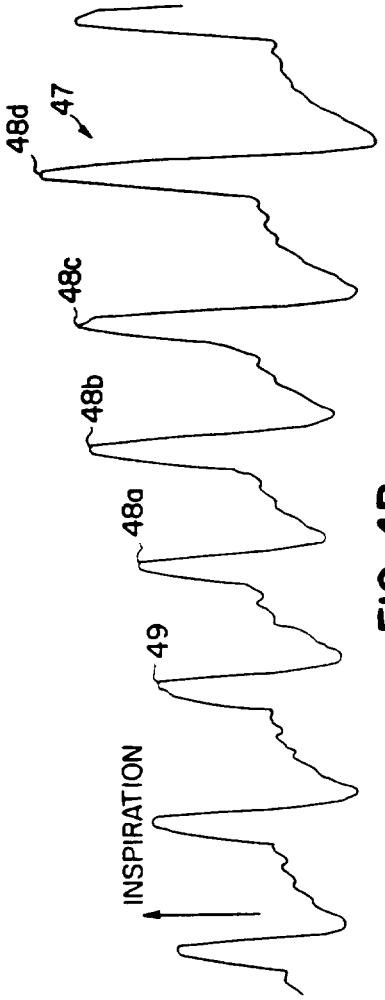


FIG. 4B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00310

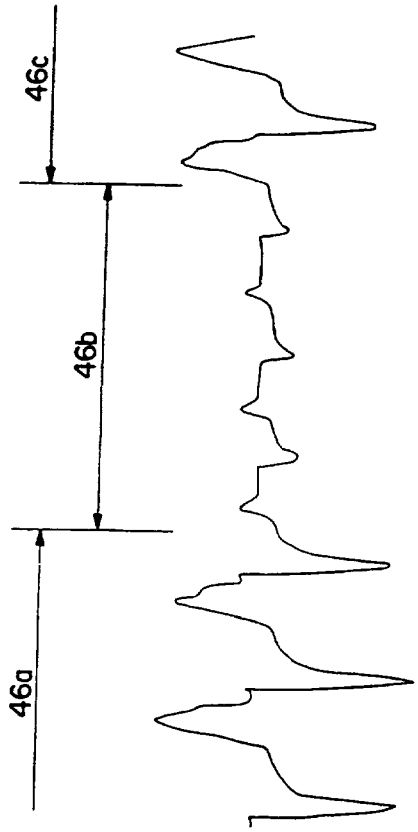


FIG. 4C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00311

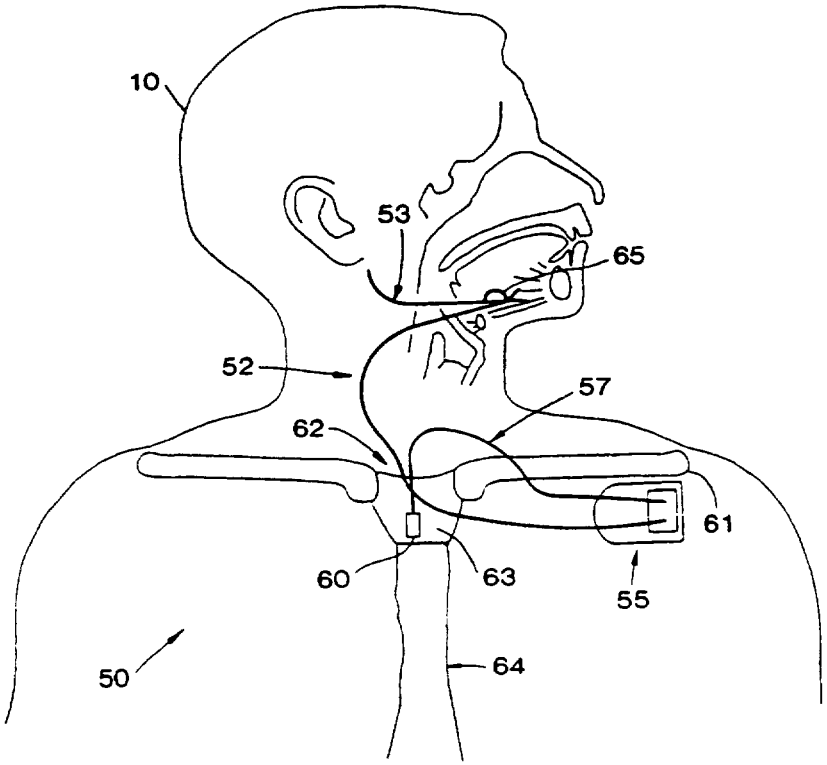


FIG. 5

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00312

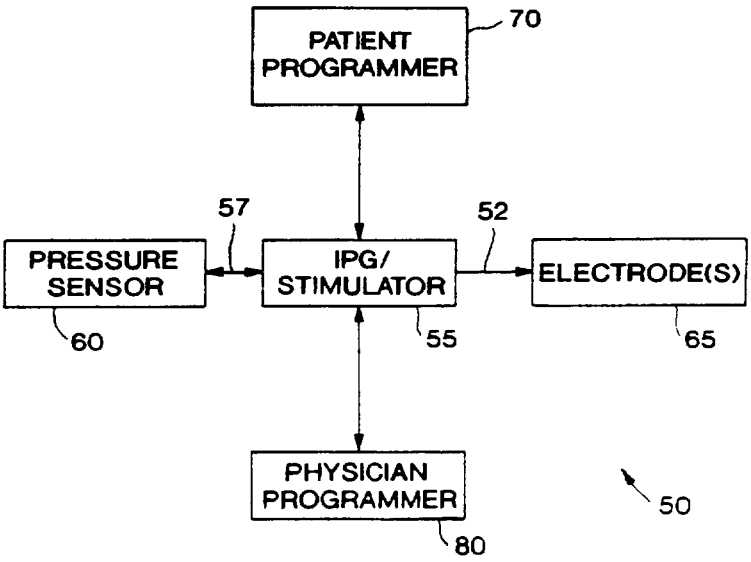


FIG. 6

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00313

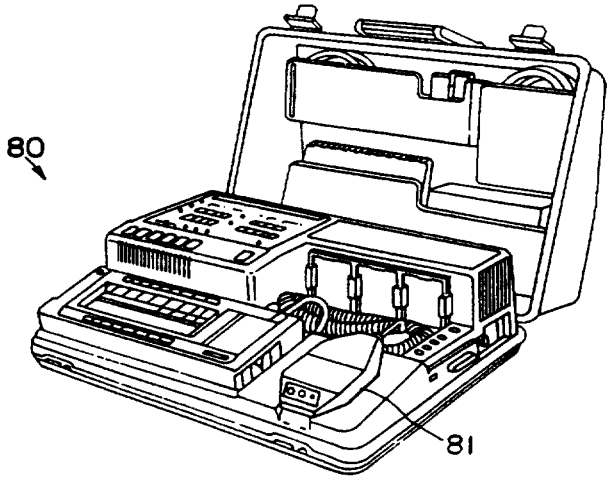


FIG. 7

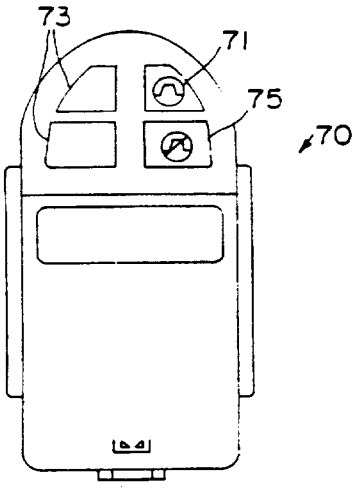


FIG. 8

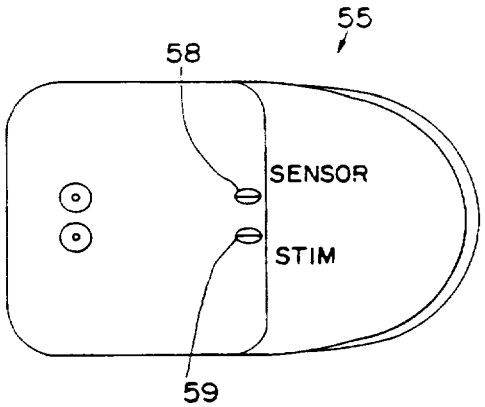


FIG. 9

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00314

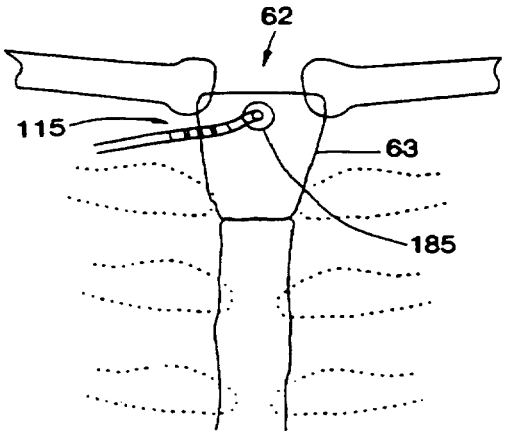


FIG. 10A

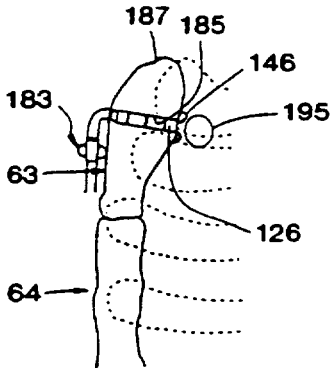


FIG. 10B

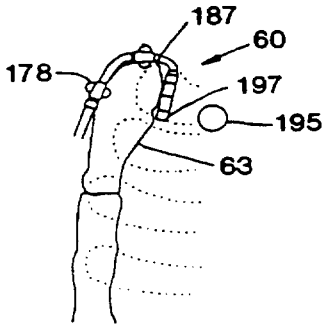


FIG. 10C

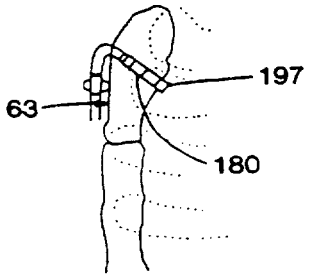


FIG. 10D

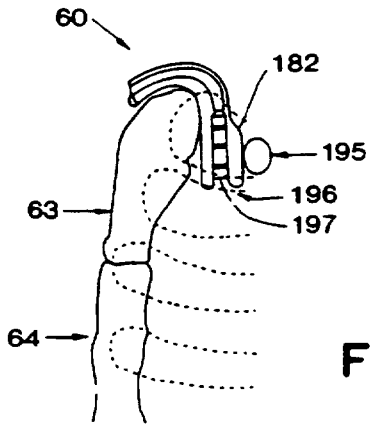


FIG. 10E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00315

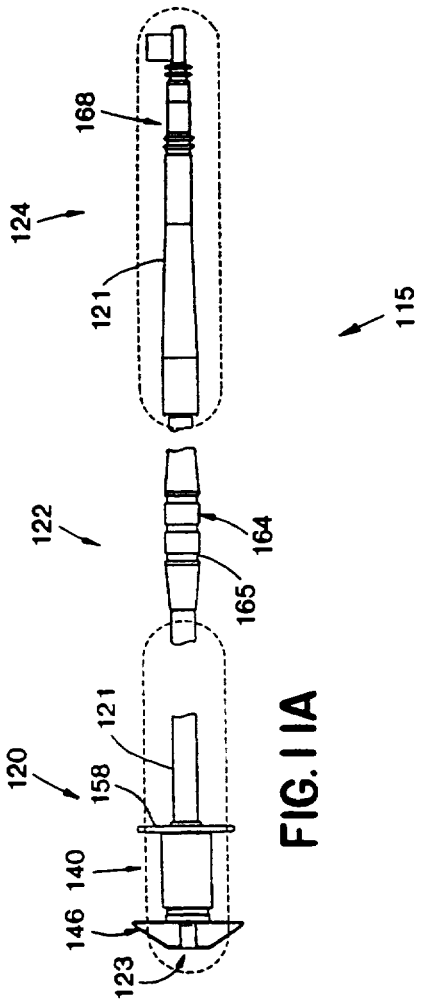


FIG. I IA

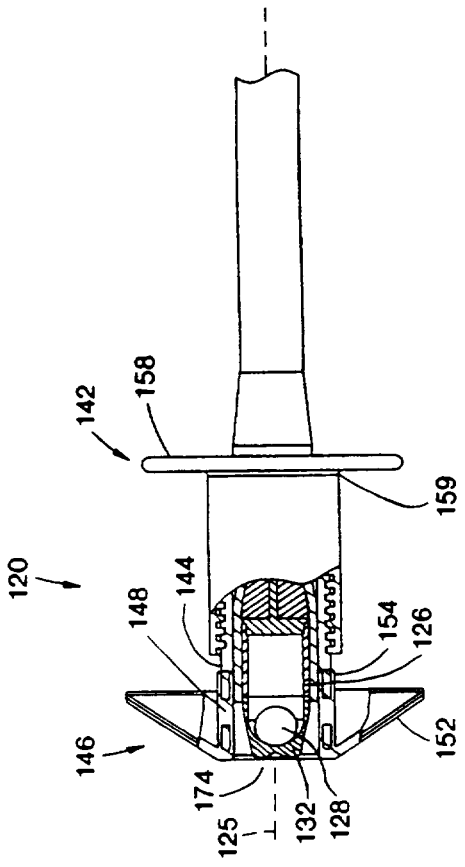


FIG. I IB

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00316

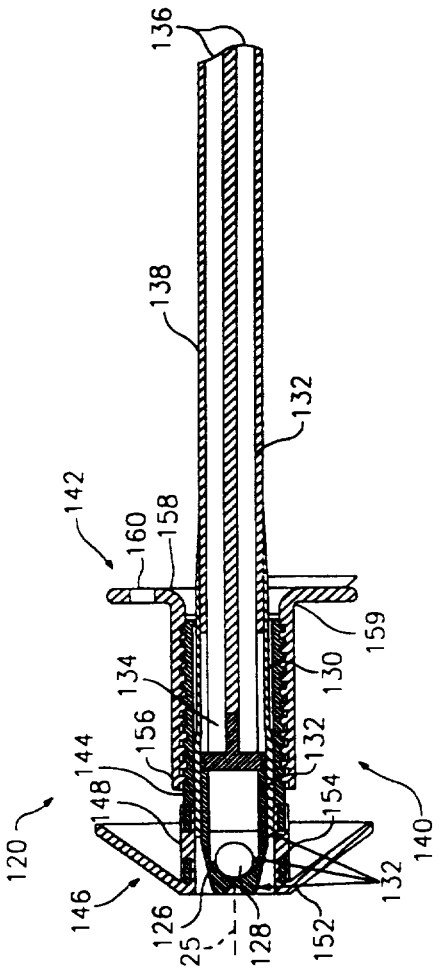


FIG. IIC

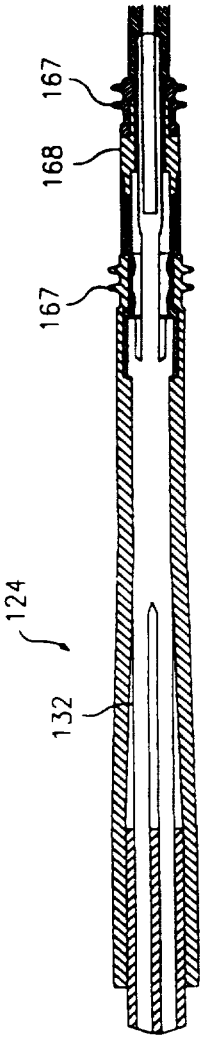


FIG. IID

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00317

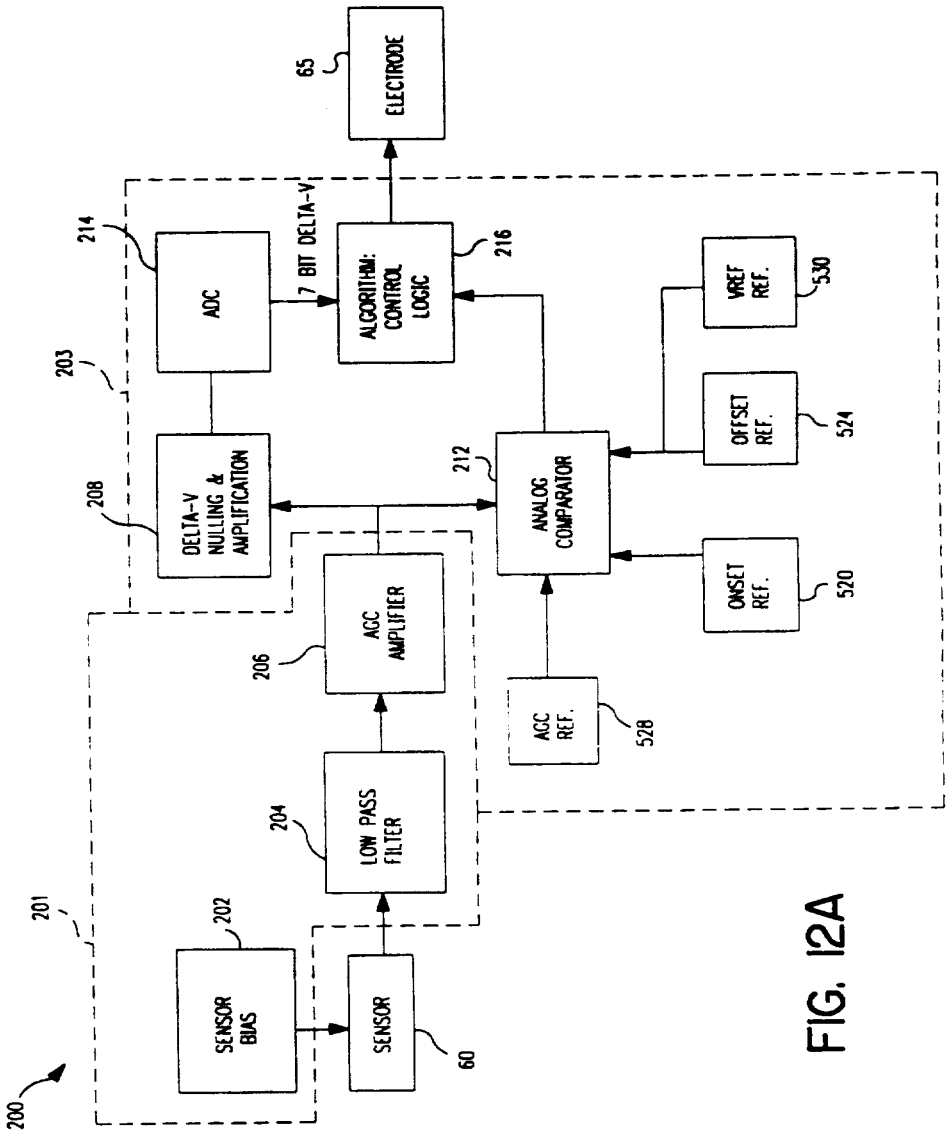


FIG. 12A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00318

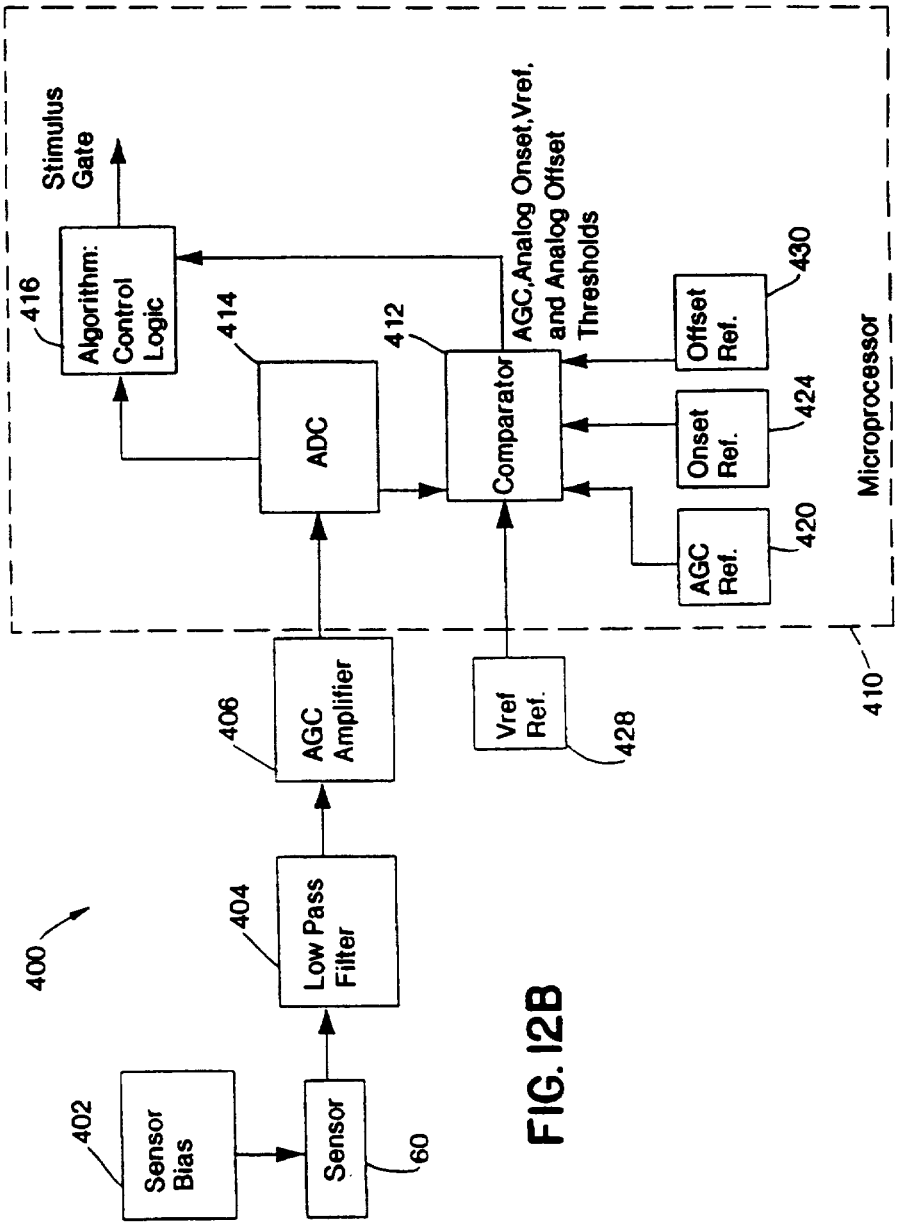


FIG. 12B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00319

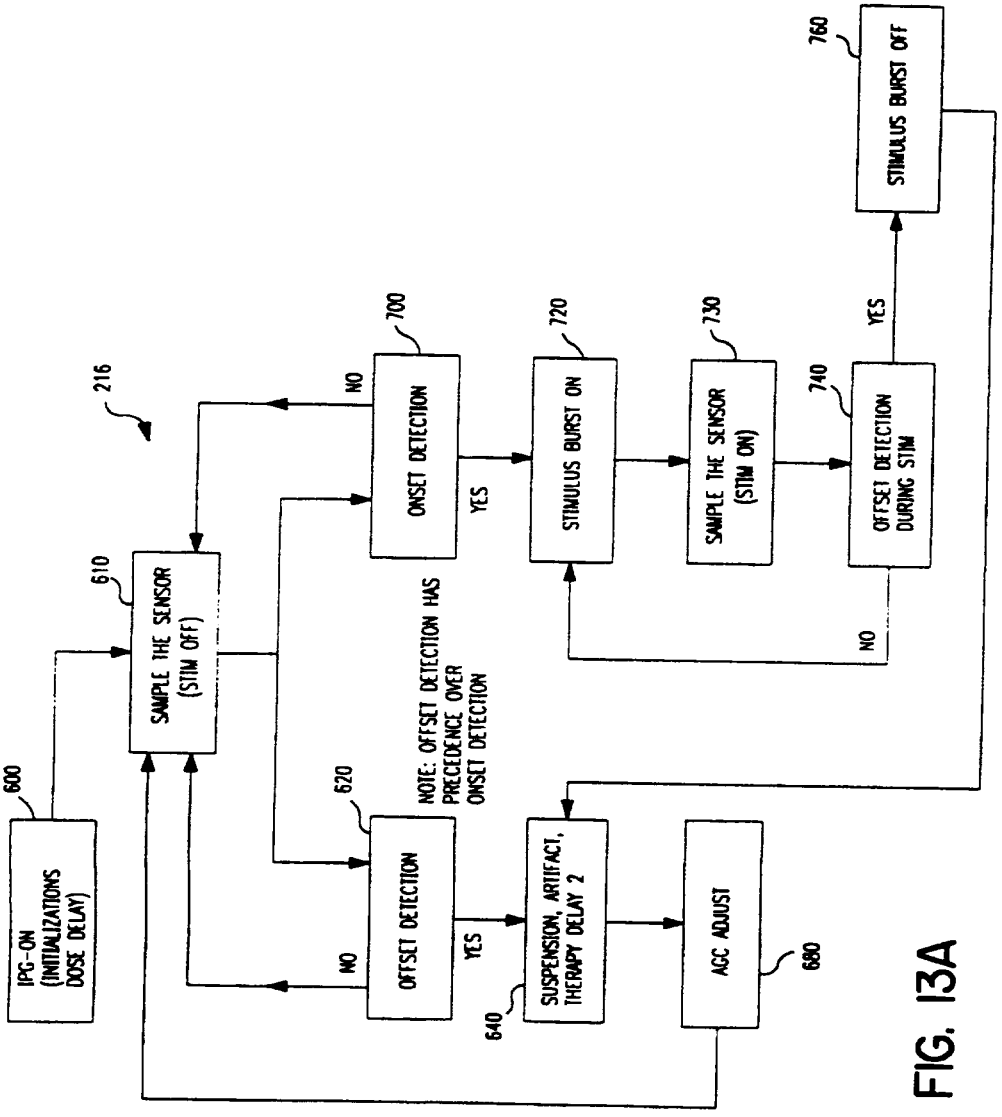


FIG. 13A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00320

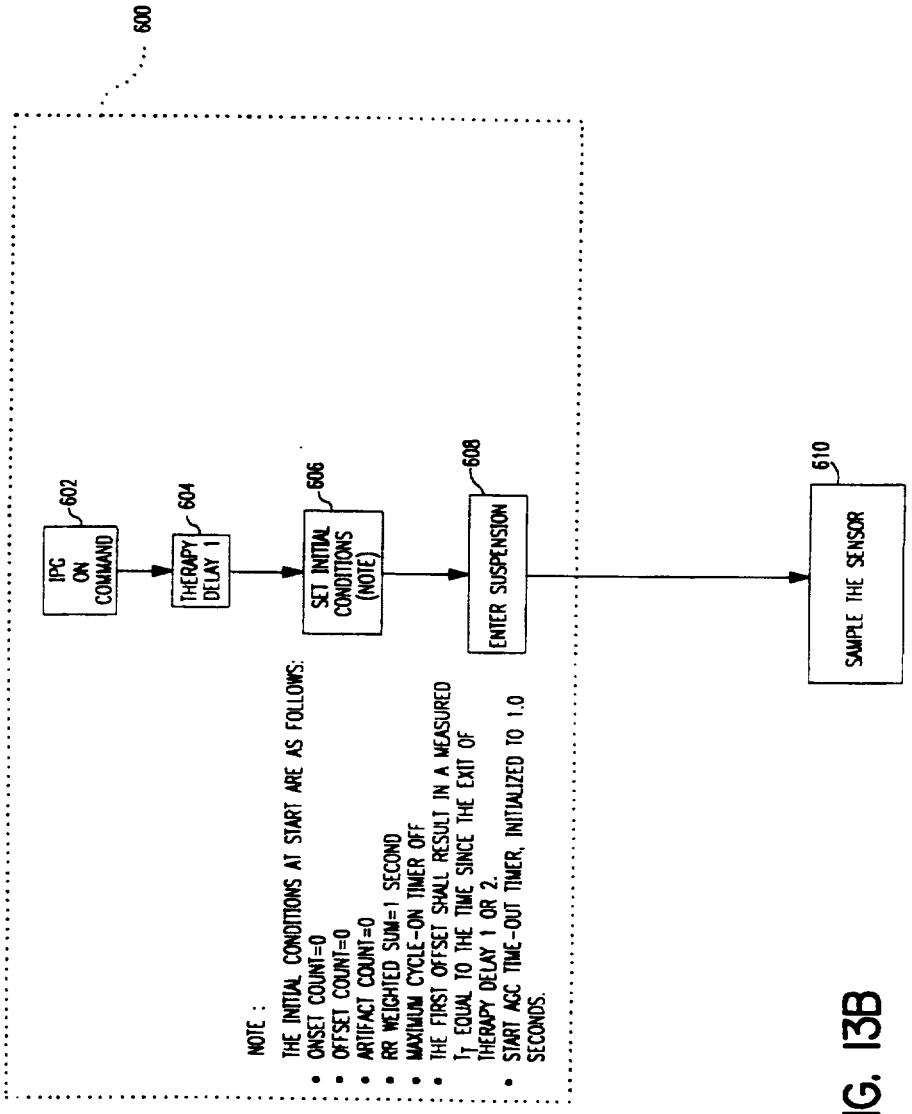


FIG. 13B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00321

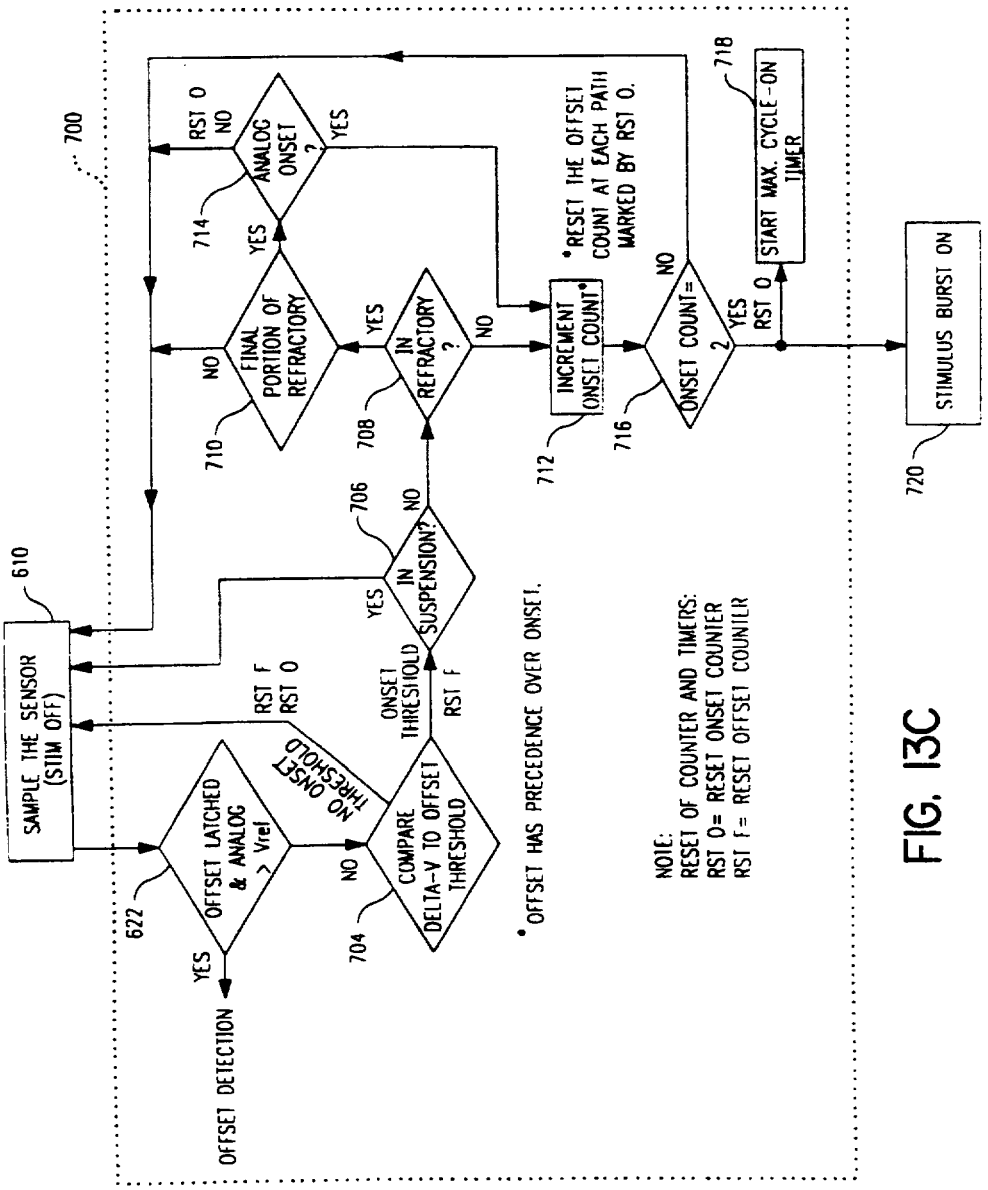


FIG. 13C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00322

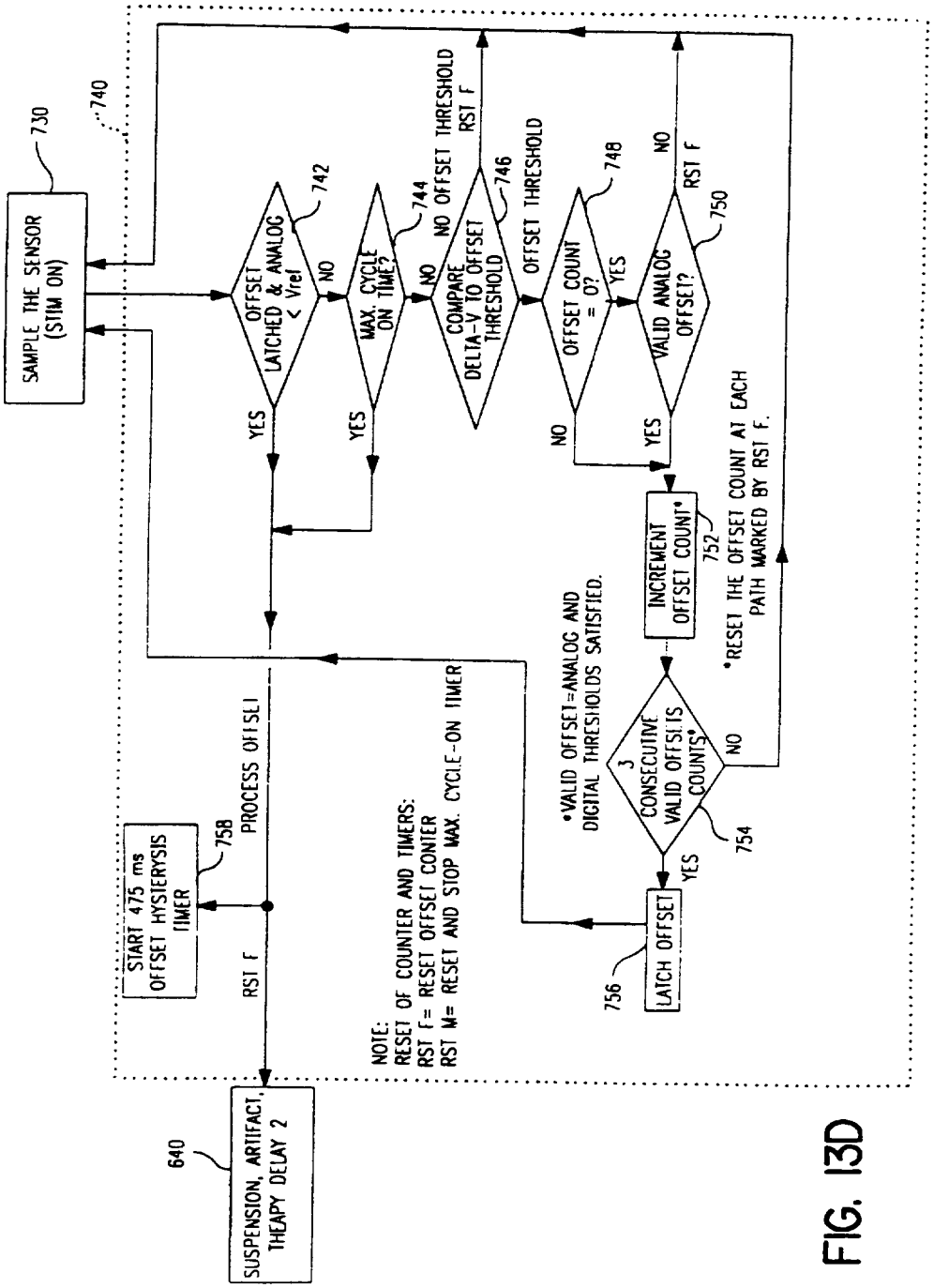


FIG. 13D

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00323

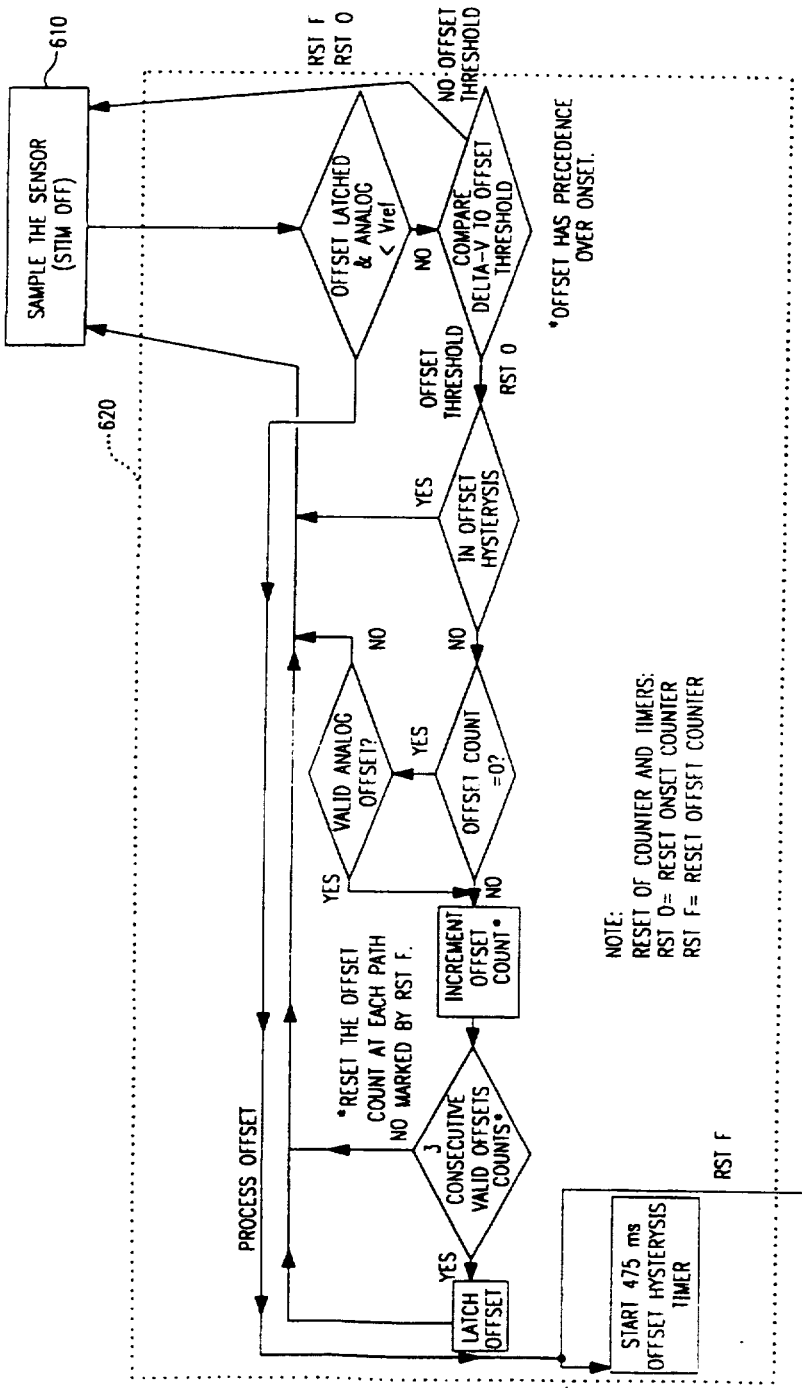


FIG. 13E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00324

FIG. 13F

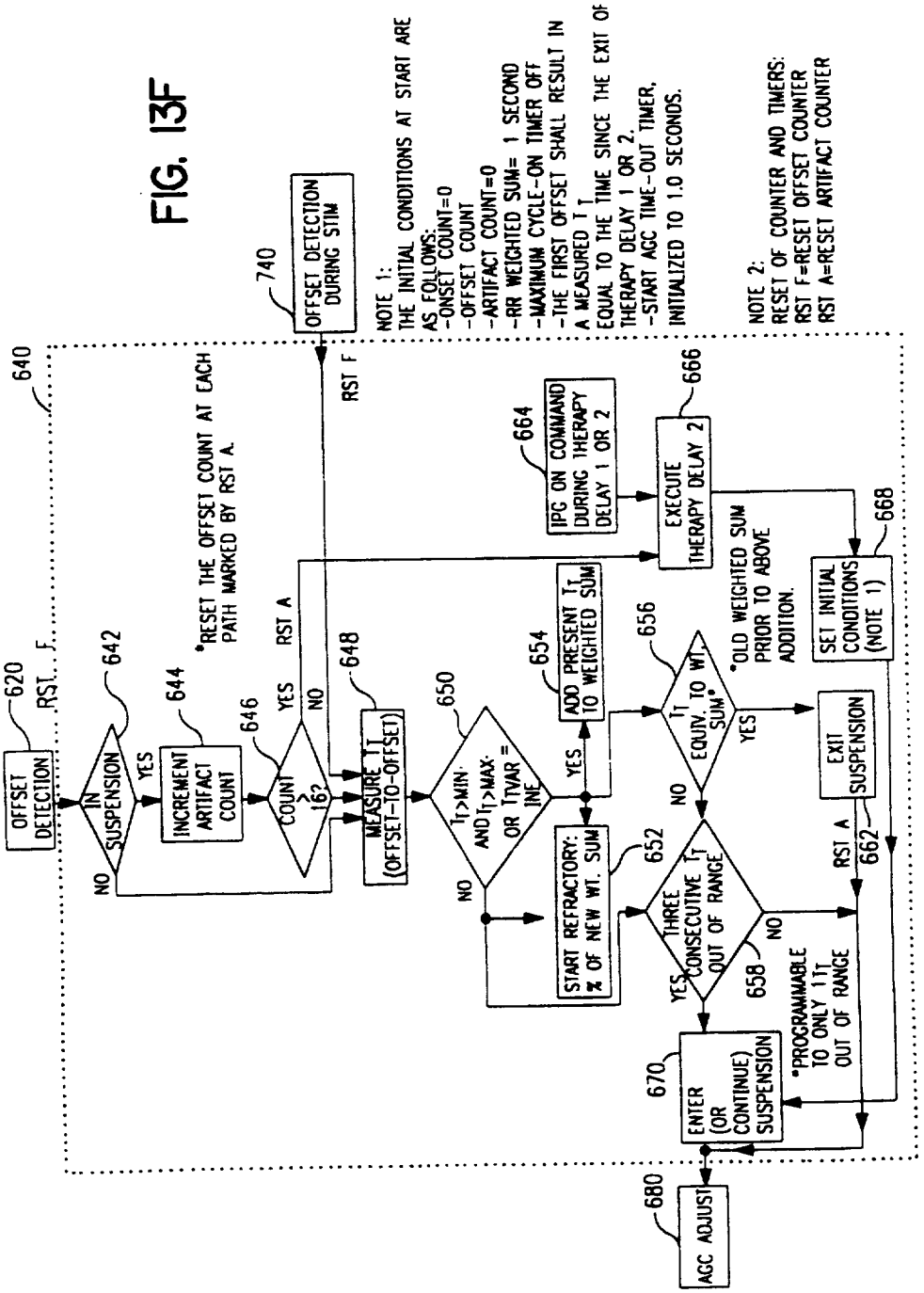


Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00325

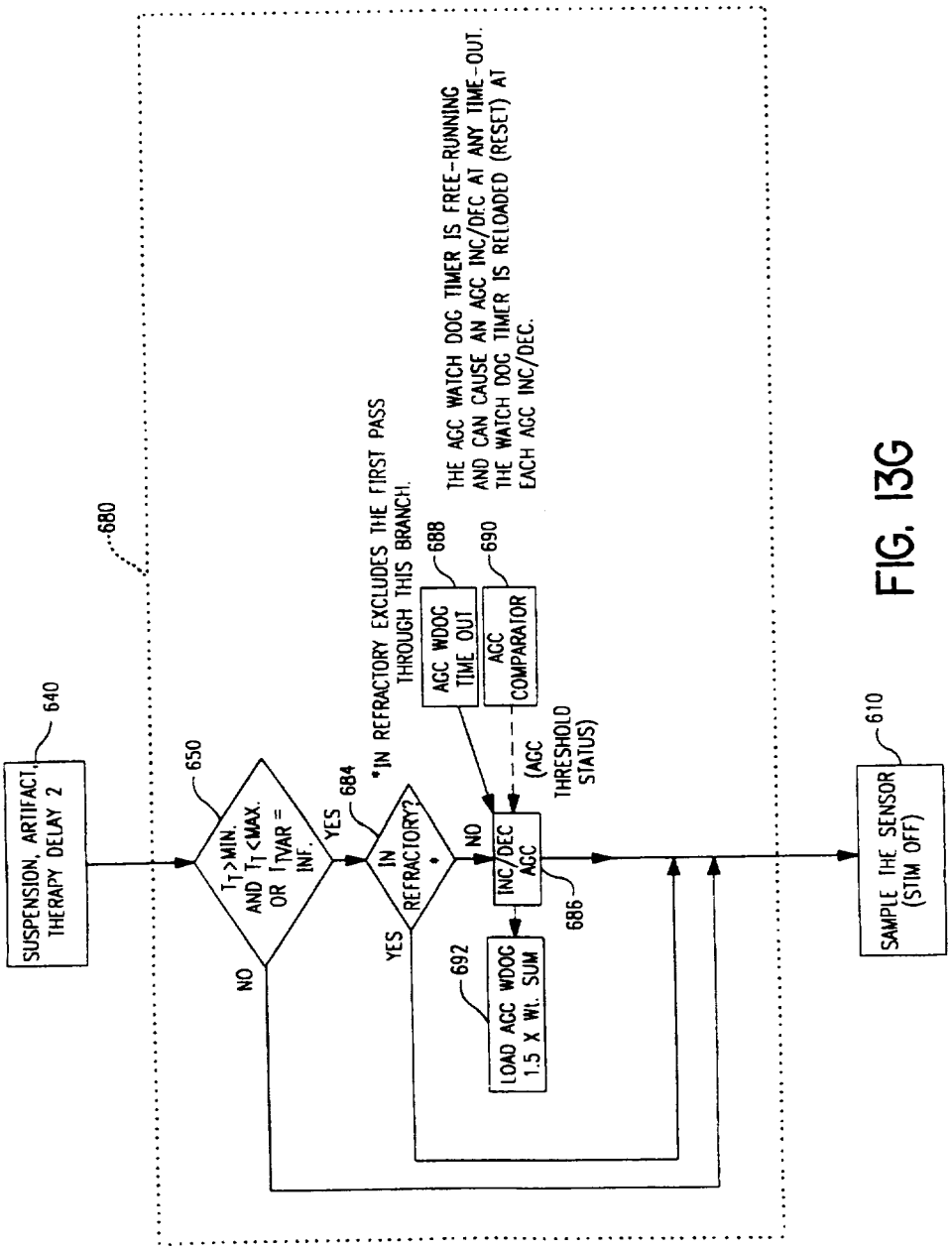


FIG. 13G

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00326

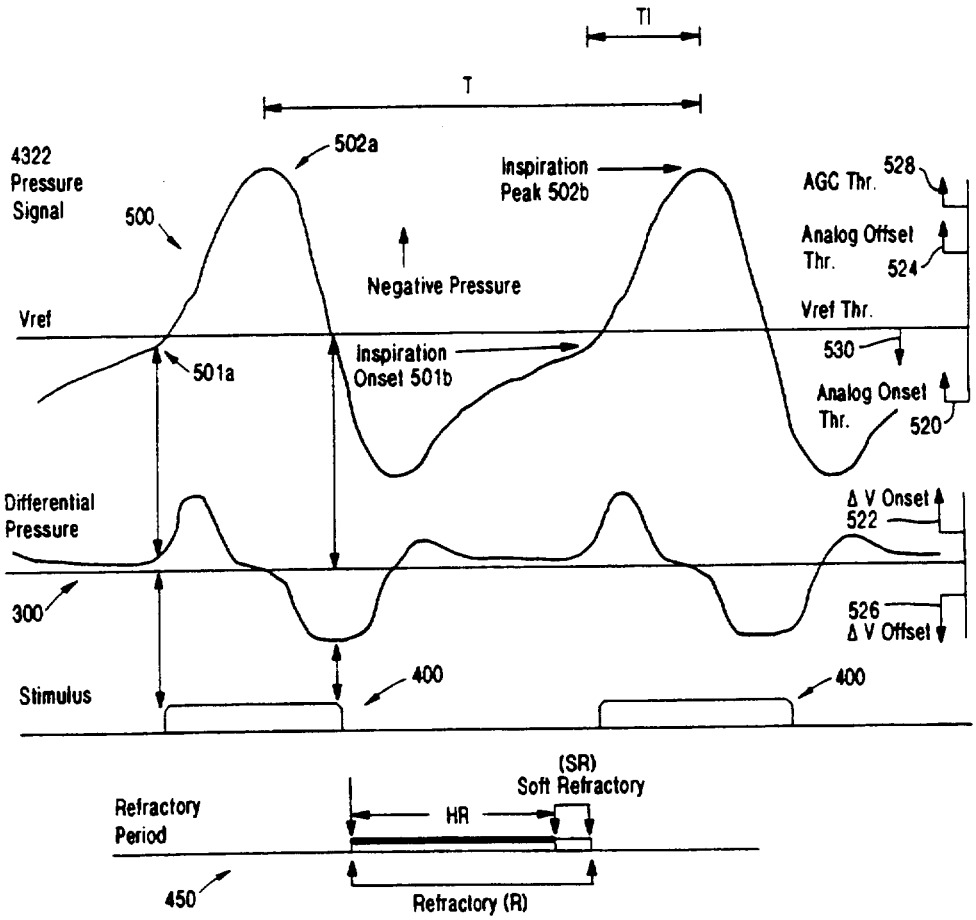


FIG. 14

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00327

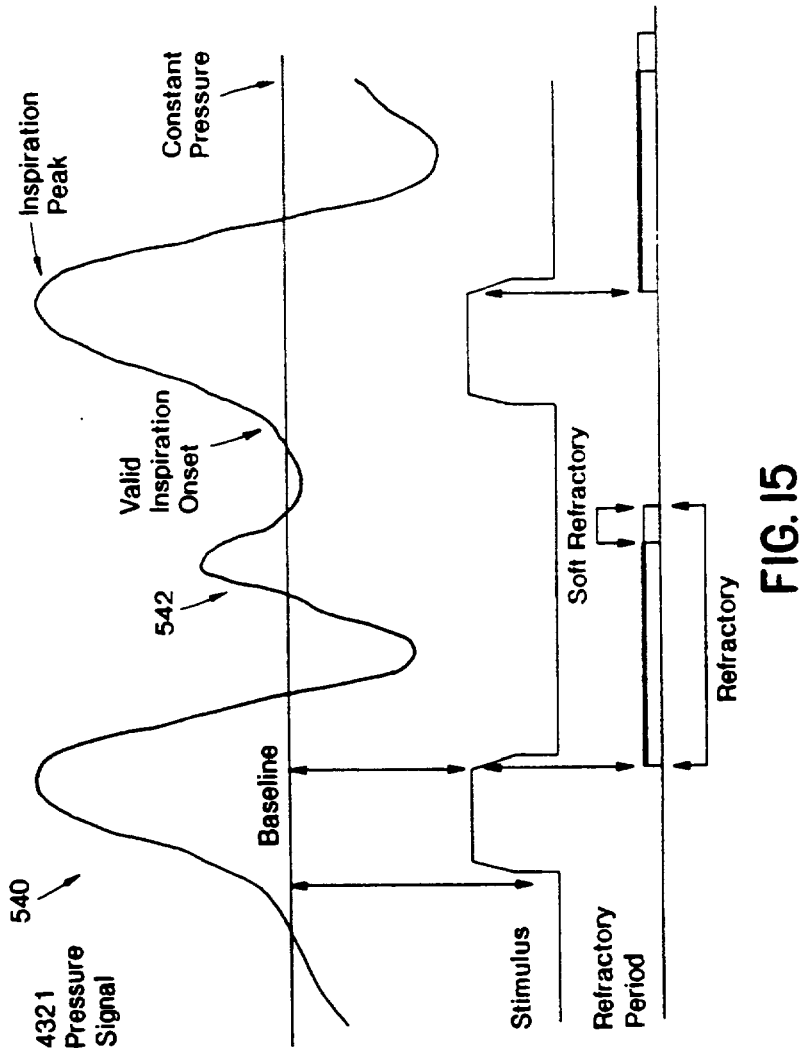


FIG. 15

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00328

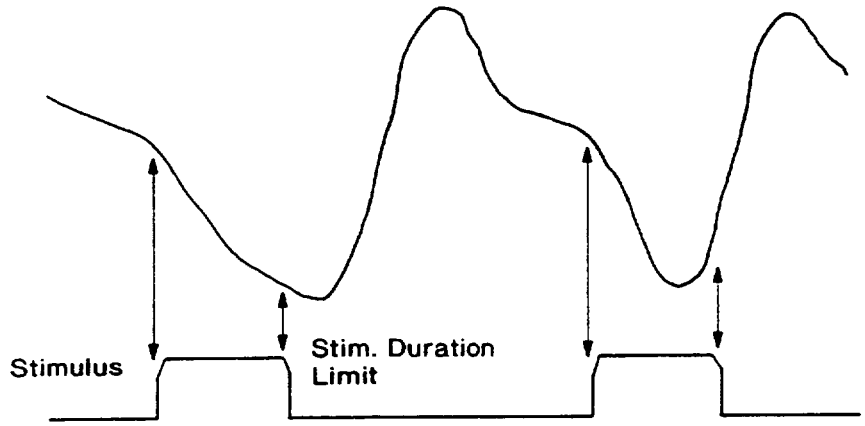


FIG. 16A

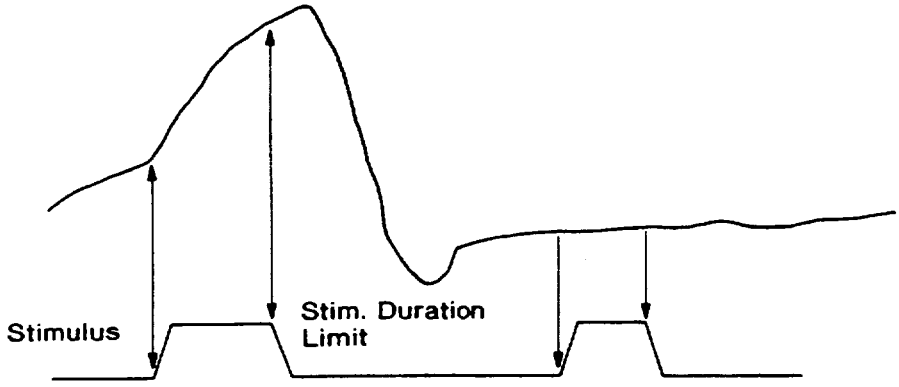


FIG. 16B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00329

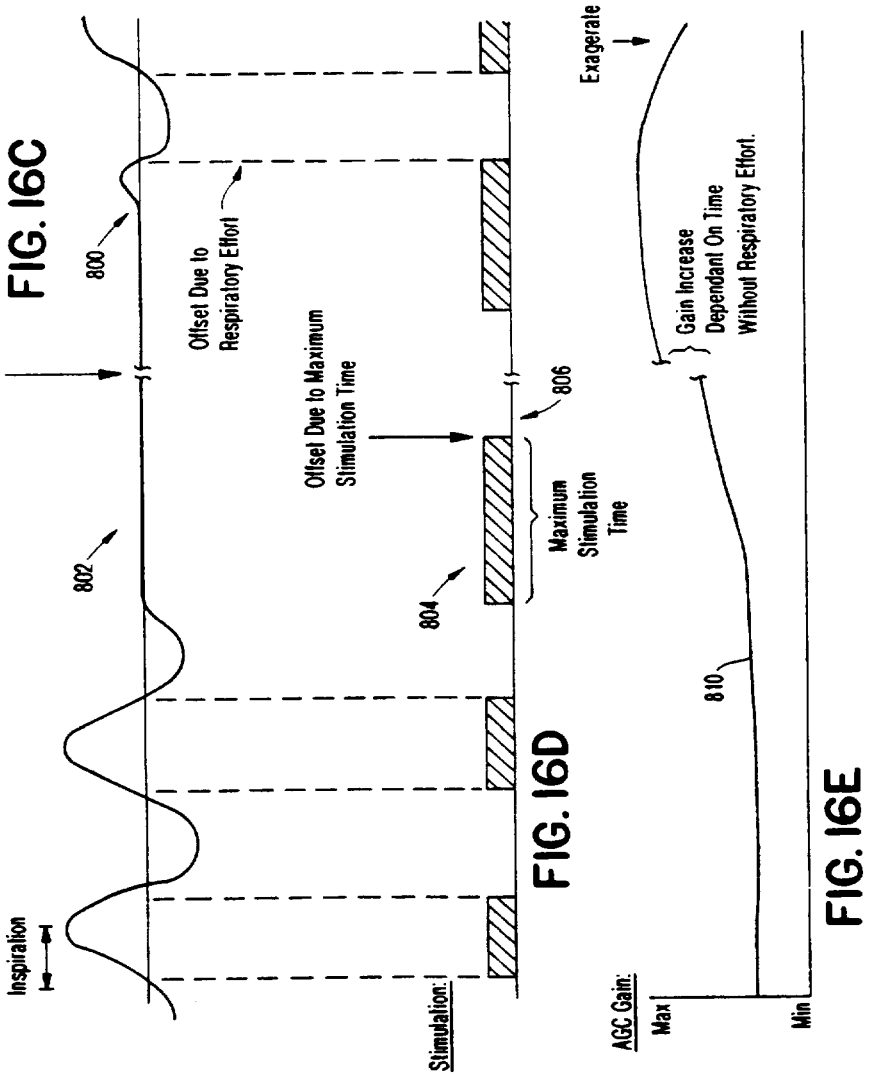


FIG. 16C

FIG. 16D

FIG. 16E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00330

FIG. 17A

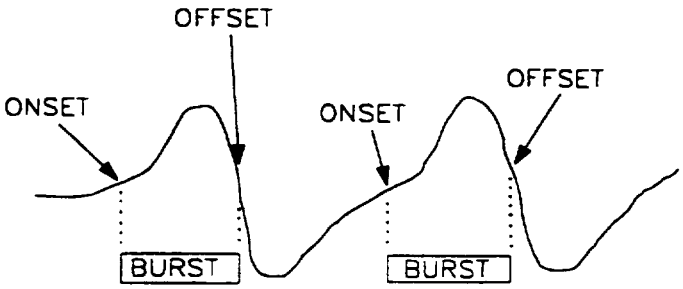


FIG. 17B

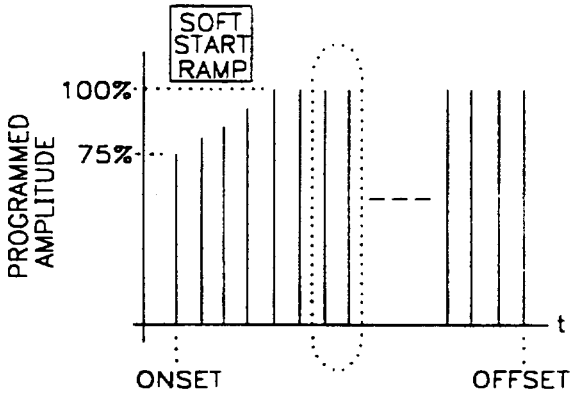


FIG. 17C

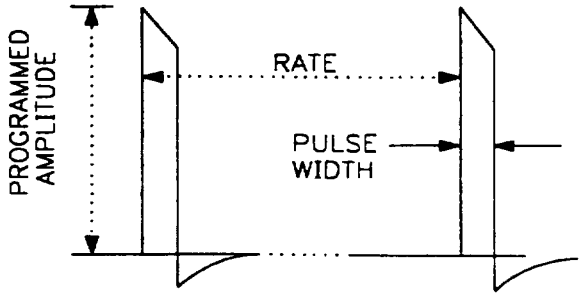


Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00331

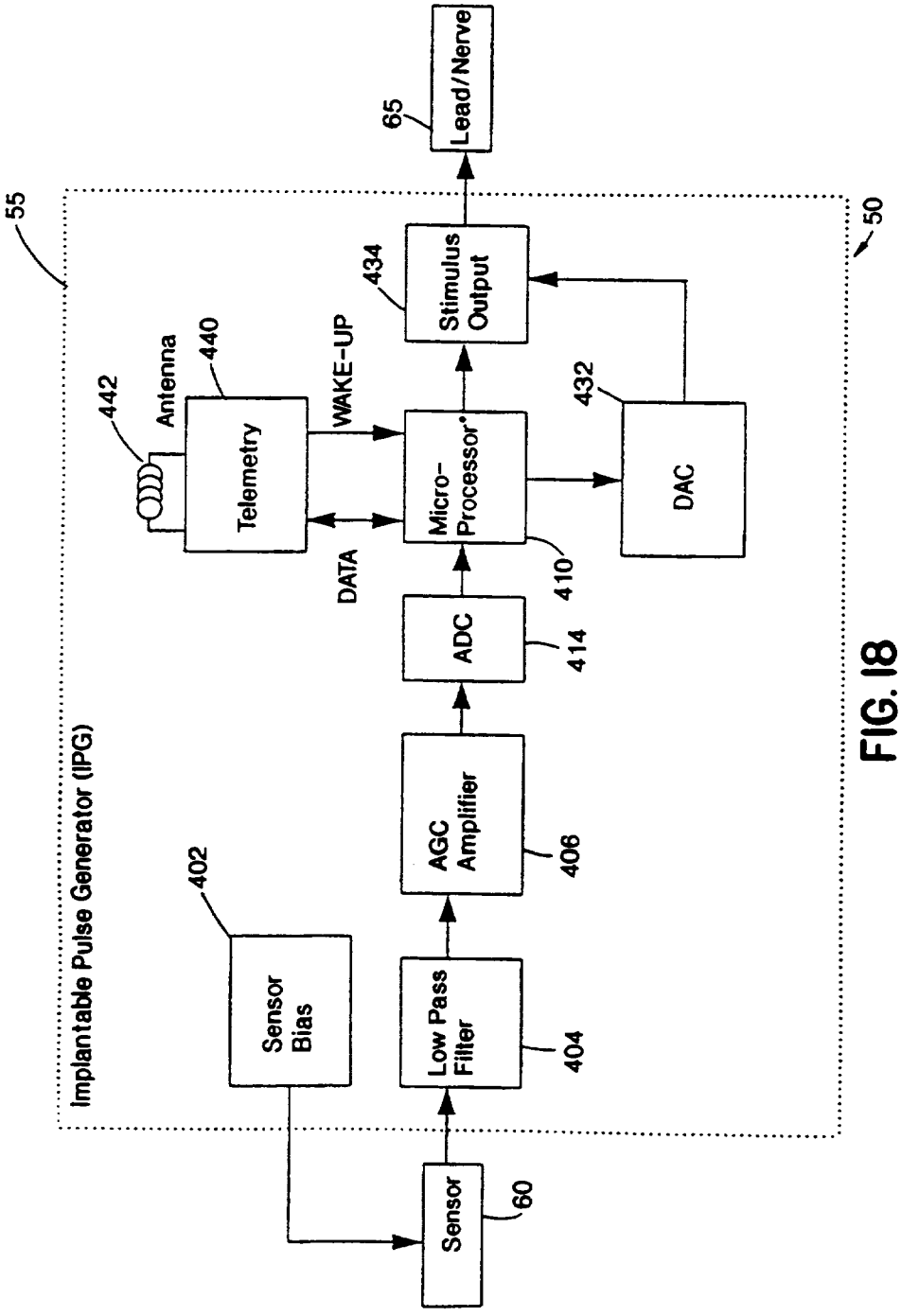


FIG. 18

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00332

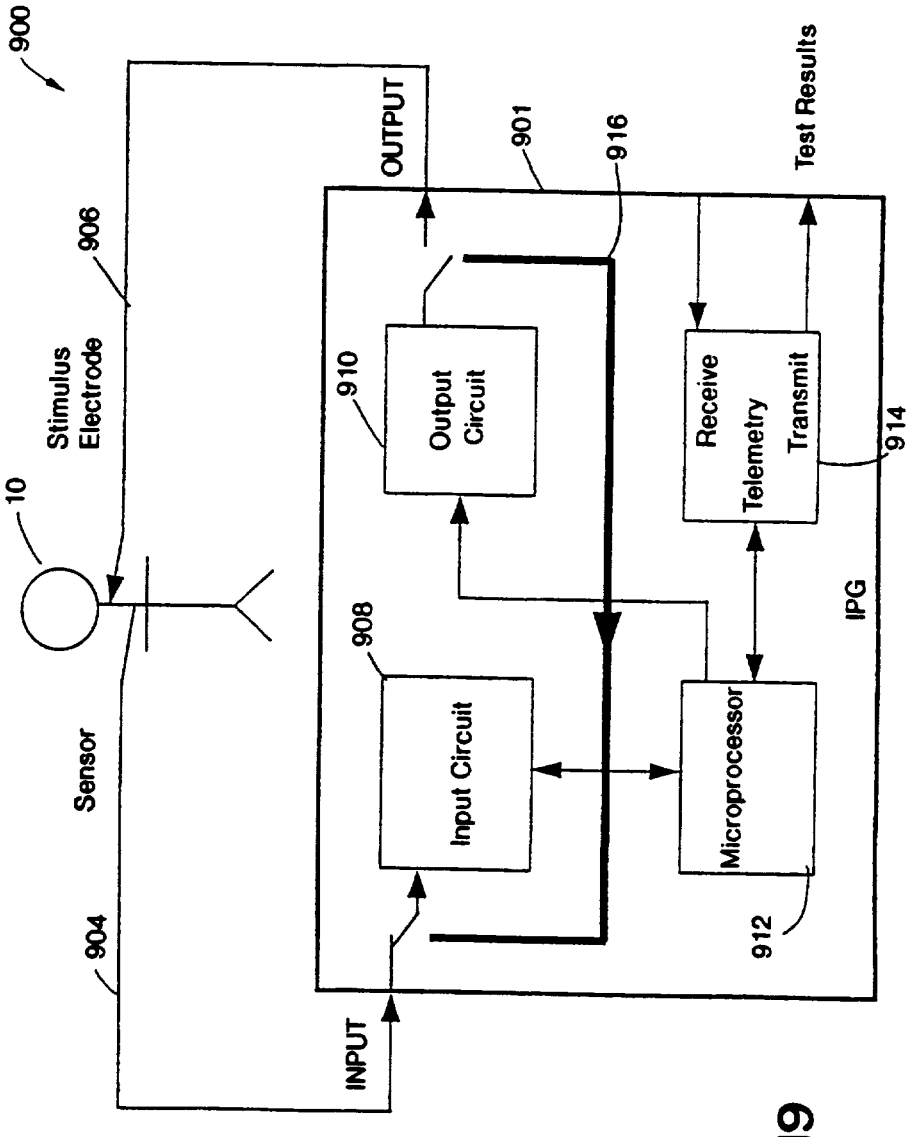


FIG. 19

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00333

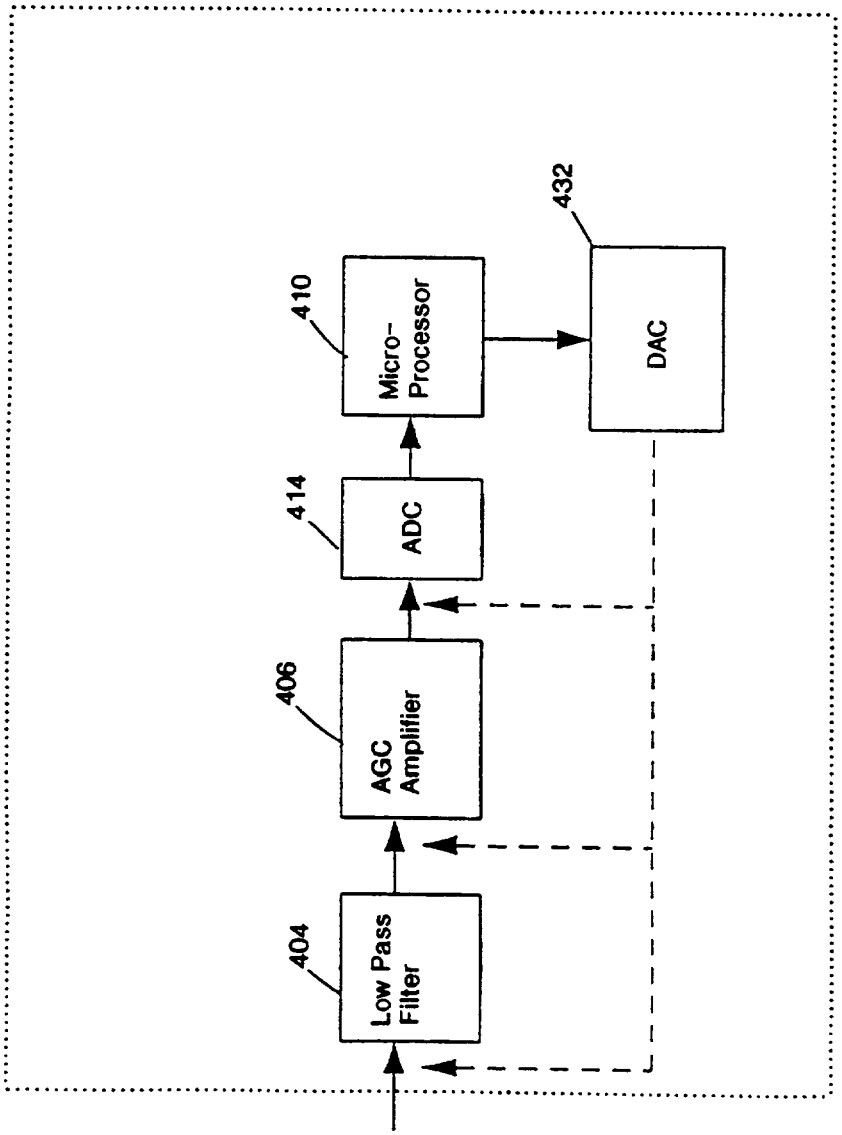


FIG. 20A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00334

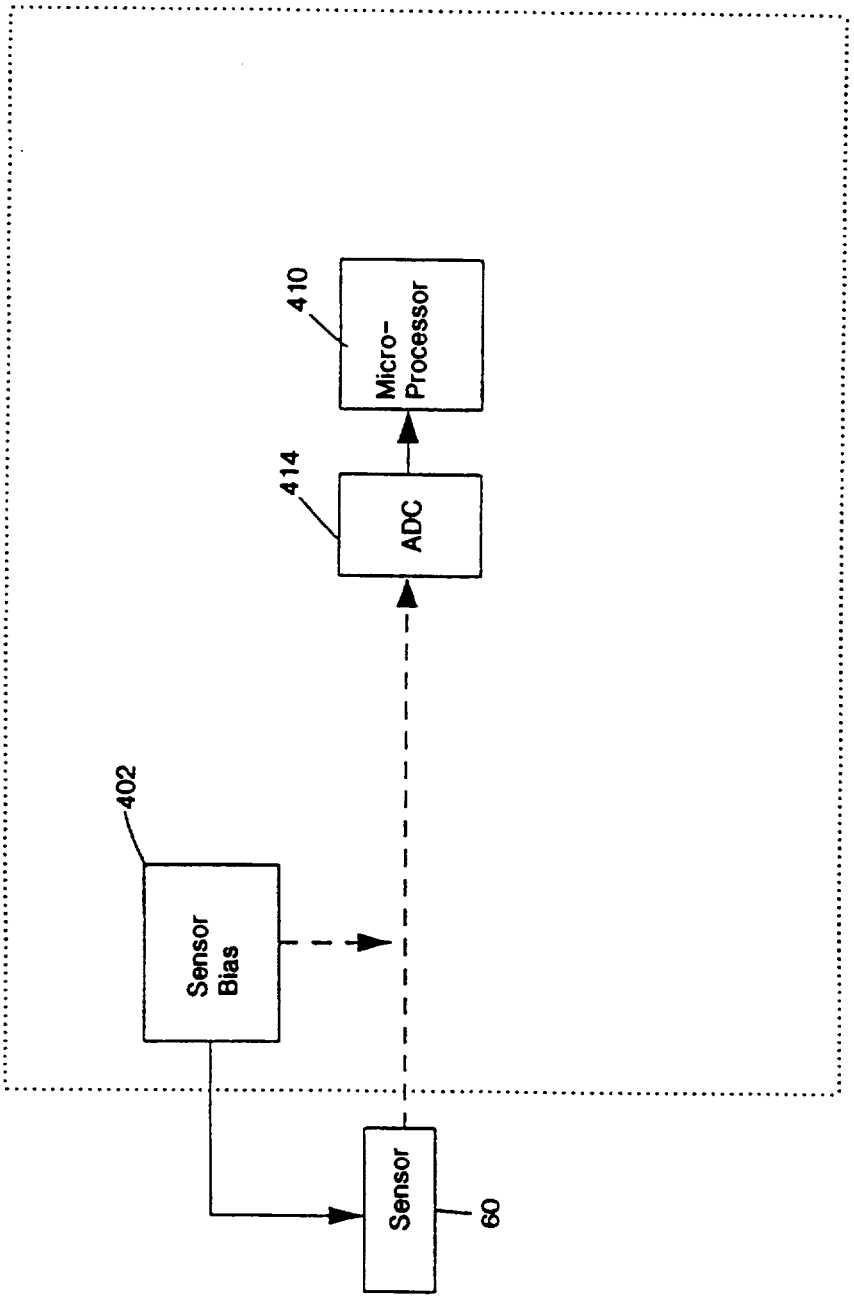


FIG. 20B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00335

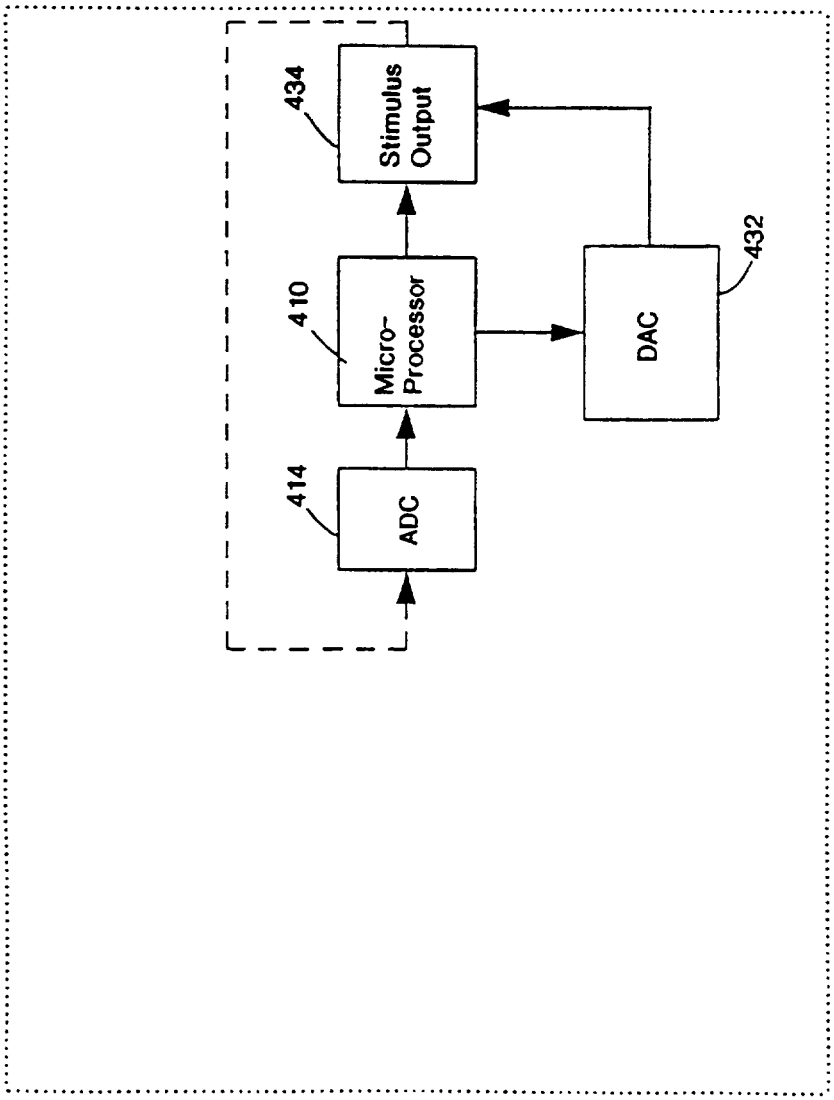


FIG. 20C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00336

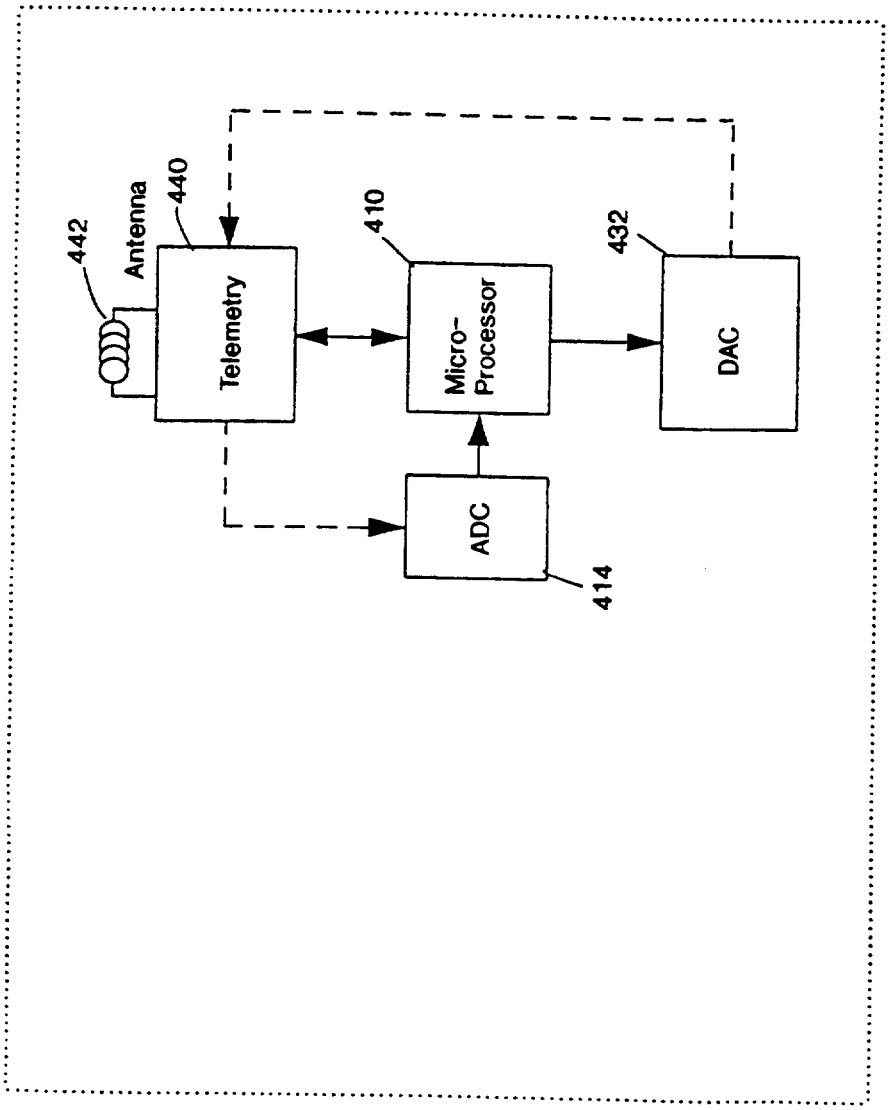


FIG. 20D

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00337

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/11618

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61N1/36 A61N1/372

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 702 979 A (MEDTRONIC INC) 27 March 1996 cited in the application see column 6, line 22-30 see column 7, line 18-21; figures 5,7	1,7
A		3-6,9, 10,13

X	WO 92 19318 A (CYBERONICS INC) 12 November 1992 see page 14, line 11-29; figures 1,4 see page 17, line 19 - page 18, line 19 see page 21, line 23 - page 22, line 24	1,3,4,6, 7,9,10, 13
A		5,11, 14-17, 22-25

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the prinoiple or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search	Date of mailing of the international search report
23 October 1997	10.11.97
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Allen, E

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Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00338

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/11618

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 483 969 A (TESTERMAN ROY L ET AL) 16 January 1996 cited in the application see column 6, line 24-53 see column 7, line 64 - column 8, line 29 see column 18, line 19-52; figures 5,6,8,34	1,3,4,6, 7,9,10, 13
X	see column 6, line 66 - column 7, line 4	14,16, 17,22
A	---	15,23-25
X	US 5 123 425 A (SHANNON JR JOHN L ET AL) 23 June 1992 see column 3, line 65 - column 4, line 5; figure 5	1,7

X	EP 0 671 687 A (SPACELABS MEDICAL INC) 13 September 1995 see page 13, line 1 - page 16, line 15; figures 1A,4A	14,22,29

X	US 5 097 830 A (EIKEFJORD ARILD J ET AL) 24 March 1992 see column 21, line 39 - column 22, line 41; figures 1,2	14,22
A		1,3,4,7, 9-11,15, 18-21, 23,26, 27,29

X	WO 94 27674 A (HEARTSTREAM INC) 8 December 1994 see page 5, line 16 - page 8, line 24 see page 10, line 22 - page 11, line 4 see page 12, line 23-34; figures 1,6,9 see page 26, line 15-29 see page 28, line 7 - page 29, line 17	14, 20-22, 27-29
A		15,18, 19,23,26

A	US 4 445 512 A (KRUPKA YAAKOV ET AL) 1 May 1984 see column 2, line 11-28 see column 2, line 40-47; figures 1,3	1,6,7,13

A	US 4 539 993 A (STANTON DAVID J) 10 September 1985 see column 2, line 63-66 see column 8, line 3-16	2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00339

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 97/11618

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0702979 A	27-03-96	US 5540731 A	30-07-96
WO 9219318 A	12-11-92	US 5335657 A	09-08-94
		AU 1904092 A	21-12-92
		CA 2103138 A	04-11-92
		EP 0584211 A	02-03-94
US 5483969 A	16-01-96	NONE	
US 5123425 A	23-06-92	AU 8427891 A	30-03-92
		WO 9203983 A	19-03-92
		US 5265624 A	30-11-93
EP 0671687 A	13-09-95	US 5579234 A	26-11-96
		CA 2144117 A	12-09-95
US 5097830 A	24-03-92	NONE	
WO 9427674 A	08-12-94	AU 6952594 A	20-12-94
		CA 2163346 A	08-12-94
		EP 0699092 A	06-03-96
		JP 9500798 T	28-01-97
		NO 954686 A	17-01-96
		US 5617853 A	08-04-97
		US 5591213 A	07-01-97
US 4445512 A	01-05-84	NONE	
US 4539993 A	10-09-85	DE 3341732 A	24-05-84
		FR 2536286 A	25-05-84

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00340

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : G06F 19/00 — A1

(11) International Publication Number: **WO 97/50049**

(43) International Publication Date: 31 December 1997 (31.12.97)

(21) International Application Number: PCT/US97/11148

(22) International Filing Date: 26 June 1997 (26.06.97)

(30) Priority Data:
08/674,494 26 June 1996 (26.06.96) US

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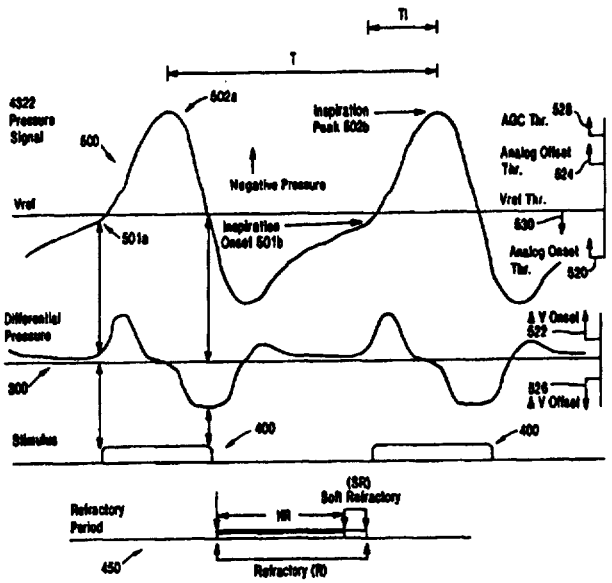
(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS

(57) Abstract

A method of predicting critical points in patient respiration includes monitoring at least one characteristic of a respiratory effort waveform of a patient to detect a respiratory event. A refractory period is defined that includes a hard refractory period during which time the respiratory event cannot be responded to and a soft refractory period following the hard refractory period. The respiratory event outside of the refractory period is detected as a function of a first set of predetermined parameters for the monitored at least one characteristic and the respiratory event within the soft refractory period is detected as a function of a second set of predetermined parameters for the monitored at least one characteristic. The respiratory event may be inspiration onset and the characteristic of the respiratory effort waveform monitored is at least one of slope and amplitude. The refractory period may be defined based on detection of inspiration offset and further may be defined based on inspiration offset, an average respiratory period, and an average time of inspiration. Further, stimulation may be provided in response to a detected inspiration onset. Another method of predicting critical points includes sampling the amplitude of the respiratory effort waveform of a patient. A sample signal is generated representative of at least one characteristic of the respiratory effort waveform based on each amplitude sample. The sample signals representative of the at least one characteristic of the respiratory effort waveform are monitored and a respiratory event is detected as a function of at least two sample signals. Apparatus and systems for use with such methods are also described.



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RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS

Field of the Invention

The present invention relates generally to medical devices and methods for use in the treatment of respiratory disorders. More particularly, the present invention pertains to methods of detecting respiratory effort for use in the treatment of respiratory disorders and devices regarding same.

Background of the Invention

Sleep apnea, an airway disorder, has been known for some time as a medical syndrome in two generally recognized forms. The first is central sleep apnea, which is associated with the failure of the body to automatically generate the neuromuscular stimulation necessary to initiate and control a respiratory cycle at the proper time. Work associated with employing electrical stimulation to treat this condition is discussed in Glenn, ADiaphragm Pacing: Present Status@, Pace, V.I, pp 357-370 (July-September 1978).

The second sleep apnea syndrome is known as obstructive sleep apnea. Ordinarily, the contraction of the dilator muscles of the upper airways (nose and pharynx) allows their patency at the time of inspiration. In obstructive sleep apnea, the obstruction of the airways results in a disequilibrium between the forces which tend to collapse airways (negative inspiratory transpharyngeal pressure gradient) and those which contribute to their opening (muscle contraction). The mechanisms which underlie the triggering of obstructive apnea include a reduction in the size of the superior airways, an increase in their compliance, and a reduction in the activity of the muscle dilator. The muscle dilators are intimately linked to the respiratory muscles and these muscles respond in a similar manner to a stimulation or a depression of the respiratory center. The ventilatory fluctuations observed during sleep (alternately hyper and hypo ventilation of periodic respiration) thus favors an instability of the superior airways and the occurrence of oropharyngeal obstruction. In sleep apnea the respiratory activation of the genioglossus muscle

has been particularly noted to be ineffective during sleep. The cardiovascular consequences of apnea include disorders of cardiac rhythm (bradycardia, auriculoventricular block, ventricular extrasystoles) and hemodynamic (pulmonary and systemic hypertension). This results in a stimulatory metabolic and mechanical effect on the autonomic nervous system. The syndrome is therefore associated with an increased morbidity (the consequence of diurnal hypersomnolence and cardiovascular complications).

A method for treatment of sleep-apnea syndrome is to generate electrical signals to stimulate those nerves which activate the patient=s upper airway muscles in order to maintain upper airway patency. For example, in U.S. Patent 4,830,008 to Meer, inspiratory effort is monitored and electrical signals are directed to upper airway muscles in response to the monitored inspiratory effort. Or, for example, in U.S. Patent 5,123,425 to Shannon, Jr. et al., a collar contains a sensor to monitor respiratory functioning to detect an apnea episode and an electronics module which generates electrical bursts to electrodes located on the collar. The electrical bursts are transferred transcutaneously from the electrodes to the nerves innervating the upper airway muscles. Or, for example, in U.S. Patent 5,174,287 issued to Kallok, sensors monitor the electrical activity associated with contractions of the diaphragm and also the pressure within the thorax and the upper airway. Whenever electrical activity of the diaphragm suggests that an inspiration cycle is in progress and the pressure sensors show an abnormal pressure differential across the airway, the presence of sleep apnea is assumed and electrical stimulation is applied to the musculature of the upper airway. Or, for example, in U.S. Patent 5,178,156 issued to Wataru et al., respiration sensing includes sensors for sensing breathing through left and right nostrils and through the mouth which identifies an apnea event and thereby triggers electrical stimulation of genioglossus muscle. Or, for example, in U.S. Patent 5,190,053 issued to Meer, an intra-oral, sublingual electrode is used for the electrical stimulation of the genioglossus muscle to maintain the patency of an upper airway. Or, for example, in U.S. Patent 5,211,173 issued to Kallok et al., sensors are used to determine the effectiveness of the stimulation of the upper airway and the amplitude and pulse width of the

stimulation are modified in response to the measurements from the sensors. Or, for example, in U.S. Patent 5,215,082 issued to Kallok et al., upon sensing of the onset of an apnea event, a stimulation generator provides a signal for stimulating the muscles of the upper airway at a varying intensity such that the intensity is gradually increased during the course of the stimulation. Or, for example, in U.S. Patent 5,483,969 issued to Testerman et al., stimulation of an upper airway muscle is synchronized with the inspiratory phase of a patient=s respiratory cycle using a digitized respiratory effort waveform. A fully implantable stimulation system is described in Testerman et al. with a sensor implanted in a position which has pressure continuity with the intrapleural space such as the suprasternal notch, the space between the trachea and esophagus or an intercostal placement.

However, even with these modes of respiratory disorder treatment, there remain many practical difficulties for implementing them and other therapy treatments in medically useful systems. In particular, if stimulation for respiratory disorder treatment occurs in response to detected points of a respiratory effort waveform, it is important to be able to accurately and reliably detect such critical points. For example, if stimulation for treating sleep apnea is to begin within a predetermined period of time of inspiration onset and no later than, for example, 200 ms after inspiration onset in order to avoid airway obstruction prior to stimulation, accurate detection is required. Although various techniques have been used for detecting critical points for initiating stimulation, such as, for example, in Testerman et al., there is always a need in the art for other and/or improved methods and devices for detection of such critical points and systems for treatment using such detection.

Summary of the Invention

A method of predicting critical points in patient respiration in accordance with the present invention is described. The method includes monitoring at least one characteristic of a respiratory effort waveform of a patient to detect a respiratory event. A refractory period is defined that includes a hard refractory period during which time the respiratory event cannot be responded to and a soft refractory period following the hard refractory period. The respiratory

event outside of the refractory period is detected as a function of a first set of predetermined parameters for the monitored at least one characteristic and the respiratory event within the soft refractory period is detected as a function of a second set of predetermined parameters for the monitored at least one characteristic.

In one embodiment of the method, the respiratory event is inspiration onset. Further, the at least one characteristic of the respiratory effort waveform monitored is at least one of slope and amplitude.

In another embodiment of the method, the step of detecting inspiration onset outside of the refractory period includes detecting inspiration onset as a function of monitored slope of the respiratory effort waveform. Further, the step of detecting inspiration onset within the soft refractory period includes detecting inspiration onset as a function of monitored slope and amplitude of the respiratory effort waveform.

In another embodiment of the method, the refractory period is defined based on detection of inspiration offset. Further, the inspiration offset is detected as a function of the monitored slope and amplitude of the respiratory effort waveform. Yet further, the detection of inspiration offset includes validating the detected inspiration offset by comparing the amplitude of the sampled respiratory waveform to a validating offset threshold.

Moreover, in another embodiment, the refractory defining step includes detecting inspiration offset, determining an average respiratory period, and providing an average time of inspiration. The refractory period, including the soft and hard refractory periods, are defined as a function of the detected inspiration offset, average respiratory period, and average time of inspiration.

A method for providing stimulation of a patient to treat respiratory disorders in accordance with the present invention includes monitoring slope and amplitude of a respiratory effort waveform of a patient to detect inspiration onset. A refractory period is defined including a hard refractory period during which time an inspiration onset cannot initiate stimulation and a soft refractory period following the hard refractory period. An inspiration onset outside of the refractory period is detected as a function of the slope of the respiratory effort waveform and an

inspiration onset within the soft refractory period is detected as a function of slope and amplitude of the respiratory effort waveform. Stimulation is provided in response to a detected inspiration onset.

In one embodiment of the method, the refractory period is defined based on detection of inspiration offset. Further, inspiration offset is detected as a function of the monitored slope and amplitude of the respiratory effort waveform.

In another method for providing stimulation of a patient to treat respiratory disorders, the method includes monitoring slope and amplitude of a respiratory effort waveform of a patient to detect inspiration onset and inspiration offset. A refractory period is defined that includes a hard refractory period during which time an inspiration onset cannot initiate stimulation and a soft refractory period following the hard refractory period. An inspiration onset is detected outside of the refractory period as a function of a first set of at least one of slope and amplitude criteria for the respiratory effort waveform and an inspiration onset is detected within the soft refractory period as a function of a second set of at least one of slope and amplitude criteria for the respiratory effort waveform. Stimulation is provided in response to detection of inspiration onset. The stimulation terminates as a function of detection of inspiration offset or a maximum stimulation time. The second set of criteria is set sufficiently sensitive relative to the first set of criteria such that stimulation, for one or more respiratory cycles, is applied as a function of the maximum stimulation time and the defined refractory period.

In another method of predicting critical points in patient respiration, the method includes sampling the amplitude of the respiratory effort waveform of a patient. A sample signal is generated representative of at least one characteristic of the respiratory effort waveform based on each amplitude sample. The sample signals representative of the at least one characteristic of the respiratory effort waveform are monitored and a respiratory event is detected as a function of at least two sample signals.

An apparatus for predicting critical points in patient respiration in accordance with the present invention is also described. The apparatus includes monitoring means for monitoring at least one characteristic of a respiratory effort

waveform of a patient and respiration detection means for detecting a respiratory event. The respiration detection means includes means for defining a refractory period including a hard refractory period and a soft refractory period following the hard refractory period, means for detecting the respiratory event outside of the refractory period as a function of a first set of predetermined parameters for the monitored at least one characteristic of the respiratory effort waveform, and means for detecting the respiratory event within the soft refractory period as a function of a second set of predetermined parameters for the monitored at least one characteristic of the respiratory effort waveform.

In various embodiments, the respiratory event may be inspiration onset, the at least one characteristic of the respiratory effort waveform monitored is at least one of slope and amplitude of the respiratory effort waveform, and/or the respiration detection means may include means for detecting inspiration offset as a function of the at least one monitored slope and amplitude of the respiratory effort waveform.

A system for providing stimulation of a patient to treat respiratory disorders in accordance with the present invention is also described. The system includes a sensor for providing a signal characteristic of a respiratory effort waveform of the patient, slope monitoring means for monitoring the slope of the respiratory effort waveform, amplitude monitoring means for monitoring the amplitude of the respiratory effort waveform, and respiration detection means for detecting inspiration onset. The respiration detection means includes means for defining a refractory period including a hard refractory period during which time an inspiration onset cannot be responded to and a soft refractory period following the hard refractory period, means for detecting inspiration onset outside of the refractory period as a function of the slope of the respiratory effort waveform, and means for detecting inspiration onset within the soft refractory period as a function of slope and amplitude of the respiratory effort waveform. The system further includes means for generating a stimulation signal in response to a detected inspiration onset and at least one electrode for delivering the stimulation signal to the patient.

Brief Description of the Drawings

Fig. 1 is a side sectional diagram of a patient having normal respiratory activity.

Figs. 2a-c are graphs of normal respiratory waveforms (shown with full normal inspiration at the peak). Fig. 2a shows a respiratory effort waveform and indicated phases of the respiratory effort waveform. Fig. 2b shows a graph of a respiratory airflow waveform with Fig. 2c showing the corresponding respiratory effort waveform.

Fig. 3 is a side sectional diagram of the patient of Fig. 1 at the onset of obstructive apnea.

Figs. 4a and 4b are respiratory waveforms of inspiratory effort showing normal inspiratory effort (Fig. 4a) and the change in normal inspiratory effort at the onset of an apnea event (Fig. 4b). Fig. 4c is a respiratory waveform showing respiratory airflow (as opposed to the respiratory effort waveform shown in Figs. 4a and 4b) in a patient during an apnea event.

Fig. 5 is a front sectional diagram of a patient showing the implantable components of the stimulation system in accordance with the present invention.

Fig. 6 is a block diagram of the stimulation system shown in Fig. 5 further including physician and patient programming units.

Fig. 7 is a diagram of one embodiment of the physician programming unit shown in block form in Fig. 6.

Fig. 8 is a diagram of one embodiment of the patient programming unit shown in block form in Fig. 6.

Fig. 9 is a diagram showing one embodiment of the IPG/stimulator shown in block form in Fig. 6.

Figs. 10a-10e are illustrations showing various positions or configurations for mounting the sensor shown in block form in Fig. 6 for sensing respiratory effort at a position in proximity to the posterior surface of the manubrium.

Figs. 11a-11d are various views of one embodiment of the sensor shown in block form in Fig. 6. Fig. 11a is a side view of the sensor, Fig. 11b is a cutaway view showing the sensing element portion of the sensor with the sleeve subassembly of the sensor cut partially away, Fig. 11c is a cross-section view of the sensing element portion of the sensor, and Fig. 11d is a cross-section view of the connector portion of the sensor.

Fig. 12a is a first embodiment of a block diagram of the signal processing circuitry of the IPG/stimulator shown in block form in Fig. 6, implemented in logic, for receiving the respiratory effort signal from the sensor and providing an inspiration synchronized stimulation signal to the electrode in accordance with the present invention.

Fig. 12b is a second embodiment of a block diagram of the signal processing circuitry of the IPG/stimulator shown in block form in Fig. 6, implemented with a microprocessor, for receiving the respiratory effort signal from the sensor and providing an inspiration synchronized stimulation signal to the electrode in accordance with the present invention.

Fig. 13a is a top level flow diagram of the algorithm/control logic shown in block form in Fig. 12a and 12b in accordance with the present invention.

Fig. 13b is a flow diagram of the IPG-ON block of the flow diagram of Fig. 13a.

Fig. 13c is a flow diagram of the Onset Detection block of the flow diagram of Fig. 13a.

Fig. 13d is a flow diagram of the Offset Detection During Stimulation block of the flow diagram of Fig. 13a.

Fig. 13e is a flow diagram of the Offset Detection block of the flow diagram of Fig. 13a when stimulation is not occurring.

Fig. 13f is a flow diagram of the Suspension, Artifact, Therapy Delay block of the flow diagram of Fig. 13a.

Fig. 13g is a flow diagram of the AGC Adjust block of the flow diagram of Fig. 13a.

Fig. 14 is a graph showing a normal respiratory effort waveform indicating various critical points detected in accordance with the present invention, various thresholds used in such detection, a normal differential pressure signal, a stimulus signal synchronously applied based on the critical points detected with respect to the respiratory effort waveform, and an illustration showing the definition of a refractory period, all in accordance with the present invention.

Fig. 15 is a graph showing a respiratory effort waveform having an artifact therein, a stimulus signal applied according to the present invention, and an illustration of the refractory period utilized to reject the artifact as an inspiration onset, all in accordance with the present invention.

Fig. 16a shows a normal respiratory effort waveform and stimulus applied according to the present invention. Fig. 16b shows a respiratory effort waveform of a patient with central sleep apnea and a stimulus applied according to the present invention utilizing a maximum stimulation time limit in accordance with the present invention. Fig. 16c shows a central sleep apnea occurring between cycles of respiratory effort. Fig. 16d illustrates stimulation periods for treatment of the central sleep apnea occurring in Fig. 16c. Fig. 16e shows AGC gain for the respiratory signal shown in Fig. 16c during the central sleep apnea.

Figs. 17a-c are graphs of one embodiment of a stimulation burst used for stimulating the patient according to the present invention.

Fig. 18 is a block diagram of one embodiment of a microprocessor based stimulation system.

Fig. 19 is a block diagram illustration of one diagnostic self test strategy for a therapy system.

Figs. 20a-d are block diagrams of various internal diagnostic self tests for the system shown in Fig. 18.

Detailed Description of the Embodiments

The following description relates generally to therapy systems including implantable therapy and stimulation systems. Although many portions of this description are particularly applicable to the treatment of respiratory disorders, such as sleep apnea, by administering stimulation of musculature in synchrony with

detected periodic events of the respiratory cycle, many portions of the system are equally applicable to other therapy systems. For example, automatic gain control, diagnostic testing, and methods for conserving energy are applicable to one or more other therapy systems such as, for example, drug delivery systems, blink stimulation systems, and cardiac related systems.

With respect to the synchronization of stimulation to the respiratory cycle of a patient to treat respiratory disorders, such synchronized stimulation requires a suitable respiratory sensor, proper placement of the respiratory sensor, and signal processing capability for converting the sensed respiratory effort signal from the sensor to a stimulation signal for use in stimulating the patient. In Fig. 1 and Figs. 2a-c, normal respiratory activity is depicted. In Fig. 1, a patient 10 has an airway 15 which remains patent during inspiration of air 20. Fig. 2a shows a typical respiratory effort waveform for two complete respiratory cycles. This analog waveform can be generated by various transducers such as, for example, a belt transducer worn snugly about the chest of the patient as used for detection and analysis of sleep apnea in sleep laboratories, an implanted pressure sensor such as that described in detail below, or any other transducer that provides a respiratory effort signal adequate for analysis to detect critical points thereof for use in the treatment of respiratory disorders, such as sleep apnea. Each wave of the waveform is characterized by a negative peak 30 on completion of expiration, a positive peak 35 on completion of inspiration (i.e. inspiration offset) and a turning point 40 which indicates the onset of inspiration (i.e. inspiration onset). Each wave of the waveform can therefore be separated into a period of respiratory pause 32, an inspiratory phase 33 and an expiratory phase 34. Respiratory effort waveforms having similar identifiable characteristics can be provided by monitoring other physiological signals such as intrathoracic pressure, intrathoracic impedance or electromyographic potentials. Other characteristics of the waveform could also be identified in connection with tracking and analyzing the respiratory waveform to monitor respiratory activity in sleep apnea treatment. In normal respiration, the respiratory effort waveform is related to airflow as set forth in Figs. 2b and 2c. In Fig. 2b a trace of normal respiratory airflow from a flow transducer is shown while

Fig. 2c shows the corresponding trace of the normal respiratory effort which produces the airflow.

In Figs. 3 and 4b, respiration in the same patient at the onset of an obstructive sleep apnea event is depicted. Fig. 3 shows the patient 10 and airway 15 with an airway obstruction 17 that is characteristic of an obstructive apnea event. Fig. 4a shows that in a normal respiratory effort waveform 43, the inspiratory peaks 45a-d are of approximately the same amplitude. By comparison in Fig. 4b, in a waveform 47, the inspiratory peaks 48a-d become significantly greater in amplitude at the onset of obstructive apnea than the immediately preceding inspiratory peak 49. This is reflective of the increased inspiratory effort undertaken by the patient in response to the difficulty of breathing through the obstructed airway.

In treatment of sleep apnea, the increased respiratory effort is avoided by synchronized stimulation of a muscle which holds the airway open during the inspiratory phase. Preferably, the muscle stimulated is an upper airway muscle, such as the genioglossus muscle stimulated by a cuff electrode placed around the hypoglossal nerve. However, there may be other upper airway muscles or nerves which can be used for stimulation to perform the same function and also other nerves or muscles apart from the upper airway which may be stimulated, such as the diaphragm, to treat respiratory disorders, such as, for example, sleep apnea. The effect of this stimulation on obstructive sleep apnea can be seen in the airflow trace of Fig. 4c. During a first period indicated as 46a, stimulation is enabled producing a normal respiratory airflow. During a second period indicated as 46b, stimulation is disabled causing obstruction of the airway and reduction in airflow volume (apnea). During a third period indicated as 46c, stimulation is resumed, restoring patency to the airway and increasing airflow volume.

Components, and one implantable configuration, of an implantable stimulation system 50 for providing inspiration synchronous stimulation treatment of sleep apnea are shown in Fig. 5. A block diagram of these components and other associated programming components of the system 50 for treating sleep apnea is shown in Fig. 6. As shown in Fig. 5, inspiration synchronous stimulation is

controlled by the implantable pulse generator (IPG)/stimulator 55. IPG 55, also shown in Fig. 9, provides inspiration synchronized stimulation, e.g. one or more stimulation pulses, through stimulation lead 52 to an electrode or electrode system 65 placed around the hypoglossal nerve 53 for stimulation of the genioglossus muscle of the upper airway. The electrode or electrode system 65 may be positioned with respect to any other respiratory nerve, or other nerve or muscle that provides the desired stimulation result for the respiratory disorder treated. The IPG 55, i.e. stimulator/controller, receives respiratory effort waveform information via a sensor lead 57 from a respiratory sensor or transducer 60 sensing the respiratory effort of a patient 10.

One associated component of system 50 includes a physician programmer 80, such as a laptop computer having programming software and communication capabilities for communicating with the IPG 55, and which is capable of programming the IPG 55 with various parameters in order to adapt the system for treatment of a particular patient. The system 50 of Fig. 5, is therefore adapted to be programmed using the physician programmer 80 as shown in Figure 7 by telemetry via transmitting/receiving element 81 electrically coupled to the processor based programmer 80. Thereafter, the system 50 is used each night by the patient to prevent the closure of the upper airway during the inspiratory phase of the respiration cycle.

It will be apparent to those skilled in the art that such a system must be made to be easy to use by the patient and since it is used without constant medical supervision, it must be able to adapt to many different operating conditions. Therefore, the system 50 includes another associated component, i.e. patient programmer 70, as shown in Fig. 8. The patient programmer 70 gives the patient the capability to turn the stimulator ON/OFF, adjust the stimulation amplitude within preset limits programmed by the physician and adjust any other stimulation parameters or parameters of the IPG 55 as may be allowed by the physician, such as, for example, stimulation pulse rate, pulse width, dose time, therapy delay time. The patient programmer 70 provides both a visual and audio confirmation of communication with the stimulator and further may include other patient control

elements for controlling parameters of the treatment of sleep apnea. In addition, as described further below, the patient turning the power on for initiation of the treatment using the patient programmer 70 starts an automatic self stimulation test and/or an automatic diagnostic self test of the components of the system 50. Such a diagnostic self test may be performed at any time, in addition to the initiation of the treatment period by the patient. Further, such self stimulation test and diagnostic tests are equally applicable to other therapy systems in addition to the treatment of respiratory disorders, such as sleep apnea.

The pressure sensor or respiratory transducer 60, may be a dynamic relative pressure sensor such as that disclosed in U.S. Patent 4,407,296 to Anderson or U.S. Patent 4,485,813 issued to Anderson et al which are incorporated herein by reference in their entirety. The pressure sensor 60 is surgically implanted in a region that has pressure continuity with the intrapleural space such as the suprasternal notch, the space between the trachea and esophagus or attached to either of the trachea or esophagus, an intercostal placement, or secured as shown in Figs. 10a-10e in a position for sensing pressure at the posterior side of the manubrium as described in further detail below. The suprasternal notch 62 and manubrium 63 of sternum 64 as shown in Figure 5, are well known structures on the upper chest that are in anatomical continuity with the intrapleural space. It is also well known that changes in intrapleural pressure provide a characteristic respiratory effort waveform. The location for placement of the sensor is, at least in part, chosen as a function of delay, i.e. propagation time of a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position and as a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. filtering necessary to remove waveforms other than the waveform of the sensed characteristic, such as cardiac waveform activity.

Preferably, the pressure sensor 60 utilized is a pressure sensor assembly or sensor lead 115 similar to the sensor lead sold under the trade designation of Medtronic Model 4321, available from Medtronic, Inc., Mpls., MN as modified and represented in Figs. 11a-11d. The pressure sensor assembly 115

includes a sensing section 120, a lead anchoring section 122, and a connector section 124. A flexible lead body 121 forms a part of each section. The sensing section 120 includes, as shown in the detail views of Figs. 11b and 11c, a relative pressure sensing element 126 which is mounted at an open distal end 123 of assembly 115 opposite the connector section 124. The relative pressure sensing element 126 senses respiration pressures through the use of piezo-electric crystals attached to a sensor diaphragm lying perpendicular to a longitudinal axis 125 extending through assembly 115. Pressures are transmitted to the diaphragm through the portholes 128 on both sides of the sensing element 126. Pressure transmits from the portholes 128 to the diaphragm via a medical adhesive 132, such as silicone rubber, which fills the nose cavity of the pressure sensing element 126. The sensor is driven, for example, with a fixed bias current on which the AC pressure signal is coupled onto. Such a fixed sensor bias can range from about 8FA to about 100FA. Such a sensor has a nominal output of about 3mV/mmHg over the usable bandwidth of about 0.1 to about 100Hz.

The sensing element 126 has coil leads 136 electrically connected thereto. The coil leads 136 are provided within bilumen tubing 138. The bilumen tubing 138 at the sensor section end and the sensing element 126 are positioned in a flexible tube 130 by medical adhesive 132 which also fills the cone of the sensing element 126 and covers the outer portions of the sensing element 126. There is no exposed metal surface of the sensing element 126 and the sensor is electrically isolated from the patient.

As shown in Fig. 11d, a connector assembly 168, such as, for example, a bipolar IS-1 compatible connector assembly, is electrically connected to the lead body 121, such as by crimping, to coil leads 136 in connector section 124 of the sensor assembly 115. Any connector assembly may be utilized that is compatible with a connector port of the IPG 55. The connector includes sealing rings 167 to ensure that body fluids do not disrupt the sensor assembly 115 and IPG 55 connection.

A sleeve attachment subassembly 140 has the sensing element 126 and a portion of the lead body 121 positioned therein. The sleeve subassembly extends from a distal surface 174 of the sensing element 126 at the open distal end 123 to beyond the interface between the lead body 121 and sensing element 126. The sleeve attachment subassembly 140 includes an outer threaded sleeve 142, an inner threaded sleeve 144, and a soft umbrella ring 146. The sleeve attachment subassembly 140 is mounted on the outer surface of the flexible tube 130 with medical adhesive 132. The inner surface of the inner threaded sleeve 144 is abraded to provide adhesion with the medical adhesive 132 to stably mount the sensing element 126 in the subassembly 140. The inner threaded sleeve 144 has holes 148 about the longitudinal axis therethrough for molding a flexible element, i.e. soft umbrella ring 146, about the distal open end of the inner threaded sleeve 144.

The soft umbrella ring 146 may be formed of silicone rubber and includes a flexible outer umbrella portion 152 that extends outward relative to the longitudinal axis and rearwardly relative to the distal open end of the inner threaded sleeve 144 and a fixed portion 154 of the umbrella ring 146. The flexible outer umbrella ring 152 performs the function of preventing tissue and bone growth over the distal open end 123 of the sensor assembly 115 when implanted. The soft umbrella ring 146 is preferably formed of a radio opaque material so that it can be seen in imaging processes throughout implantation and explanation. Further, the umbrella ring 146 may include a treatment to prevent tissue and bone overgrowth of the sensor 126. Such treatment may include treatment with a steroid, such as heparin, chemical coatings, surface roughening, or any other treatment that reduces such tissue and bone overgrowth.

The flexible element, i.e. umbrella ring 146, may be of any configuration that prevents bone and tissue overgrowth. Further, if the sensor is implanted into a drill hole in the manubrium as described below, the flexible element must be capable of being inserted and removed through the drilled hole. For example, the flexible element may be a donut shape or a simple flange

extending outward relative to the longitudinal axis 125 at the distal open end of inner threaded sleeve 144.

The outer threaded sleeve 142 includes a threaded portion 156 and an unthreaded flange portion 158 extending substantially perpendicular to and outward relative to the longitudinal axis 125 of the sensor assembly 115. The outer and inner threaded sleeves 142 and 144 are utilized for adjusting the length of the subassembly 140 along the longitudinal axis 125. Further, they provide for anchoring the sleeve subassembly, i.e. securing the sensor, in the manubrium as described further below with the unthreaded flange portion 158 of the outer threaded sleeve 142 providing means for direct or indirect contact at the anterior side of the manubrium and with the flexible element 146 providing for direct or indirect contact at the posterior side of the manubrium. The adjustability is important as the thickness of the manubrium varies from patient to patient. One or more holes 160 in the flange portion 158 are available for anchoring the sensor section 120 by suture to tissue or by bone screw to the anterior side of the manubrium. The outer threaded sleeve 142 and the inner threaded sleeve 144 are preferably formed of stainless steel, but can be any biocompatible material, preferably a rigid biocompatible material.

In alternative configurations, the flange portion 158 may include a soft cover thereabout or may be formed of a different shape as long as it still performs the function of direct or indirect contact with the manubrium to hold the sensing element 126 in position and/or includes means for attachment by a bone screw, suture, or other securing means. For example, the flange portion 158 may be a tab structure or multiple tabs extending away from and substantially perpendicular to the longitudinal axis 125 from the end 159 of threaded portion 156.

Further, the adjustability function of the inner and outer sleeves 142 and 144 may be provided by any structure that allows a length of the sleeve to be adjusted and then capable of being fixed at a particular length. For example, two telescoping members or sliding members may be used with, for example, a ratchet technique coupling the two and providing fixation at a particular length.

The anchoring section 122 includes lead body anchoring sleeve 164 slidably mounted on the lead body 121 and having suture grooves 165 for the anchoring of the lead body 121 when implanted. The lead body 121 is flexible such that it can make a sharp right angle from the sleeve subassembly 140 at the anterior region of the manubrium when the sensor assembly 115 is implanted to avoid skin erosion and bulge thereat. For example, the lead body 121 may include pentifilar conductor coils 136 in a bilumen silicon tubing. Alternatively, the lead body 121 may include a right angle attachment at the anterior region of the manubrium 63 for providing direction to the lead body as it extends from the drilled hole at the anterior of the manubrium 63.

One skilled in the art will recognize that various connection techniques for connecting the sensing element 26 to the IPG 55 may be utilized. For example, fiber optic connection may be used, RF techniques may be used, and also techniques using the body mass itself to propagate a signal between components may be used. With use of at least some of these connection techniques, a lead extending from the anterior of the manubrium would not be present. Without the need for a lead, the sleeve subassembly 140 for positioning and anchoring the sensor in the drilled hole of the manubrium 63 could take the form of any mounting element having an adjustable length. The mounting element would no longer need to have an opening therethrough, such as a sleeve, but could take the form of, for example, a spring loaded elongated member with one open end for holding the sensor. In other words, the mounting elements used to mount the sensing element may take any elongated form with an adjustable length and elements for securing it in the manubrium hole by direct or indirect contact with the anterior and posterior surfaces of the manubrium.

The pressure sensor 60, such as pressure sensor assembly 115, or any other suitable sensor for providing a signal characteristic of respiratory effort, may be implanted in various positions, such as those previously mentioned and further including attachment to the esophagus or trachea or in a position therebetween, or to any other soft tissue in the suprasternal notch. Various positions for the sensor are described in U.S. Patent Serial No. 08/310,177 entitled

AMethod and Apparatus For Detecting and Treating Obstructive Airway Disorders@ incorporated herein by reference in its entirety. Further, the sensor 60 may be positioned as shown in the Figs. 10a-10e. Preferably, the pressure sensor assembly 115 is implanted through a drilled hole in the manubrium 63 as shown in Figs. 10a and 10b. However, the sensor assembly 115 could be implanted through the sternum 64 at any location thereof or through any other bone such that the sensing element 126 is in communication with the intrathoracic region or a region with pressure changes characteristic of respiratory effort.

As shown in Fig. 10b, the brachiocephalic vein 195, also known as the inominant vein, is located in a region on the posterior side of the manubrium 63 and erosion of the vein is to be avoided. The present invention is configured to allow sensing in the region where this vein is located. The pressure sensor 60 is positioned in proximity to the vein, however, the term in proximity to the vein means that the sensing element is positioned in the region of the vein but is configured and/or positioned such that erosion of the vein is avoided.

To implant the pressure sensor assembly 115, a small pocket posterior to the manubrium 63 via the suprasternal notch 62 is created, such as by blunt dissection. A hole 185 is drilled perpendicularly through the superior aspect of the manubrium 63 and at the midline of the manubrium 63. It is desired that the sensor element 126, be placed near the top 187 of the manubrium 63 so that the pocket created on the posterior side of the manubrium 63 is minimized lessening surgical excavation risk and lessening the effects of cardiac signals which are stronger at lower portions. Further, by implanting the sensor assembly 115 toward the top of the manubrium 63, the implanter can see the position of the umbrella ring 146 easily, especially with mirrors. During drilling, a retractor is placed on the posterior side of the manubrium 63 to protect intrathoracic structures. Although placement of the sensing element 126 near the top 187 of the manubrium is preferred, the sensing element may be positioned anywhere along the length of the sternum 64, although the manubrium is preferred. More preferably, the sensing element is positioned about 0.5 cm to about 3 cm from the top 187 of the manubrium.

When implanting the sensor, the length of the sensor section 120 of the pressure sensor assembly 115 (i.e. length of subassembly 140) is maximized by turning the outer threaded sleeve 142 with respect to the inner threaded sleeve 144 of the sleeve attachment subassembly 140. The sleeve attachment subassembly 140 of the sensing section 120 is then inserted in the drilled hole 185 and the sensor section length is adjusted such that the soft umbrella ring 146 is in direct or indirect contact with the posterior surface of the manubrium 63. When the sensor section 120 is inserted into the drilled hole 185, the umbrella ring 146 collapses or is compressed against the side of the sleeve subassembly 140 and will spring outward upon protruding into the posterior side of the manubrium 63. The umbrella ring portion 152 will act as an anchor and will prevent bone and tissue growth over the sensor opening. The implanter can utilize a finger to make sure the umbrella ring 146 is flush with the posterior surface and to stabilize the sensor while the outer threaded sleeve 142 is turned to adjust the length of the sleeve attachment subassembly 140 of the sensor section 120 to the thickness of the patient=s manubrium 63. The distal tip 174 of the sensing element 126 should protrude in the range of about 1 mm to about 3mm posteriorly from the manubrium 63. A position less than 1 mm results in a greater chance of tissue or bone overgrowth of the sensing element 126. The distal tip 174 of the sensing element 126 is flush with the open end of the inner threaded sleeve 144. The sensor assembly 115 can then be anchored on the anterior side of the manubrium by a suture or bone screw through the hole 160 of the unthreaded flange 158 of the outer threaded sleeve 142. The lead body 121 can be anchored with use of suture grooves 165 on the anchoring sleeve 164.

With the IPG 55 implanted in a position on the upper chest, such as just below the clavicle 61 as shown in Fig. 5, the lead body 121 of the pressure sensor assembly 115 is inserted in a tunnel created from the manubrium 63 to a pocket created for implanting the IPG 55. When the IPG 55 is implanted, the connector section 124 of the pressure sensor assembly 115 is connected to sensor port 58 of the IPG 55.

Figs. 10c-10e show alternative configurations for implanting the pressure sensor 60 of the implantable stimulation system 50. As shown in Fig. 10c, a pressure sensor 60 has a sensing element 197 positioned posterior to the manubrium 63 with the lead body extending over the top 187 of the manubrium 63. The lead is then brought down the anterior portion of the manubrium 63. Various anchors 178 are utilized to hold the sensing element 197 in place behind the manubrium 63.

As shown in Fig. 10d, the sensor 60 is positioned in a manner similar to that shown with respect to the drill through technique described with reference to Figs. 10a and 10b. However, in this configuration, the drill hole 180 is made at an angle through the manubrium 63.

As shown in Fig. 10e, the sensor 60 is positioned substantially as described in Fig. 10c. However, in order to protect against erosion of fragile veins posterior of the manubrium, the sensing element 197 and a portion of the lead body extending therefrom are covered with a soft guard 182. The guard 182 may serve the function of anchoring the sensor 60 as well as preventing any erosion of the brachiocephalic vein 195. The distal end 196 of the guard is open.

As demonstrated by the various configurations shown, many various positions for implant of the sensor 60 are possible behind the manubrium yet while avoiding the fragile veins. The present invention contemplates the positioning and securing of various sensing elements with respect to the manubrium 63 to sense pressure or any other characteristic for obtaining a respiratory effort waveform at a region posterior of the manubrium 63. The sensing elements are preferably placed in close proximity to the posterior surface of the manubrium 63.

The electrode or electrode system 65 of the implantable stimulation system 50 may be any conventional electrode system for stimulation of muscles to treat respiratory disorders, such as sleep apnea. As previously described, although various respiratory muscles may be stimulated, stimulation of the genioglossus muscle is utilized herein for treatment of sleep apnea. For example, the electrode system 65 utilized may be a Model 3990B Half Cuff Nerve Electrode available from Medtronic, Inc., Mpls., MN. This electrode and other suitable electrode

configurations are described in U.S. Patent 5,344,438 to Testerman et al., entitled ACuff Electrode@ and incorporated entirely by reference herein. This electrode is utilized for placement around a respiratory motor nerve, such as the hypoglossal nerve 53, with the stimulation lead 52 for connection to the stimulation port 59 of IPG 55 as shown in Figs. 5 and 9. One or more stimulation pulses are delivered to the electrode 65 by the IPG 55 and transferred to the nerve resulting in opening of the airway during respiration. It should be readily apparent to one skilled in the art that any suitable electrode for stimulating the desired muscle may be utilized with the stimulation system 50 according to the present invention. For example, the electrode may be a full cuff electrode or any other electrode configuration for capturing a respiratory motor nerve, such as the hypoglossal nerve. Further, with respect to any other neuromuscular stimulation systems which may benefit from the present inventions described herein, the electrode(s) may include any electrode(s) that provide the desired stimulation for such systems.

The IPG 55 includes signal processing circuitry 200, including detection algorithm or control logic 216, as shown in block diagram form in Fig. 12a, respectively, and functionally shown in the flow diagrams of Figs. 13a-13g. The signal processing circuitry 200 processes the respiratory effort signal provided by the pressure sensor 60, such as pressure sensor assembly 115, and provides inspiration synchronized stimulation via electrode or electrode system 65 for the treatment of respiratory disorders.

To achieve adequate treatment of sleep apnea, the stimulation is initiated by detection of inspiration onset, for example, within a predetermined time of the actual physiological onset, for example 200 ms. Sensing onset 200 ms early (i.e. >predictive=) is desired. Stimulation is terminated as a function of a detected inspiration offset. Slight errors of approximately 300 ms or less in timing causing early offsets, late offsets, or early onsets are typically permitted by the treatment system. Late onsets, however, are preferably no later than, for example, 200 ms. The requirement that detection of onsets be no later than, for example, 200 ms, is necessary to avoid airway obstruction prior to stimulation. The timing to recruit a muscle to overcome obstructions which occur prior to stimulation force such a

requirement. The present invention provides means for predictively detecting onsets to meet this requirement. In addition to rigid timing requirements, the detection algorithm operates reliably in the presence of cardiac artifacts and motion artifacts.

The description herein is set forth in a manner such that stimulation for treatment of sleep apnea occurs substantially continuously and synchronous with inspiration throughout the treatment period, except for time of nonstimulation such as suspension, dose, therapy delay, etc. as determined by the algorithm described below. The treatment period is the time period from when the treatment is turned on to when the treatment is turned off. However, many of the concepts described herein are equally applicable to sleep apnea treatment systems wherein the onset of apnea is detected in some manner and stimulation only performed after such detection of apnea. For example, waveform analysis could be performed to determine when an apnea is about to occur and then treatment by stimulation could be initiated using concepts described herein. Such detection of the onset of sleep apnea is described in U.S. Patent 5,483,969 to Testerman et al. which is incorporated herein by reference in its entirety.

The detection algorithm or control logic 216 of the signal processing circuitry 200, which will be described in detail below, makes significant reference to Fig. 14. Therefore, a brief description of Fig. 14 is appropriate at this point to introduce the elements thereof and provide a brief description of some of the functionality of the control logic 216. Fig. 14 includes a normal respiratory effort waveform 500 characteristic of the signal sensed by the pressure sensor 60, a differential pressure signal 300, an illustrative stimulus window 400 during which one or more pulses are generated for treatment of airway disorders synchronized with inspiration onset 501a and inspiration offset 502a, and a refractory period illustration wherein a refractory period (R) is defined during at least a part of the expiratory and pause periods 34 and 32 (Fig. 2a) of the respiratory cycle.

Further, Fig. 14 shows the respiratory period (T) which is represented as the period from inspiration offset 502a to inspiration offset 502b, the time of inspiration (TI) which is shown as the time from inspiration onset 501b to

inspiration offset 502b, and a variety of thresholds which are utilized by the detection algorithm/control logic 216 to control and provide inspiration synchronous stimulation. Such thresholds include analog onset threshold 520 and)V (i.e. slope) onset threshold 522 used for detection of inspiration onset, analog offset threshold 524 and)V offset threshold 526 used for detection of inspiration offset (i.e. latched offset), Vref threshold 530 or zero crossing threshold used for validating or declaring a detected latched inspiration offset, and AGC amplitude threshold 528 used in updating gain of the respiratory signal from the sensor 60.

)V is representative of the slope of the respiratory effort waveform 500. For illustration, the)V values can be generated by sampling the sensor output during a sample period, such as for example every 10 to 70 ms. The sampled value is then compared to the previously sampled value to obtain the net change in voltage (i.e. change in intrathoracic pressure) over the sample period. The net change,)V, is thus the pressure signal slope and therefore, representative of slope of the respiratory effort waveform.

The normal respiratory effort waveform 500 shows the amplitudes and slopes which are characteristic of inspiration onset and offset. The polarity of the voltage respiratory effort waveform 500 in Figure 14 is inverted with respect to the polarity of the actual physiologic pressure measured by sensor 60. Inspiration is represented as a positive going voltage which indicates a negative inspiration pressure. Expiration is shown as a negative going voltage which indicates a positive expiration pressure. The stimulation system 50 includes automatic gain control (AGC) that references or normalizes the respiratory effort signal. For example, the signal may be normalized such that the positive signal peak is 1.2 volts, baseline (Vref) is 0 volts (DC), and the negative signal peak is at approximately -1.2 volts. In other words, a 2.4 peak to peak signal is provided. The AGC is described in further detail below and is applicable to any variable input signal characteristic of a periodic physiological parameter and is not limited to only the respiratory effort pressure signal described herein. The normalization of such signals is particularly advantageous when used in systems where timing detection is based on comparison to signal thresholds.

Inspiration onset 501 is characterized as a rapid change in slope at an amplitude above a predetermined level, i.e. analog onset threshold 520 (Figure 14), and is detected by the control logic of the present invention as a function of such characterization. Inspiration offset 502 is characterized by a negative change in slope above a predetermined amplitude, i.e. analog offset threshold 524 (Figure 14). A sustained non-positive slope and an amplitude above the predetermined amplitude typically indicate an offset 502 and an offset is detected and latched by the control logic of the present invention as a function of such characterization.

Physiological artifacts caused by cardiac pressures and body motions add complexity to the respiratory effort waveform. Cardiac artifacts produce slope changes very similar to onset and offset slope changes. However, the slope is not typically sustained for the same duration. The respiratory amplitude level is typically not altered by the cardiac artifacts. Therefore, the combination of sustained slope and amplitude provides information to differentiate between inspiration events (onsets and offsets) and cardiac artifacts to avoid stimulation at the improper time. The control logic, for example, by using consecutive)V samples to detect offsets and onsets, utilizes such characteristics to prevent misdetection of valid onsets and offsets, i.e. offsets and onsets that are not artifact onsets and offsets.

Motion artifacts are similar to inspiration in both sustained slope and amplitude. Figure 15 displays a motion artifact 542 on a respiratory waveform 540. Depending on the source of the artifact (slow or fast body movement, etc.) the slope and amplitude may be sufficient to satisfy the characteristics of either an inspiration onset and/or offset and stimulation based on such an artifact is to be avoided. As illustrated in Fig. 15, the control algorithm in accordance with the present invention utilizing a defined refractory period minimizes stimulation from occurring based on artifacts like artifact 542. Such distinguishing of the artifact from normal respiration will become apparent from the detail description of the control logic 216 below.

The techniques used by the algorithm or control logic 216 to distinguish motion artifacts are based on known physiological parameters of breathing during sleep. First, respiratory rate is known to be very stable and consistent during sleep. For example, a typical breath-to-breath rate variation of 15 % has been established, with maximum variations as high as 35 %. Periods of wakefulness will have more breath-to-breath variations, coughs, sighs, etc., but stimulation is not necessary nor desirable while the patient is awake. The detection algorithm establishes the presence of a stable respiratory rate or respiratory period in order for stimulation to occur when signal onset characteristics are present, i.e. stimulation is suspended if a stable respiratory rate or respiratory period is not detected. Second, as the ratio between time of inspiration / total respiratory period (TI/T) is generally known, such as for example, between 0.30 and 0.40, a refractory period (i.e. blanking period after inspiration has occurred), that includes both hard and soft refractory periods, is utilized to detect or predict onset at a time just prior to the next expected onset. These two ideologies, along with others as will become apparent from the further detail below, are utilized by the algorithm to reject motion artifacts.

The IPG 55, shown in Fig. 9, is any IPG or stimulator capable of being configured for control of stimulation as required herein for treatment of sleep apnea. The IPG 55 may be, for example, a Medtronic nerve stimulator sold under the trade designation ITREL II Model 7424 or a Medtronic nerve stimulator sold under the trade designation ITREL III Model 7425, both available from Medtronic Inc., Mpls., MN., modified to include an input from the respiratory sensor 60 and modified to include all the signal processing capabilities as shown in Fig. 12a for control of stimulation as required herein. Each of these nerve stimulators include circuitry for providing a wide range of stimulation therapies which can be used with the present invention. The stimulator utilized should be capable of implementing the signal processing with minimum power consumption. Many various hardware configurations may be utilized to implement the described signal processing circuitry. For example, various designs incorporating hardware, software, processors, analog circuits, digital circuits, combinations of the aforementioned,

etc. may be used to perform the necessary signal processing and the present invention is not limited to any particular configuration. Any IPG 55 utilized requires an energy source.

The IPG 55 is implanted in the patient at a location such as shown in Figure 5. However, any location normally utilized for implanting an IPG can be used for the location of IPG 55 as would be readily apparent to one skilled in the art. A suitable implantable neurostimulator has advanced programmable features permitting mode changes by transcutaneous RF telemetry. The patient-controllable parameters of the IPG=s operation, such as the amplitude of stimulation, can therefore be controlled by the patient through a small hand-held telemetry device, i.e. patient programmer 70, shown in Figure 8. Likewise, the physician can preset additional operational parameters of the IPG 55 through a handheld telemetry device 81 of the physician programmer 80, as shown in Fig. 7, held over the implanted IPG 55.

As shown in Fig. 9, the IPG 55 includes two connector ports 58 and 59. The connector port 58 is for insertion of the sensor lead 57 and the connector port 59 is for insertion of the stimulator lead 52.

Fig. 12a is a first embodiment of a block diagram of the processing circuitry 200 that includes sensor input circuitry 201 necessary to acquire a respiratory signal from the pressure sensor 60 including means for biasing the sensor, filtering the sensor output and providing a normalized sensor signal. Processing circuitry 200 further includes monitoring circuitry 203 for monitoring the sensed signal to synchronize stimulation with respiration.

In this first embodiment, as shown in Fig. 12a, a combination of analog and digital circuits is used. Logic functions are provided without use of a microprocessor, i.e. purely analog and digital circuits. The analog front end or sensor input circuitry 201 for obtaining a respiratory effort signal includes sensor bias 202 required for biasing the pressure sensor 60. The pressure sensor 60, for example, the sensing element 126, requires a stable bias current in the range of 8.8 :A to 100 :A. One method of sensor bias 202 includes providing a static bias current in the range of, for example, 15 :A to 25 :A. Currents of this magnitude

provide the best trade-off in terms of battery life and adequate immunity from noise. Alternatively, a second manner of sensor bias 202 includes providing a duty-cycled bias current. In this manner of operation, for example, a 80 :A to 100 :A bias is applied to the sensor just prior to the sampling the respiratory signal. Such duty cycling provides lower power operation, i.e. saves battery life, and provides noise immunity benefits.

The pressure induced AC voltage from the sensor 60 is AC coupled with a high pass filter pole at 0.1 Hz from the sensor bias current to a filter 204, for example, a 2 pole, 3 Hz RC low pass filter. The filter 204 is for anti-aliasing the signal prior to providing the signal to the AGC amplifier 206 and to remove the higher frequency edges of non-respiratory artifacts, such as cardiac artifacts, and also motion artifacts.

The AGC amplifier 206 (Fig. 12a) may operate at a sampling frequency using switched capacitor techniques or may be operated continuously. The AGC amplifier 206 is responsible for normalizing the sensor output, such as, for example, to a consistent 2.4 volt peak-to-peak signal. The amplitude of this signal is then sampled and used by the analog threshold comparator 212 for comparison to various thresholds and is presented to the ADC 214 for conversion into digital delta voltage measurements ()V's) via the)V nulling amplifier 208 for providing an indication of the slope of the waveform. The outputs from the analog comparator 212 and ADC 214 are then utilized by algorithm/control logic 216 to provide inspiratory synchronous stimulation as further described below.

The AGC amplifier 206 compensates for patient-to-patient and inter-patient respiration amplitude variabilities. For example, pressure amplitudes will vary as a patient changes sleeping positions. The AGC amplifier 206 provides adaptivity to the variable amplitudes and thus the physician is not required to program a gain setting. The AGC amplifier 206 also makes the detection algorithm much easier to implement as the thresholds, as described above and also further below, become relative to the normalized peak-to-peak signal and will operate the same even as the true pressure varies throughout the night.

In the first embodiment of processing circuitry 200, the measurement of the pressure sensor signal amplitude is implemented in analog circuitry. The analog amplitude of the pressure signal is measured by comparison to various thresholds and digital outputs are provided to the detection algorithm 216 as a function of such comparisons. Because of the fixed nature of the AGC amplitude threshold 528, the signal amplitude is easily determined and readily comparable to the various analog thresholds in the analog domain. The one comparator 212 can be multiplexed between the onset analog reference 520, offset analog reference 524, Vref threshold 530, and AGC analog reference 528. As mention above, digital outputs are provided by the comparator 212 to the algorithm/control logic 216 to indicate the crossing of such amplitude thresholds.

The sampled signal amplitudes of the signal from AGC amplifier 206 are used by the)V nulling amplifier 208 and ADC 214 to generate)V values of a desired bit size, for example, a 7 bit or 8 bit)V value. Configuring the amplifier prior to the ADC 214 and nulling the present amplitude sample value with the previous sample amplitude value allows for digitally converting a change in voltage (i.e. slope) to)V=s. The nulling amplifier 208 has a gain, for example, of 16, to restore amplitude to the differenced value. The ADC 214 sampling period is synchronized (non-overlapping) to the stimulus to avoid degrading the ADC sensitivity with stimulus circuitry noise. The stimulator frequencies of the IPG 55 may be, for example, and thus the sampling frequencies may be, for example, 20, 30, 33, and 40 Hz. One skilled in the art will readily recognize that the ADC 214 and)V nulling and amplification block 208 could be switched, with the ADC 214 digitally converting the sampled amplitude to a digital value and the digital values from the present sample and previous sample used to determine a digital)V value.

The)V values represent the change in amplitude over the sampling period. Several consecutive)V values can be evaluated to confirm the sustained slope characteristic of inspiration onset or offset as described further below with reference to the detection algorithm. By using several, for example, two or more, consecutive)V samples, short duration (higher frequency) noise or cardiac artifacts can be rejected and thus misdetection of a valid onset or offset is avoided. The

tradeoff for considering more than one sample is that delay is added by waiting to use multiple samples for detection of an onset or offset.

As an alternative to using digital)Vs for representation of slope of the respiratory waveform to the detection algorithm 216, an analog differentiator and peak detector could be utilized for slope measurement. However, the availability of the)V's in the digital domain allows for precise threshold settings and variation in bandwidth by choosing the number of samples to evaluate.

A second embodiment of signal processing circuitry 400 for performing the signal processing with substantially equivalent results to signal processing circuitry 200 is shown in Fig. 12b. The sensor input circuitry, including the sensor bias 402, low pass filter 404, and AGC amplifier 406, is substantially the same as previously described with respect to the first embodiment. However, the monitoring circuitry 203, as indicated by the dashed line in Figure 12a, is performed with the use of a microprocessor 410 and associated code. The microprocessor 400 includes an internal analog to digital convertor (ADC) 414 which presents a converted sampled amplitude to the algorithm/control logic 416 and comparator 412, i.e. the logic and comparison are implemented in software. In this embodiment,)V=s are still determined based on the sampled signal from the AGC amplifier representative of slope of the respiratory effort waveform, and sampled amplitude comparisons are still made with the various thresholds. However, the sampled amplitude of the respiratory effort signal is immediately converted to the digital domain by the ADC 414 and processed digitally by the algorithm to obtain the)V=s. Further, the digitally converted sampled amplitude is digitally compared to digital thresholds 420, 424, 430, and 428 as necessary to carry out the functions as described further below. The algorithm 416 then processes the)V, i.e. slope, information which it generated, and the amplitude comparison information generated by digital comparison 412, as described further below. Also as described further below, the processor 400 can be powered down at certain times when it is not required; conserving energy. Although both the first and second embodiment may be utilized in accordance with the present invention, along with various other configurations of digital or analog circuits, whether with

the use of a processor or without, the remainder of the description shall be made with reference to Fig. 12a for simplification, except as otherwise noted and for specific features which are particularly beneficial to the processor based configuration, such as processor power down.

The detection algorithm as shown in the flow diagrams of Figs. 13a-13h shall now be described with reference thereto and with reference to other figures herein as required. The detection algorithm or algorithm logic 216 as shown in Fig. 12a resides in the IPG 55 of the implantable system 50 shown in Fig. 5. The detection algorithm 216 detects inspiration onset and offset using comparisons of sampled amplitude to multiple thresholds and)V values representative of the slope of the respiratory effort signal. As described previously with reference to Fig. 12a, in the first embodiment, the digital outputs used by detection algorithm 216 to track the respiratory effort waveform, are the onset and offset amplitude threshold comparison outputs from the analog comparator 212 and the digital)V slope value output from the ADC 214 (Fig. 12a). With respect to the second embodiment utilizing the microprocessor and associated code, the digital comparison of the digitally converted sampled amplitude to the various digital thresholds along with the)V values generated using the digitally converted sampled amplitude, all generated inside the microprocessor, are utilized by the processor control logic algorithm 416. This respiratory effort signal information concerning amplitude and slope and the knowledge of respiratory timing parameters during sleep are used by the algorithm to reject cardiac and motion artifacts and control stimulus of muscle in the treatment of sleep apnea.

A top level flow diagram of the detection algorithm/control logic 216 is shown in Fig. 13a. Generally, the detection algorithm is initiated at IPG-ON (block 600). The sensor signal is then sampled (block 610) at a programmed sample rate and the appropriate outputs (i.e.)V=s and analog threshold outputs) are generated by the associated components of the system. Offset detection (block 620) and onset detection (block 700) are then performed, with offset detection taking precedence over onset detection. If neither offset nor onset is detected then the sensor signal is further sampled and offset and onset detection repeated. If offset is

detected, then various functions are performed such as determining whether suspension mode is to be entered, therapy delayed, or AGC updated (blocks 640, 680). If onset is detected (block 700), then stimulation is initiated (block 720). The stimulation is continued and the sensor sampled during stimulation (blocks 730) until an offset is detected (block 740) and stimulation is terminated (block 760). The various functions performed after an offset is detected (blocks 640, 680) are then performed.

The IPG ON command block 600 is a patient or physician controlled function, where he/she turns the IPG "ON" via the patient programmer 70 or physician programmer 80. The IPG 55 recognizes the IPG ON command (block 602) and begins a start-up sequence including dose control timer (block 603), a dose delay (block 604), a setting of initial conditions 606, and the entrance of suspension mode until a regular breathing pattern is recognized. The IPG ON command may also initiate a patient self stimulation test and/or a diagnostic self test, as described further below.

Dose control timer (block 603) is immediately started by the on command, i.e., IPG-ON state. Dose is considered the treatment time over which the IPG 55 is on and stimulation synchronous with inspiration can occur as the patient sleeps. A patient typically uses the system 50 during a regular night=s sleep. A patient may sleep anywhere from, for example, 1 to 15 hours. The dose period is initiated by the patient programmer 70 or a physician programmer 80 transmitting an IPG-ON command to the IPG. Dose is terminated or dose timer timeout occurs by either reaching a maximum programmed dose time or the patient programmer 70 transmits an IPG-OFF command, i.e. IPG-OFF state. The dose time-out provides an automated method for turning off stimulation in the morning after a night=s sleep. The maximum dose time is physician programmable and may be for example, from 1 hour to 15 hours in 1 hour increments.

The initial IPG-ON command also initiates the dose delay period (block 604). The delay waits a sufficient amount of time before starting stimulation to allow the patient time to fall asleep. Dose delay 604 is physician programmable from, for example, 0 to 75 minutes, in 5 minute increments. If stimulation were to

start too soon, the patient may be disturbed and may have difficulty sleeping. The detection algorithm does not operate during dose delay 604 and minimal battery power is consumed during this delay period, for example, in a microprocessor based design, the microprocessor could be powered down.

At the end of the dose delay (block 604), the detection algorithm parameters are initialized (or reset). The initial conditions include: Onset Count = 0, Offset Count = 0, Artifact Count = 0, Average Respiratory Period Weighted Sum (TWS) = 1 second, Max Stimulation On Timer = OFF. In addition, the start AGC watchdog timeout timer as described further below is initialized to 1 second and AGC gain is initialized to a mid-gain setting as described further below. After initialization of the conditions (block 606), as indicated above, stimulus is indefinitely suspended, i.e. suspension mode is entered, until a regular breathing pattern is recognized (block 608).

Generally as will be explained further below, in suspension mode, stimulation is disabled in the presence of artifacts or non-periodic respiration. Suspension is defined as a state where stimulation is suspended due to the lack of a stable respiratory pattern. If the present measured respiratory period (T) is not within a specified minimum and maximum time or if it is not relatively equivalent, i.e. within a certain tolerance (Tvar) of, a stored weighted sum respiratory period (TWS), then stimulus is suspended or suspension mode is entered. The detection algorithm does not exit suspension mode until a measured respiratory period (T) is within the allowed variability from the weighted sum respiratory period (TWS).

As shown in Fig. 13a, during the sampling of the sensor 60 (block 610), the detection algorithm looks for a valid onset so that stimulation can be initiated (block 720). The onset of inspiration is characterized as a sustained increase in slope greater than a physician programmable)V onset threshold value and an amplitude greater than a physician programmable analog onset threshold as shown in Figure 14. An offset detection takes precedence over onset detection, as reflected by Offset Latched & Analog Vref block 622 (Fig. 13c).

As shown in block 700 of Fig. 13c, two consecutive)V's greater than the physician programmed)V onset threshold value are required to indicate a sustained increase in slope. The comparison of sampled)V=s to the)V onset threshold is shown as block 704. The time required to obtain the two samples, for example, may be between 40 ms and 80 ms, depending on the sampling rate; the stimulus rate and sampling rate being the same. The stimulus rate is programmed or fixed by the physician and the)V onset threshold can be adjusted at the same time to compensate for shorter or longer sampling rates. For example, a faster stimulus/sampling rate would result in smaller)V's since less change is seen over the shorter sampling period. Thus, a lower)V onset threshold may be appropriate.

As shown in block 704, if a)V does not exceed the)V onset threshold, the onset counter for counting the number of times the)V onset threshold is exceeded is reset. If the)V onset threshold is exceeded, it is determined whether the stimulation has been suspended (block 706). Although a valid)V onset threshold level was detected, if the IPG 55 is in suspension mode, the onset counter is not incremented. Further sampling and comparisons are then performed to detect offsets. The offsets are detected to determine if a stable respiratory signal is present. If the IPG is not in suspension mode then it is checked to see whether the IPG is in refractory, i.e., a period of time between offset declaration and onset as described further below. Refractory (R), as shown in Fig. 14, includes both a hard refractory (HR) and a soft refractory (SR), i.e. a final portion of refractory (R). Refractory (R) is a processed time, based on a preprogrammed percentage of measured patient respiratory periods (T), during which time the patient is typically denied access to stimulation, except possibly in soft refractory.

As shown in block 708, if the IPG is in refractory (R), then it is checked to see whether it is in hard refractory (HR) or soft refractory (SR) (block 710). If the IPG 55 is in hard refractory (HR), the onset counter is not incremented and more)V comparisons are made. If the respiratory effort signal is in soft refractory (SR), then the amplitude of the signal is compared to the programmed analog amplitude onset threshold (block 714). If the signal does not exceed the

analog onset threshold, the onset counter is not incremented but rather reset to zero and sampling is continued. If the signal exceeds the analog onset threshold, then the onset counter is incremented (block 716). Also as shown by blocks 708 and 712, if the)V onset threshold is exceeded and the IPG is not in the refractory period, then the onset counter is also incremented (block 712). If the onset counter is equal to a count of two, a valid onset is declared (block 716), the counter is reset to zero, a stimulation timer is initiated for controlling the maximum stimulation length (block 718) as described further below, and stimulation is initiated (block 720).

The illustrative 200 ms onset previously described is obtainable, particularly by adjusting the programmable)V and analog amplitude onset thresholds along with refractory (R) and soft refractory (SR) discussed further below. By such adjustment, the algorithm can be made to be >trigger happy= or predictive such that onset detection is not late and the refractory (R) is maximized to save battery life. For example, with use of the soft refractory period, the analog threshold may be set lower to allow a lower signal to exceed the threshold and increment the onset counter. This still, however, blocks motion artifacts from being detected as an onset is detected only if both slope and amplitude thresholds are exceeded during soft refractory, as opposed to just slope out of refractory (R).

Generally, to declare an onset and thus start stimulation, in addition to the)V onset threshold being exceeded by two consecutive samples, the algorithm must be out of refractory (R) during the two consecutive)V samples above threshold or the pressure signal amplitude must be greater than the analog amplitude onset threshold and the algorithm must be in soft refractory (SR). Further, the algorithm must be out of dose delay, therapy delay, and suspension for stimulation to occur.

It should be apparent to one skilled in the art, that variations of onset detection may provide suitable detection. For example, the number of counts may vary, the sampling rate may vary, more)V values may be used alone to detect onset in soft refractory as opposed to the use of both)V and amplitude information in soft refractory and other variation as would be readily apparent to one skilled in the art.

During stimulation, the sensor signal is still being sampled (block 730). Offset detection (block 740) is being performed using the sampled signal during stimulation (block 740). If an offset is detected and latched while stimulation is on, stimulation is terminated (block 760) when the latched offset is validated or declared a valid offset. If offset is not detected, stimulation proceeds until a maximum stimulation period is reached as timed by max-stimulation on timer (block 718), at which time an offset is automatically declared.

Therefore, maximum stimulation time is used in the event that an offset of the inspiratory phase is not detected. A maximum stimulation time shall terminate the stimulation and algorithm functions which typically occur at a regularly detected and validated offset are initiated. In other words, if maximum stimulation time is reached, an offset is declared and functions such as calculating weighted sum, starting refractory, etc. are initiated. When an offset is detected and latched (block 740) and stimulation is terminated (block 760) after the latched offset is validated, the algorithm proceeds to suspension, artifact, therapy delay block 640 as will be described further below.

The detection and declaration of an offset during stimulation (block 740) and when stimulation is off (block 620) shall be described together, as the flow of both blocks is substantially similar with the exceptions as noted. Such description shall be set forth with reference to Figs. 13d and 13e.

Inspiration offset is the most reliable and repeatable signal characteristic to detect as the respiratory waveform slope changes from a positive slope to a sharp negative slope and the amplitude of the respiratory waveform signal reaches a peak value which is controlled by the AGC, for example, the 1.2 volts. Therefore, detection algorithm operation and timing is centered around the detection of offsets, although other periodic events in the respiratory signal may also be used.

Respiration timing, AGC control, and the accuracy, for example, of the prediction of the next onset are all dependent on offset detection. Generally, the detection of offset requires three consecutive)V samples below the physician programmed)V offset threshold 526 (Figure 14) and the first of the three)V

samples is required to have an amplitude greater than the analog amplitude offset threshold 524 (Figure 14). Once these requirements are achieved, an offset is detected and latched. The algorithm then waits for the respiratory effort signal level to fall below the Vref or zero crossing threshold 530 before validating the latched offset, i.e. declaring a valid offset and terminating stimulation. Waiting for the signal to fall below the Vref threshold 530 discriminates against cardiac artifacts riding on the signal, which may cause another offset to be prematurely detected. Alternatively, the offset could also be validated at any amplitude after the offset requirements are met, such as for example, onset threshold or even immediately upon latching the offset.

With reference to the flow diagram of Fig. 13d, as the sensor signal is sampled during stimulation (block 730), if an offset has not been declared or validated (block 742) and the maximum stimulation on time for stimulation has not been reached (block 744), a comparison of)V samples to the programmed)V offset threshold 526 is performed (block 746). If the programmed)V offset threshold is not met, then the algorithm resets the offset counter to zero and sample and comparison continues. If the programmed)V offset threshold is met, then the state of the offset counter is queried (block 748). If the offset count is at zero and the analog respiratory effort signal is not greater than the analog offset threshold to produce a first offset count (block 750), then the offset counter is reset to zero, the offset counter is not incremented and sampling and comparison is continued to detect an offset. If the offset count is equal to zero and the analog respiratory signal is greater than the analog offset threshold, then a first count is made (block 752). If the offset count is not equal to zero (i.e., a first offset count has been made), then such consecutive)V samples that meet the)V offset threshold increment the offset counter (block 752). If the counter registers three consecutive counts during three consecutive sample periods (block 754) with the first offset crossing the analog offset threshold 524, an offset is detected and latched. Once the amplitude falls below Vref (block 742) the latched offset is validated and stimulus is terminated. If the three consecutive offset count requirement is not met, then the offset counter is reset, and sampling and comparison is continued for detecting offsets.

The offset declared or validated is then processed further by Suspension, Artifact, Therapy Delay block 640 and an offset hysteresis timer is started (block 758). Offset hysteresis is utilized to prevent artifacts from declaring two offsets in a very short period of time. For example, if the offset slope was too shallow, multiple offsets could be triggered by artifacts in the signal waveform (e.g., if 6 consecutive)V=s satisfied the)V offset threshold and the analog offset threshold was met for at least the first of each set of three, then two offsets could be declared). Therefore, offset hysteresis provides a blanking period, for example, about 475 ms, after an offset has been declared during which no other offset can be declared. The blanking period is to provide a form of hysteresis such that the algorithm will only >see= one offset per respiratory cycle. The offset hysteresis should be sufficiently short to resume the detection of possible artifact signals for proper suspension mode and artifact counting operation.

Various alternatives to the offset detection portion of the algorithm can be made. For example, the number of counts necessary for an offset to be detected may be modified, the analog threshold may be required to be satisfied for all three)V samples as opposed to just one, the sampling rate may be different, different levels of analog thresholds may be used for declaration or validation of an offset to terminate stimulus and any other variation may be made that would be apparent to one skilled in the art.

The offset detection when stimulation is off (block 620) is substantially the same as described above with the exception that maximum stimulation on time does not need to be checked (block 744) as stimulation is off.

As mentioned previously, the detection algorithm/control logic 216 uses at least two ideologies including that the respiratory period (T) of respiration is known to be stable and consistent during sleep and that the ratio of the time of inspiration (TI) to the respiratory period (T) is typically known or can be evaluated with statistical measures. The detection algorithm 216 uses at least these two ideologies and also respiratory timing statistics of sleeping humans to make the algorithm robust and exclusionary of misdetecting artifacts for onset and offset. As part of implementing the ideologies, the weighted sum respiratory period (TWS) is

used to build a running average of measured patient respiration periods (T) and is utilized in connection with various algorithm functions to control stimulation and reject artifacts. The various functions which employ the use of TWS include refractory (R)/soft refractory (SR) function, suspension function, AGC control, and the artifact counter function. After a general discussion of the these functions, the suspension function, AGC control and artifact counter function will be described further with reference to the flow diagram of Fig. 13f and 13g. The use of refractory (R)/soft refractory (SR) function has been previously described with reference to the flow diagram for onset detection (Fig. 13c).

The detection algorithm 216 evaluates the equivalence of every patient respiration period (T) by comparison of measured periods (T) to the continuously calculated weighted sum respiratory period (TWS) and to bounds for a respiratory period to evaluate whether respiration is stable. The detection algorithm having knowledge of the weighted sum respiratory period (TWS) and a substantially constant inspiration time (TI), also approximates the time between each offset and onset such that onsets can be predicted.

The geometric-series weighted sum used to generate the weighted sum respiratory average (T) is weighted more heavily by the most current measured T periods. The algorithm adds the present weighted sum to the present T period and then divides by 2. The result is expressed in the following equation: T Weighted Sum (n) = [T Weighted Sum (n-1) + T Interval (n)] / 2. The maximum number of T periods contained in one sum is ten, but the T periods beyond the fifth have an insignificant contribution to the sum. Not all measured T periods are utilized in determining TWS. The algorithm measures the patient respiratory period (T) at each offset. If T falls out of the predetermined bounds set for T, i.e. Tmin and Tmax, for example, in the range of 1 second to 16 seconds, indicating nonperiodic respiration, then the algorithm will consider the T period invalid. The invalid T periods are not added to the weighted sum (TWS).

With the weighted sum average respiratory period (TWS) calculated, the refractory period (R) can be approximated as described below. Onsets (and thus stimulation) can be kept from occurring for a period of time in the refractory period

(R) following the declaration of offset of inspiration. This time frame is in the expiration phase of respiration. Any physiologic or sensor disturbances (artifacts, noise, etc.) during this time period can be rejected as onsets. Stimulation is thus inhibited during at least a portion of refractory (R), but sampling continues in order to detect the presence of artifacts and enter suspension mode, if necessary.

The refractory period (R) begins at the offset of inspiration (i.e. the end of stimulus) and continues almost until when the next inspiration onset is expected. A percentage of the weighted sum (TWS) is used to calculate the refractory (R) duration. For example, with TI/T ranges known from, for example, statistical analysis, the expiration portion of respiration and thus the refractory period (R) can be calculated as a fraction of the weighted sum (TWS). For example, the calculated refractory period (R) may be implemented based on the weighted sum by multiplying a physician programmable refractory multiplier of 0.375, 0.50, 62.5, or 0.75 times the weighted sum: refractory (R) = (Refractory Multiplier x Respiratory Period Weighted Sum (TWS)). Such particular refractory multipliers are for illustration only and any portion of T may be designated as refractory, such as from 0.1 to 0.75, particularly depending upon the individual patient=s respiratory cycle.

The weighted sum respiratory period (TWS) is initialized upon the on command for the IPG 55 to be 1 second. The algorithm remains in suspension mode as described further below until the TWS is equivalent to the present measured T, i.e. periodic respiration is determined. The algorithm does not use refractory (R) to blank onsets until suspension mode is exited. This insures that the weighted sum (TWS) will have established a valid value and thus the refractory (R) will also be a valid duration for predicting onsets and blanking artifacts.

Refractory (R) is limited to a minimum time. This is achieved by only updating the weighted sum (TWS) for T periods greater than 1 second and therefore the weighted sum (TWS) has a minimum of 1 second. As such the refractory (R) minimum time is given by: Minimum Refractory = (Refractory Multiplier x 1 second). The establishment of a minimum refractory time is a safety guard against over stimulation by establishing some minimum of blanking time.

Soft refractory (SR) is implemented in the final portion of the refractory period (R). The other portion of refractory (R) is referred to as hard refractory (HR) and is shown in Fig. 14. In hard refractory (HR), stimulation is not allowed, i.e. onsets are not responded to. In the soft refractory (SR) period of refractory (R), as shown in Fig. 14, an onset (i.e. stimulation) is allowed if the analog onset threshold and the)V comparison as described with reference to Fig. 13c both indicate an onset. The soft refractory (SR) portion of refractory period (R) may be a fraction of, for example, 12.5 % of the weighted sum (TWS). Therefore, for illustration, if refractory (R) is 75% of the weighted sum, then the soft refractory (SR) is during the 62.5% to 75% portion of refractory (R).

Alternatively, the soft refractory (SR) could be a function or percentage of refractory (R). Further, the refractory functions may be based on stimulus duration as opposed to respiratory rate. With this alternative, the algorithm would measure the duration of the previous stimulus interval and multiply the interval by a predetermined value. A further alternative for refractory could be based on both stimulus duration and the respiratory period (T) or any other alternative respiratory timing parameter that would be suitable for defining a refractory, hard refractory, and/or soft refractory period following offset detection, such as TI.

Suspension mode, which also utilizes TWS, provides several benefits. For example, the suspension function keeps the patient from being overly stimulated, i.e. patient comfort. Further, this technique also conserves energy to increase battery life. In suspension mode, stimulation is disabled in the presence of artifacts or non-periodic respiration. Suspension is defined as a state where stimulation is suspended due to the lack of a stable respiratory pattern. If the present measured patient respiratory period (T) is not within a specified minimum and maximum time or if it is not relatively equivalent to, i.e. within an allowed variability of, a stored weighted sum respiratory period (TWS), then stimulus is suspended, i.e. suspension mode is entered. The detection algorithm does not exit suspension mode until a measured patient respiratory period (T) is within the allowed variability from the weighted sum respiratory period (TWS) . The

programmable values of allowed T variability (hereafter referred to as Tvar) may be for example, 25 %, 33 %, 50 %, and infinite. Each and every offset is considered as a measure of the respiratory period (T) and/or the presence of artifacts. While in suspension mode, the algorithm continues all other signal processing tasks such as threshold comparisons, AGC adjustments, and weighted sum calculations.

Generally, suspension is entered by the algorithm under the following conditions indicative of nonperiodic respiration. First, upon initialization of the IPG 55, the algorithm is in the suspension state, as shown in Fig. 13b, block 608, after the IPG 55 is turned ON and dose delay (block 604) is completed. Second, if the presently measured respiratory period (T) is less than the minimum or greater than the maximum bounds programmed for T, suspension mode is entered, i.e. the bounds of 1 second and 16 seconds as previously mentioned. Third, if the present respiratory period (T) is not within a programmed allowed variability, i.e. Tvar, suspension mode is entered. And last, suspension is entered after the completion of a therapy delay initiated with use of the artifact counter as described below. It should be readily apparent to one skilled in the art that the number of respiratory violations of, for example, Tmin, Tmax or Tvar, which are required for suspension mode to be entered may vary. For example, more than one violation may be required to enter suspension.

The above described suspension mode technique disables stimulus in the presence of physiologic artifacts such as arm movements and head movements. Such movements occur only when the patient is in shallow sleep or awake. An example of the benefit of suspension mode is the case of a sleeping patient awakening to a phone call. Suspension mode will be entered as the patient moves about and stimulation will be inhibited while the patient speaks on the phone. Suspension mode is also intended to disable stimulus in the presence of non-physiologic and environmental noise sources. During suspension mode, the algorithm continues to evaluate the signal and will exit suspension mode and return to stimulus as soon as a periodic respiratory signal is re-established. Therefore, only the prevention of stimulus conserves energy as the sensor must still be operated.

As mentioned above, an artifact counter is used to initiate a therapy delay during which time stimulation is disabled. This is technique also conserves energy, lengthens battery life, and rejects artifacts. If the respiratory waveform continues to be too variable or multiple motion artifacts are occurring while in suspension mode, then the artifact counter will cause the algorithm to enter therapy delay. While in suspension mode, the number of offsets are counted by the artifact counter, in which case an offset is defined as the falling peak of either a respiratory or artifact event. If a maximum number of offsets are counted during suspension mode, then the algorithm enters a therapy delay period. The maximum artifact count is physician programmable, for example, to 10, 20, 40, or 80. During therapy delay, initiated by the artifact counter, the algorithm does not process the respiratory waveform signal and therefore, energy is conserved by turning the pressure sensor off and by preventing stimulation. Upon completion of the therapy delay period, the algorithm resets to an initial state (AGC gain and weighted sum reset, etc.) like when the IPG 55 was first turned on. Sampling the signal in the suspension mode is then resumed.

The counting of offsets during suspension mode is a simple method for determining the extent of non-respiratory activity. If frequent offsets are occurring, then this indicates that extensive movement exists and the algorithm shall transition quickly into therapy delay. If suspension mode occurs due to a short duration event, the offset artifact count will not reach the maximum, and stimulus will resume after the steady respiration rate has been re-established. If suspension mode is maintained by a variable respiratory rate, the offset artifact count will eventually lead to a maximum artifact count and therapy delay from counting of offsets. It should be noted that the artifact count is reset to zero upon exiting suspension mode.

The artifact counter function also provides the patient a method to quickly terminate stimulation without the use of the patient programmer 70. This is accomplished by tapping in the proximity of the pressure sensor to induce artifact counts. Such tapping allows the patient to terminate stimulus for the duration of therapy delay in the event that the patient programmer 70 is lost or fails during the

night. Such termination could also be accomplished by use of a magnet being passed over a reedswitch built into the IPG 55.

Offset hysteresis, as previously described, is also used to conserve energy, as during this period of time the sensor can be shut down. Further, although some functions described herein may depend on the sensor functioning during refractory, with some modifications to the algorithm, the sensor may also be shut down during refractory, particularly hard refractory, as stimulation is prohibited. Thus, energy can also be conserved by shutting down the sensor whenever the respiratory waveform is not needed by the remainder of the system.

With reference to Fig. 13f, the flow of the suspension and artifact counting techniques in the detection algorithm shall be described. If offset is detected while stimulation is off (block 620), then it is determined whether the algorithm is in suspension as described above. If the unit is in suspension mode, artifacts (i.e. offsets, both inspiratory and artifact) are counted to determine if the algorithm should go into therapy delay (block 644). If the count exceeds some predetermined number, such as, for example, 16 counts, then the artifact counter is reset to zero, suspension mode is exited and activation of programmed therapy delay is entered (block 666). The therapy delay time is also started upon receiving the IPG on command during either an already occurring therapy delay (block 666) or dose delay (block 604) (Fig. 13b). After the therapy delay is exited, the initial conditions are set, substantially the same as when the IPG is turned on with the patient programmer (Fig. 13b).

If an offset has been detected either during stimulation or when stimulation is off, respiratory period (T) is measured (i.e. offset-to-offset or the time from the last offset to the current offset) (block 648). The current measured respiratory period (T) is then compared to Tmin and Tmax (block 650). If the current respiratory period (T) is not greater than Tmin and less than Tmax, then refractory (R) is started (block 652) based on a percentage of the previous weighted sum respiratory period (TWS). Further, if three consecutive current respiratory periods (T) measured do not meet these requirements, then the algorithm goes into

suspension mode and stimulation is not allowed, otherwise, artifact counter is reset to zero and suspension mode is exited.

If the current respiratory period (T) is greater than Tmin and less than Tmax, then the current measured respiratory period (T) is added to the weighted sum average respiratory period and a weighted sum (TWS) of the previous breaths is calculated to determine a new average weighted sum respiratory period (block 654). Refractory is started (block 652) based on a percentage of the new average weighted sum, as updated. Further, the current respiratory period (T) measured is compared to the weighted sum from the previous offsets (i.e. the old weighted sum prior to the addition of the current T) (block 656). If the current T is equivalent, i.e. meets Tvar, indicating periodic respiration, then the artifact counter is reset to zero and suspension mode is exited. Otherwise, it is once again determined if three current respiratory periods (T) measured do not meet the Tmin, Tmax and Tvar requirements (block 658). As before, if three consecutive T=s do not meet the Tmin, Tmax, and Tvar requirements, then the algorithm goes into the suspension mode or suspension mode is continued (block 670) and stimulation is not allowed, otherwise, artifact counter is reset to zero and suspension mode is exited (block 662).

The number of consecutive out of tolerance T=s necessary to enter suspension mode is programmable. For example, the number can be set at one or other suitable values. Further, Tvar can be set to infinity which overrides the suspension feature and suspension is never entered.

In either case, whether suspension mode is entered or exited, the automatic gain control (AGC) is continually utilized or adjusted (block 680) as shall be described with reference to Fig. 13g. However AGC is not operational during treatment delays, i.e. dose delay or therapy delay, as the pressure sensor need not be operated during this delay time, conserving battery life. The AGC control described herein is applicable to the provision of any signal characteristic of a periodic physiological parameter for use in a therapy system. For example, the normalization provided by the AGC control is particularly applicable to systems which perform functions based on comparing the signal to the thresholds.

The AGC amplifier 206 (Fig. 12a), as described previously, is required to normalize the pressure sensor output to a consistent peak to peak signal, for example, 2.4 volt peak-to-peak signal. The operation of the AGC for the system 50 is dependent on the detection algorithm for synchronizing gain increment and decrements. The AGC consists of a plurality of gain steps, for example, 64 gains steps. Gain is incremented exponentially such that each gain step increases by the same percentage, for example, about 5.3 %. However, gain may be performed by other than exponential techniques, such as, for example, techniques that produce equivalent increases as opposed to equivalent percentage increases.

Generally, the AGC functions in the following manner. The gain is incremented or decremented once per respiratory period (T). The AGC gain is changed immediately following detection of a periodic event in the waveform, i.e. a >true= offset. True offset is defined here so as to indicate those offsets which are likely to be from an actual, stable inspiration offset and not a motion artifact or irregular breathing. The algorithm determines an offset is true if it does not occur during refractory (R) (including both soft refractory and hard refractory), as during refractory (R) it is assumed that the offset is an artifact offset. Offsets resulting in a respiratory period (T) outside of the predetermined bounds set for the periods, such as, for example, less than 1 second or greater than 16 seconds, are also considered invalid.

It is desirable to not change gain during refractory as the offsets which occur in this period may be of large amplitude, due to a motion artifact, and gain may be unnecessarily updated. Also, the refractory sets a limit on how fast the gain can be changed. Thus, if a rapid burst of artifacts occurs during refractory (R) then there will be no rapid change in gain. If a burst of artifacts occurs while the algorithm is not in refractory (R), then the first artifact will be considered an offset and subsequent artifacts will not change the gain as they will be in refractory (R). Thus, rapid offsets can only change the gain once during a respiratory cycle, i.e. increment or decrement once. AGC control is performed during suspension mode, along with offset detection and refractory, as only stimulus is inhibited and an

exceeding of the artifact counter results in a therapy delay while in suspension mode.

An AGC watchdog timer also forms a part of AGC control. The AGC watchdog timer is reset each time a valid offset occurs resulting in the AGC gain being updated. The watchdog timer will otherwise time-out at, for example, 1.5 times the respiratory period weighted sum (TWS) or in other words, the watchdog timer time-outs at 50 % beyond the point where an offset is expected. At time-out an AGC threshold is used to determine if the AGC gain should be incremented or decremented by one step. The watchdog timer will continue to time-out and increment or decrement until offsets begin occurring. The offsets then take control of the AGC operation. Therefore, the watchdog timer gets the gain to a level such that offsets can be detected and normal AGC control via offsets can be established, particularly when the IPG 55 is first turned on.

The AGC is initialized to a mid-range setting. If this initial gain is too low, the watchdog timer may have to cycle several times before offsets begin to occur and equilibrium is reached. The watchdog timer is loaded with a predetermined time, for example, 1 second at the initialization of the algorithm. Thus, the gain will increment one step per second until offsets are achieved, unless the initialized gain is too high, in which case each offset and/or the watchdog timer will decrement the gain until equilibrium is reached. The AGC is reset or reinitialized at each exit of therapy delay or dose delay.

Generally, therefore, gain is updated when an offset is detected following onset, even while in suspension mode or gain is updated when a watchdog time out occurs if an offset is not detected within a predetermined period of time. However, offsets detected while in refractory (R), whether or not in suspension mode, do not initiate gain update. Further, since offsets are not even looked for in dose delay or therapy delay, AGC is not updated during this time period. Typically, after initialization, the gain is incremented with use of the watchdog timer until valid offsets can be detected. Thereafter, the AGC typically controls the gain by toggling between increments and decrements to keep the gain at a particular level, i.e. the AGC threshold 528 (Fig. 14) and the waveform is normalized.

The flow of AGC control 680 is shown in Fig. 13g. AGC is run virtually simultaneously with the determination after an offset is detected of whether the algorithm should be in suspension or not as described previously with reference to Fig. 13f. As such, block 650 (Figs. 13f and 13g) appears in both flow diagrams. AGC is not performed until the current measured respiratory period (T) meets the requirements of being greater than Tmin and less than Tmax (block 650), i.e. a somewhat stable periodic signal is sensed. Further, AGC update is performed if Tvar is set to infinity (block 650), regardless of the Tmin and Tmax requirements, i.e. if Tvar is set to infinity then all requirements for T are disabled for suspension and AGC functions. If the gain is not updated the sensor is continued to be sampled (block 610) and offset and onset detection is performed (blocks 620 and 700). If such requirements are met, then it is determined whether the algorithm is in refractory (R). If the algorithm is in refractory (R), then the gain is not updated (block 684). If the algorithm is not in refractory, then gain is either incremented or decremented based on a comparison with a predetermined AGC amplitude threshold (Fig. 14) (blocks 686 and 690). If the amplitude of the respiratory effort signal is less than the AGC threshold at any time since the previous update, then gain is incremented at, for example, offset, watchdog timeout or any other periodic event in the respiratory cycle. If the amplitude of the signal is greater than the threshold at any time since the previous update, then the gain is decremented at offset, watchdog timeout or any other defined periodic event in the cycle. The watch dog timer is reset at each and every AGC increment or decrement. However, at any time when no offsets are detected in a specified period of time, then the gain is incremented or decremented using the watchdog timer, i.e. a time based on the weighted sum respiratory period (block 692). Generally, therefore, for a signal characteristic of a periodic physiological parameter, such as respiration, which include multiple periodic cycles, gain is updated when a periodic event is detected. The gain, however, is updated only once during a periodic cycle. Further, a watchdog timeout occurs if the periodic event is not detected and gain is updated even though a periodic event is not detected. Thus, the gain will be

adjusted once per periodic cycle upon detection of a periodic event or at a watchdog timeout.

Other alternative methods of AGC implementation may be utilized with the present invention. For example, the AGC may adjust the amplifier gain after each amplitude sample has been taken. The magnitude of the sample would then be processed digitally to adjust the gain such that the amplifiers operate in mid-dynamic range. This technique has the advantage of quick gain adjustments and continuous digital knowledge of the signal amplitude. However, the AGC would not provide normalization and thus relative threshold measurements are not possible.

In general, the algorithm must be in the following state for stimulation to occur. A valid onset consisting of a certain number of)V=s, for example, two)V=s, above)V onset threshold must be detected. The refractory period (R) must be complete or the analog onset threshold must be crossed if the algorithm is in soft refractory (SR). The algorithm must not be in suspension mode and the algorithm must not be in either dose delay or therapy delay.

Further, any one of the following events will terminate stimulation: a predetermined consecutive number of)V=s, for example, three consecutive)V=s, below)V offset threshold with the first)V sample below the)V offset threshold satisfying the analog offset threshold (the offset must also be validated by comparison to another threshold level such as zero crossing); maximum stimulation time is reached; a patient initiates therapy delay by giving another IPG on command when treatment is on; end of the dose timer period after a night=s sleep; and an IPG-OFF command.

Moreover, in general, implantable stimulation system 50, operates in the following manner. At some point following the IPG 55 implant, the patient will undergo a sleep laboratory evaluation where algorithm parameters, such as those programmable parameters described herein (onset and offset thresholds, refractory, dose times, etc.) are optimized to achieve proper stimulation for the individual patient. The stimulation parameters (amplitude, rate, and pulse width) are also adjusted to achieve the muscle stimulation necessary to overcome respiratory

obstructions. After being programmed by the physician, the patient is provided with a hand-held patient programmer 70 which is primarily used to turn the IPG ON and OFF each evening and morning, respectively. The patient programmer 70 also may provide the patient with display indications regarding system information such as battery life warnings, failed stimulus components, etc., and further may be used to automatically initiate other diagnostic and stimulation testing as described further below. The implanted stimulation system 50, upon initialization of treatment, then utilizes the sensed respiration effort waveform to detect critical points in the waveform to provide inspiration synchronous stimulation for treating respiratory disorder in accordance with the algorithm as described above.

The system 50 can also be used for patients with central apnea, or patients whose central nervous system provides no drive to breath. Central apneas often occur in obstructive sleep apnea patients in what are call mixed apneas. To ensure effective therapy, the patient must be stimulated over the first breaths following the central apnea, in order to prevent obstructive apneas. Patients with such conditions generate a respiratory effort waveform somewhat as shown in Fig. 16b or Fig. 16c as compared to a normal respiratory waveform (Fig. 16a). Because of the relative flatness of the waveform, offset and onset detection is difficult and almost unusable for providing stimulation to treat the upper airway condition. However, the detection algorithm can be adjusted to continue stimulation asynchronously when the signal amplitude becomes small. By making the)V and analog onset thresholds sensitive to flat sensor signals, stimulation can be maintained for such a patient. Although offsets are not detected, the maximum stimulation time can be used to terminate stimulation. Further, stimulation occurs, i.e., turns on, either at the end of hard refractory (HR) or refractory (R). The average respiratory period weighted sum (TWS) is approximately maintained by the repetitive stimulation occurring based on the maximum stimulation time and asynchronous stimulation will continue until the patient=s periodic respiration returns. Further, the maximum stimulation time can be adjusted to forego overstimulation.

A central sleep apnea is shown in Fig. 16c. For example, the central sleep apnea 802 may occur over a time period of 5 seconds to 30 seconds. As shown in Fig. 16d, stimulation is synchronized to inspiration during the first and second cycles of respiration prior to central apnea occurring. Stimulation, in accordance with the present invention, then occurs for the maximum stimulation time 804 as offset is not detected during central apnea. The offset is then due to maximum stimulation time being reached. Refractory then occurs after the maximum stimulation time, during which time no stimulation is allowed. This particular refractory period 806 is shown by the time period between the two maximum stimulation times during the central sleep apnea. During this time, i.e. central sleep apnea, the AGC is operating by means of the watchdog timer and/or the maximum stimulation time offsets which update gain when no inspiration offsets are detected for a particular period of time. This operation of the AGC, increases the signal amplitude, and allows the algorithm to detect an onset with use of a smaller amplitude respiratory signal. Once a first onset is detected (or offset) then stimulation can be continued synchronous with inspiration as opposed to stimulating based on maximum period of stimulation and refractory. This ability to increase gain to detect offsets or onsets of a smaller respiratory signal is important because the first breaths 800, Fig. 16c after central apnea are typically shallow (low effort) and thus the algorithm compensates for the low effort by increasing the gain of the signal using the watchdog timer. The increase in gain 810 during the central apnea is shown in Fig 16e.

The stimulation control using the detection algorithm described above and synchronized to the respiratory effort waveform allows for the provision of a preprogrammed train of pulses, i.e., voltage, current, power, to the electrode 65 (Fig. 5) as shown in Fig. 17a. This train of pulses, also referred to as a burst, stimulate the nerve/muscle, such as a muscle in the upper airway, the diaphragm, or any other muscles which are suitable for use in treatment.

Fig. 17b shows characteristics of a typical train of pulses that is initiated upon onset detection as previously described. The train of pulses is shown to begin upon onset at an amplitude of about 75% of the programmed value. The

amplitude is then ramped to 100% of the programmed value. This ramped function provides added comfort during the nerve stimulation. However, alternatively, the train of pulses may be started at any percentage of the programmed value or any percentage of the programmed value, i.e. 100%, 110%, 150%. The train of pulses ends upon the declaration of an offset, when maximum stimulation time is reached or the IPG off command is entered as described previously.

Fig. 17c shows the characteristics of the individual pulses within the train of pulses. Amplitude, the rate at which the pulses are delivered and the width of the individual pulses all impact the stimulation of the muscle. Minimizing the programmable amplitude, pulse width and rate of stimulation increases the longevity of the system. As one of ordinary skill in the art will recognize there are various manners of providing the train of pulses or a single pulse, and the present invention is not limited to any particular manner of generating such pulses. Any suitable circuit configuration for providing such pulses may be utilized, such as those available with the ITREL platforms.

Fig. 18 shows the system 50, as shown in Fig. 5, including the IPG 55 which is a processor based IPG such as shown in Fig. 12b, sensor 60, and lead/electrode 65. The microprocessor 410 as previously described internally includes ADC 414. The IPG also includes the other components previously discussed including sensor bias 402, low pass filter 404, and AGC amplifier 406. Further included in the IPG 55 are telemetry components 440 coupled to antenna 442, stimulus output circuit 434 and digital to analog convertor (DAC) 432 which is used to produce the correct stimulus output amplitude for the system. The microprocessor 410, in addition to controlling stimulation, also controls the sensor bias 402, AGC amplifier 406 and diagnostic self test functions as described further below.

With reference to the system of Fig. 18, an energy conserving technique shall be described which is not only applicable to this particular system, but also to other implantable therapy systems, such as, for example, drug delivery systems, other stimulation systems, and any other systems which could benefit from such an energy conservation technique. The processor based IPG 55 enters an off

state, i.e. a treatment period is not occurring, as a result of various events. For example, the off state in the system 50 is entered when the patient programmer 70 is used to send an IPG off command via telemetry using the telemetry circuitry and antenna 442. Further, the treatment period may end as a result of a dose timer timing out at the end of a dose period, such as in the morning after a nighttime treatment period, or the treatment period may end as a result of some other event. In such cases, the microprocessor 410 goes through a shut-down sequence and enters an off or >sleep= mode during which it is not required to function.

The shut down sequence includes turning off power to all non-essential circuits of the system 50. Such non-essential circuits during the sleep mode include the amplifier 406, sensor bias 402, ADC 414, DAC 432, and stimulus output circuits 434. In the microprocessor based system, the microprocessor can also enter the sleep mode or stop mode where very little current is consumed, but the microprocessor will awake when an interrupt line is toggled. The telemetry block 440 remains on to listen for telemetry communication, such as from the patient programmer 70, and then wakes the microprocessor 410 when the external communication, i.e. telemetry command, is received. During operation of the sleep mode, energy is conserved.

This sleep mode can also be used with the IPG having processing circuitry that is not microprocessor based. For example, the logic circuits could be shut down or powered down. Further, methods other than telemetry could be used to wake up the processor. For example, a patient held magnet and a reedswitch trigger located in the IPG could be used, or a background timer in the IPG could be used to automatically turn the IPG on at a certain time. Further, as previously indicated above, this sleep mode could be used with other implantable therapy systems. For example, a blink stimulation system could enter sleep mode at night when essential circuits are not used or a drug delivery system could use sleep mode when there is a period of time that the essential components are not needed.

The patient programmer 70, Fig. 8, and the physician programmer 80, Fig. 7, communicate with the IPG 55 via telemetry. The physician programmer 80 allows the programmable parameters of the system to be adjusted by the physician to conform to the needs of the patient. Such programming devices are readily known to those skilled in the art. Examples of such devices are described in U.S. 4,236,524 to Powell et al., U.S. Patent 4,250,884 to Hartlaub et al., U.S. Patent 4,305,397 to Weisbrod et al., U.S. Patent 4,323,074 to Nelms, U.S. Patent 4,432,360 to Mumford et al., and U.S. Statutory Invention Registration No. H1347 to Greeninger et al., all incorporated herein by reference in their entirety. For example, all the programmable parameters mentioned with respect to the detection algorithm and also the stimulus pulse amplitude, stimulus pulse duration, stimulus pulse frequency, and stimulus ramp on/off times can be adjusted through the physician programmer 80. In addition, the physician programmer 80 can be used to access any stored data and retrieve such data stored in the implanted system. For example, the patient=s name, the code number of the hospital or clinic, the prescription date, and the last follow-up date could be stored in hardware of the system. Further, patient compliance data, system performance data, diagnostic testing data could be accumulated by the system and read out through use of the programmer 80. For example, the total time the power is on, total stimulation time for the patient, the number of power cycles or reset cycles, the average battery voltage and fault detection could be stored and retrieved through the physician programmer 80.

Fig. 8 shows the patient programmer 70 for patient control of the system 50. The control panel of programmer 70 includes on and off switches 71, 75 which allow the patient to turn the system on or off. Turning switch 71 on initializes the treatment period using the above described control logic. The buttons 73 allow the patient to adjust the amplitude of stimulation for comfort level and other controls could be added to allow the patient to control other parameters such as, for example, pulse rate, pulse width, delay times.

The power on switch 71 also may be utilized to initiate various self test functions as well as initiating a dose delay (block 604) if the device is already operating. One self test function initiated by the power on switch is a patient stimulation self test function, wherein when the patient turns the stimulation system on with the patient programmer 70 for a treatment period, i.e. before going to bed, the stimulator immediately thereafter automatically provides stimulation to the patient, such as to the hypoglossal nerve. This stimulation may be based on the maximum stimulation time or any other predetermined time period. Such power on stimulation, gives the patient the ability to verify that the system is capable of stimulating properly. For example, the stimulation verifies that the nerve/muscle was captured, that the lead placement is correct, that the lead from the IPG 55 to the electrode 65 is operative, and also that the IPG stimulator output circuits for providing the pulse are functioning properly. At any time during the treatment, if the patient did not think that the system 50 was functioning properly, the patient could, by pushing the power on switch, provide a stimulus to check the device. Further, the stimulation self test could be performed at IPG-OFF.

The patient stimulation self test is not only applicable to respiratory treatment systems as described herein, but is equally applicable to any stimulation systems that provide patient treatment. For example, such a self test could be used with a muscle therapy or conditioning system, a blink electrode stimulation system, or any other neuromuscular stimulation system. With respect to the respiratory disorder treatment system described herein which, for example, stimulates the hypoglossal nerve, the stimulation automatically provided provides stimulation sufficient to evoke tongue protrusion, which the patient senses and thus can verify that the stimulator is on and stimulation is functional.

Any faults detected by the stimulator using the stimulation self test or by any of the other tests described herein, such as the diagnostic self tests, can be reported to the patient via the patient programmer 70. Further, since the patient by the power on stimulus has tested the adequacy of the stimulation, the patient can adjust the amplitude of stimulation by buttons 73, for example, within certain bounds set by the physician. This adjustment would allow the patient to increase

stimulation amplitude if capture of the nerve was not occurring or decrease amplitude of stimulation if adequate capture was occurring, in order to increase battery longevity. Such patient adjustment may be used for any other physician programmable parameters that the physician would want the patient to be able to control. For example, stimulus rate, pulse width, therapy delay periods, etc. Moreover, if the system is not functioning properly, a visit to the physician can be made for evaluation of the system, i.e. such as by accessing test data or fault data stored in the system.

The power on switch 71 may also be utilized to initiate an internal diagnostic self test for testing the system to determine whether the components and circuit functions, along with the detection algorithm are operating properly. However such diagnostic self test can also be run whenever the system is not interactive with the patient. For example, a diagnostic self test of the system described with reference to Fig. 18 could be run during a dose delay, a sleep mode, a therapy delay, at IPG-OFF or anytime during the day when the patient is awake. During the diagnostic self test, components and functions of the system can be tested, for example, with reference to the system of Fig. 18, the amplifier 406, the filter 404, and all the rest of the components can be tested as described further below. Typically, such testing is performed at the physicians office using the physician programmer 80. However, since this treatment is performed during the sleep period of a patient=s day, it may not be known whether the system is functioning properly or not as the patient is asleep when it is operating. Therefore, a diagnostic self test during a period of time when the system is not interacting with the patient, i.e. stimulation or sensing, or in other words when the patient is not dependent on the treatment, is beneficial. With, for example, a fault indication sent to the patient programmer 70 when faults are detected, the patient has some assurance that the system is functioning properly.

The diagnostic self test strategy as shown in Fig. 19, is applicable to many different therapy systems. For example, as shown therein, a typical therapy system 900 includes a therapy device 901, i.e. IPG 55, having an input circuit 908 for receiving an input such as a sensed signal 904 of a patient 10. The device 901

further includes a microprocessor or some other logic circuitry 912 for processing the sensed signal and generating an output 906 via output circuit 910. Further, the device may include telemetry circuitry 914 for receiving and transmitting information from and to an external source.

The general diagnostic test strategy for such a generally described therapy system, includes applying the generated output 906 from the output circuit 910 to the patient 10. The result of the therapy due to the generated output 906 is sensed via the input circuit 908 to verify operation of the system. For example, a stimulus output, i.e. a cardiac pace, could be applied to the patient and the input circuit could sense whether the cardiac pace resulted in a physiological response in the patient. Further, for example, the stimulus output could be a train of pulses to the genioglossus muscle to treat sleep apnea. The input circuit would then provide the sensed signal characteristic of respiratory effort to the microprocessor to verify that a correct respiratory response was achieved with the stimulus of the genioglossus muscle, i.e. open airway and proper respiratory action. If a correct response is not indicated, the system could be further tested. An internal attenuated feedback output 916 (shown as a thicker line than the lines of system normal configuration) from the output to the input can be used to determine if the input or output circuits are operating properly. This general test strategy will detect faults internal and external to the device 601. For example, a broken stimulus or sense lead could be detected or a faulty output circuit could be detected.

Figs. 20a-d show various block diagrams of other more specific internal diagnostic self tests for testing various components of the system shown in Fig. 18. Fig. 20a shows the blocks of Fig. 18 involved in a front end amplifier self test. The DAC 432 sends a voltage or voltage pulse to the input of filter 404, amplifier 406, or ADC 414. The microprocessor 410 then verifies the correct response. The DAC 432 is also verified by its participation in these loops.

Fig. 20b shows the blocks involved in a sensor bias self test. A bias signal from sensor bias 402 is directed to the ADC 414 and measured and compared to set references by the microprocessor 410. A sensor signal from sensor 60, for example, a DC static voltage resulting from sensor bias, can also be directed to the

ADC 414, measured and compared to set references by the microprocessor 410 for verification.

Fig. 20c shows the blocks involved in a stimulus output self test. The output from the stimulus output 434 with its amplitude under control of DAC 432 is directed to the ADC 414 and verified by the microprocessor 410. The output can be ramped to its maximum stimulus and then attenuated for input to ADC 414 for measurement.

Fig. 20d shows the blocks involved in a telemetry self test. The telemetry circuitry 440 can be tested in a couple of ways. First, known voltage pulses are applied to the telemetry circuit 440 via the DAC 432 to drive the circuit, i.e. simulate a received ping, and telemetry reception is verified via the microprocessor 410 and a demodulated voltage measured on the ADC 414. Likewise, the microprocessor 410 could initiate a telemetry uplink, i.e. ping on antenna, and the ADC 414 will verify the signal on the antenna 442. Second, a telemetry uplink can be initiated with the microprocessor 410, i.e. ping the antenna, and then immediately enable the telemetry demodulator of circuitry 440 to detect the ringing of the antenna 442 with verification of the detection performed by the microprocessor 410. This second test would not use the ADC 414 or the DAC 432.

Further tests could be performed to verify other components and functions. For example, the AGC could be calibrated by switching in a known signal, analog offset and onset detection could be verified by a DAC generated signal, and lead and battery measurements could be made. Further, diagnostic self test results can be stored and uplinked to allow quick fault identification at either a patient or a physician programmer.

It will be appreciated by those skilled in the art that while the invention has been described above in connection with particular embodiments and examples, the invention is not necessarily so limited and that numerous other embodiments, examples, uses, modifications and departures from the embodiments, examples and uses may be made without departing from the inventive concepts.

What is claimed is:

1. A method of predicting critical points in patient respiration, the method comprising the steps of:

monitoring at least one characteristic of a respiratory effort waveform of a patient to detect a respiratory event;

defining a refractory period including a hard refractory period during which time the respiratory event cannot be responded to and a soft refractory period following the hard refractory period;

detecting the respiratory event outside of the refractory period as a function of a first set of predetermined parameters for the monitored at least one characteristic; and

detecting the respiratory event within the soft refractory period as a function of a second set of predetermined parameters for the monitored at least one characteristic.

2. The method according to claim 1, wherein the respiratory event is inspiration onset and further wherein the at least one characteristic of the respiratory effort waveform monitored is at least one of slope and amplitude.

3. The method according to claim 2, wherein the step of detecting inspiration onset outside of the refractory period includes the step of detecting inspiration onset outside of the refractory period as a function of monitored slope of the respiratory effort waveform, and further wherein the step of detecting inspiration onset within the soft refractory period includes the step of detecting inspiration onset within the soft refractory period as a function of monitored slope and amplitude of the respiratory effort waveform.

4. The method according to claim 1, wherein the refractory period is defined based on detection of inspiration offset.

5. The method according to claim 2, wherein the refractory period is defined based on detection of inspiration offset and further wherein the method includes the step of detecting inspiration offset as a function of the monitored slope and amplitude of the respiratory effort waveform.

6. The method according to claim 5, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration offset includes the steps of:

comparing the slope values to a predetermined slope value offset threshold in a first comparison step;

comparing the amplitude of the sampled respiratory effort waveform to a predetermined amplitude offset threshold in a second comparison step;

detecting inspiration offset as a function of the first comparison step and second comparison step.

7. The method according to claim 6, wherein the detection of inspiration offset further includes validating the detected inspiration offset by comparing the amplitude of the sampled respiratory waveform to a validating offset threshold.

8. The method according to claim 6, wherein the detecting inspiration offset step further includes the step of detecting inspiration offset if a predetermined number of slope values satisfies the slope value offset threshold and the amplitude of at least the first of the predetermined number of slope values satisfies the amplitude offset threshold.

9. The method according to claim 2, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform signal and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration onset outside of the refractory period includes the step of detecting an inspiration onset as a function of a comparison of the slope values to a predetermined slope value onset threshold.

10. The method according to claim 9, wherein the detection of inspiration onset outside of the refractory period includes detecting inspiration onset if a

predetermined number of slope values satisfy the predetermined slope value onset threshold.

11. The method according to claim 2, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration onset within the soft refractory period includes the step of detecting inspiration onset as a function of a comparison of the slope values to a predetermined slope value onset threshold and comparison of the amplitude thereof to a predetermined amplitude onset threshold.

12. The method according to claim 11, wherein the detection of inspiration onset within the soft refractory period includes detecting inspiration onset if a predetermined number of slope values satisfy the predetermined slope value onset threshold and the amplitude thereof satisfies the amplitude onset threshold.

13. The method according to claim 1, wherein the defining step includes the steps of:

detecting inspiration offset;

determining an average respiratory period;

providing an average time of inspiration; and

defining the refractory period, including the soft and hard refractory periods, as a function of the detected inspiration offset, average respiratory period, and average time of inspiration.

14. The method according to claim 13, wherein the refractory period is defined as a portion of the average respiratory period and the soft refractory period is defined as a portion of the refractory period.

15. The method according to claim 13, wherein the refractory period is defined as a portion of the average respiratory period and the soft refractory period is defined as a portion of the average respiratory period.

16. The method according to claim 13, wherein the average respiratory period is a weighted sum average respiratory period.

17. The method according to claim 1, wherein the refractory period is defined as a function of an average time of inspiration, the average time of inspiration being a physician programmable value.

18. The method according to claim 1, wherein the defining step includes defining the refractory period, including the soft and hard refractory periods, as a function of time of stimulation.

19. The method according to claim 2, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the method includes setting an amplitude onset threshold and a slope value onset threshold, and yet further wherein the detection of inspiration onset outside of the refractory period is performed by comparing the slope values to the slope value onset threshold and the detection of inspiration onset within the soft refractory period is performed by comparing the slope values to the slope value onset threshold and the amplitude thereof to the amplitude onset threshold.

20. A method for providing stimulation of a patient to treat respiratory disorders, the method comprising the steps of:

monitoring slope and amplitude of a respiratory effort waveform of a patient to detect inspiration onset;

defining a refractory period including a hard refractory period during which time an inspiration onset cannot initiate stimulation and a soft refractory period following the hard refractory period;

detecting inspiration onset outside of the refractory period as a function of the slope of the respiratory effort waveform;

detecting inspiration onset within the soft refractory period as a function of slope and amplitude of the respiratory effort waveform; and

stimulating in response to a detected inspiration onset.

21. The method according to claim 20, wherein the refractory period is defined based on detection of inspiration offset.

22. The method according to claim 21, further including the step of detecting inspiration offset as a function of the monitored slope and amplitude of the respiratory effort waveform.

23. The method according to claim 22, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration offset includes the steps of:

comparing the slope values to a predetermined slope value offset threshold in a first comparison step;

comparing the amplitude of sampled respiratory effort waveform to a predetermined amplitude offset threshold in a second comparison step; and

detecting inspiration offset as a function of the first comparison step and the second comparison step.

24. The method according to claim 23, wherein the detection of inspiration offset further includes validating the detected inspiration offset by comparing the amplitude of the sampled respiratory waveform to a validating offset threshold and terminating stimulation as a function of such comparison.

25. The method according to claim 24, wherein the validating offset threshold is one of the detected inspiration offset, zero crossing of the respiratory waveform, or an inspiration onset threshold.

26. The method according to claim 23, wherein the detecting inspiration offset step further includes the step of detecting inspiration offset if a predetermined number of slope values satisfies the slope value offset threshold and the amplitude of at least the first of the predetermined number of slope values satisfies the amplitude offset threshold.

27. The method according to claim 20, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform signal and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration onset outside of the refractory period includes the step of detecting an inspiration onset as a function of a comparison of the slope values to a predetermined slope value onset threshold.

28. The method according to claim 27, wherein the detection of inspiration onset outside of the refractory period includes detecting inspiration onset if a predetermined number of slope values satisfy the predetermined slope value onset threshold.

29. The method according to claim 1, wherein the monitoring step includes sampling the amplitude of the respiratory effort waveform signal and generating slope values representative of the respiratory effort waveform based on the amplitude samples, and further wherein the detection of inspiration onset within the soft refractory period includes the step of detecting inspiration onset as a function of a comparison of the slope values to a predetermined slope value onset threshold and comparison of the amplitude thereof to a predetermined amplitude onset threshold.

30. The method according to claim 29, wherein the detection of inspiration onset within the soft refractory period includes detecting inspiration onset if a predetermined number of slope values satisfy the predetermined slope value onset threshold and the amplitude thereof satisfies the amplitude onset threshold.

31. The method according to claim 20, wherein the defining step includes defining the refractory period, including the soft and hard refractory periods, as a function of time of stimulation.

32. The method according to claim 20, wherein the stimulation is continued until at least inspiration offset is detected or until a maximum stimulation time is reached.

33. A method for providing stimulation of a patient to treat respiratory disorders, the method comprising the steps of:

monitoring slope and amplitude of a respiratory effort waveform of a patient to detect inspiration onset and inspiration offset;

defining a refractory period including a hard refractory period during which time an inspiration onset cannot initiate stimulation and a soft refractory period following the hard refractory period;

detecting inspiration onset outside of the refractory period as a function of a first set of at least one of slope and amplitude criteria for the respiratory effort waveform;

detecting inspiration onset within the soft refractory period as a function of a second set of at least one of slope and amplitude criteria for the respiratory effort waveform;

stimulating in response to detection of inspiration onset, stimulation terminating as a function of detection of inspiration offset or a maximum stimulation time; and

setting the second set of criteria sufficiently sensitive relative to the first set of criteria such that stimulation, for one or more respiratory cycles, is applied as a function of the maximum stimulation time and the defined refractory period.

34. The method according to claim 33, further including the step of updating gain of the respiratory effort waveform during the one or more respiratory cycles such that stimulation can be controlled by detecting inspiration onset during later respiratory cycles.

35. A method of predicting critical points in patient respiration, the method comprising the steps of:

sampling the amplitude of the respiratory effort waveform of a patient;

generating a sample signal representative of at least one characteristic of the respiratory effort waveform based on each amplitude sample,

monitoring the sample signals representative of the at least one characteristic of the respiratory effort waveform; and

detecting a respiratory event as a function of at least two sample signals.

36. The method according to claim 35, wherein the respiratory event is inspiration onset, and further wherein the at least one characteristic of the respiratory effort waveform is at least one of slope and amplitude.

37. The method according to claim 36, wherein inspiration onset is detected as a function of at least two sample signals representative of slope of the respiratory effort waveform.

38. The method according to claim 35, wherein the respiratory event is inspiration offset and further wherein the at least one characteristic of the respiratory effort waveform is at least one of slope and amplitude.

39. The method according to claim 38, wherein the generating step includes generating slope values representative of the respiratory effort waveform based on the each amplitude sample, and further wherein the detection of inspiration offset includes the steps of:

comparing the slope values to a predetermined slope value offset threshold in a first comparison step;

comparing the sampled amplitude of the respiratory effort waveform to a predetermined amplitude offset threshold in a second comparison step; and

detecting inspiration offset as a function of the first comparison step and the second comparison step.

40. The method according to claim 39, wherein the step of detecting inspiration offset further includes validating the detected inspiration offset by comparing the sampled amplitude of the respiratory waveform to a validating offset threshold, whereby the validated inspiration offset as opposed to the detected inspiration offset triggers an associated activity.

41. The method according to 40, wherein the validating offset threshold is one of the detected inspiration offset, zero crossing of the respiratory waveform, or an inspiration onset threshold.

42. The method according to claim 40, wherein the detecting inspiration offset step further includes the step of detecting inspiration offset if a predetermined number of slope values satisfies the slope value offset threshold and the amplitude of at least the first of the predetermined number of slope values satisfies the amplitude offset threshold.

43. An apparatus for predicting critical points in patient respiration, the apparatus comprising:

monitoring means for monitoring at least one characteristic of a respiratory effort waveform of a patient; and

respiration detection means for detecting a respiratory event, the respiration detection means including:

means for defining a refractory period including a hard refractory period and a soft refractory period following the hard refractory period;

means for detecting the respiratory event outside of the refractory period as a function of a first set of predetermined parameters for the monitored at least one characteristic of the respiratory effort waveform; and

means for detecting the respiratory event within the soft refractory period as a function of a second set of predetermined parameters for the monitored at least one characteristic of the respiratory effort waveform.

44. The apparatus according to claim 43, wherein the respiratory event is inspiration onset.

45. The apparatus according to claim 44, wherein the at least one characteristic of the respiratory effort waveform monitored is at least one of slope and amplitude of the respiratory effort waveform.

46. The apparatus according to claim 45, wherein the respiration detection means further includes means for detecting inspiration offset as a function of the at least one monitored slope and amplitude of the respiratory effort waveform.

47. The apparatus according to claim 46, wherein the inspiration offset detection means includes:

means for comparing the slope to a predetermined slope offset threshold; and

means for comparing the amplitude of the respiratory effort waveform to a predetermined amplitude offset threshold.

48. The apparatus according to claim 45, wherein the means for detecting the respiratory event outside of the refractory period includes means for comparing the monitored slope of the respiratory effort waveform to a predetermined slope onset threshold to detect inspiration onset.

49. The apparatus according to claim 45, wherein the means for detecting the respiratory event within the soft refractory period includes means for comparing the monitored slope of the respiratory effort waveform to a predetermined slope onset threshold and means for comparing the amplitude of the respiratory effort waveform to a predetermined amplitude onset threshold to detect inspiration onset.

50. A system for providing stimulation of a patient to treat respiratory disorders, the system comprising:

a sensor for providing a signal characteristic of a respiratory effort waveform of the patient;

slope monitoring means for monitoring the slope of the respiratory effort waveform;

amplitude monitoring means for monitoring the amplitude of the respiratory effort waveform;

respiration detection means for detecting inspiration onset, the respiration detection means including:

means for defining a refractory period, the refractory period including a hard refractory period during which time an inspiration onset cannot be responded to and a soft refractory period following the hard refractory period;

means for detecting inspiration onset outside of the refractory period as a function of the slope of the respiratory effort waveform;

means for detecting inspiration onset within the soft refractory period as a function of slope and amplitude of the respiratory effort waveform;

means for generating a stimulation signal in response to a detected inspiration onset; and

at least one electrode for delivering the stimulation signal to the patient.

51. The system according to claim 50, wherein the respiration detection means includes means for detecting inspiration offset as a function of at least one of monitored slope and amplitude, and further wherein the refractory period is defined based on detection of inspiration offset.

52. The system according to claim 50, wherein the means for detecting inspiration onset outside of the refractory period includes means for comparing the slope of the respiratory effort waveform to the predetermined slope onset threshold.

53. The system according to claim 51, wherein the means for detecting inspiration offset includes means for comparing the slope of the respiratory effort waveform to a predetermined slope offset threshold and means for comparing the amplitude of the respiratory effort waveform to a predetermined amplitude offset threshold.

54. The system according to claim 50, wherein the respiration detection means further includes means for terminating stimulation after a maximum predetermined stimulation time period.

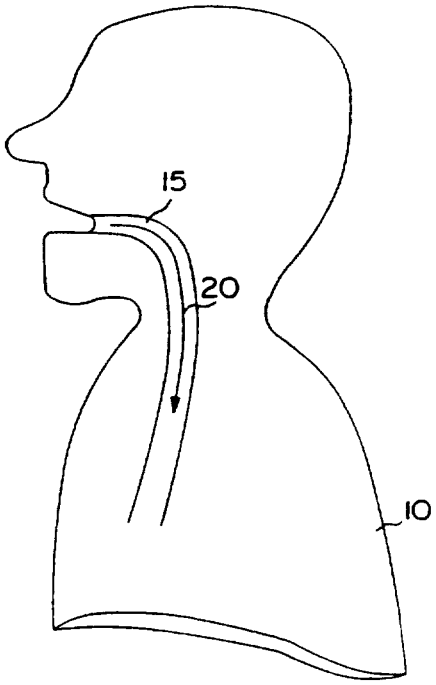


FIG. 1

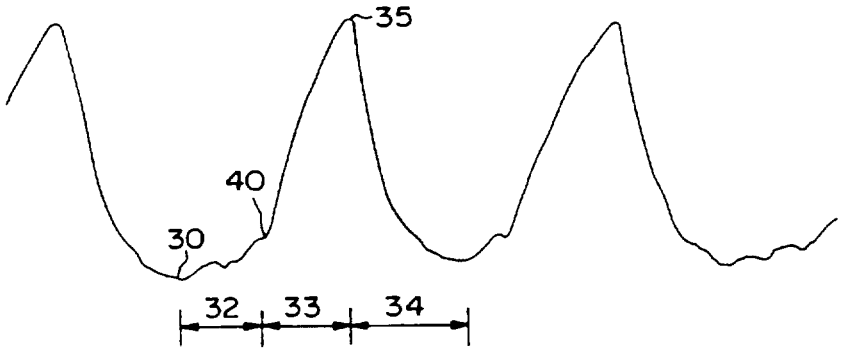


FIG. 2A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00411

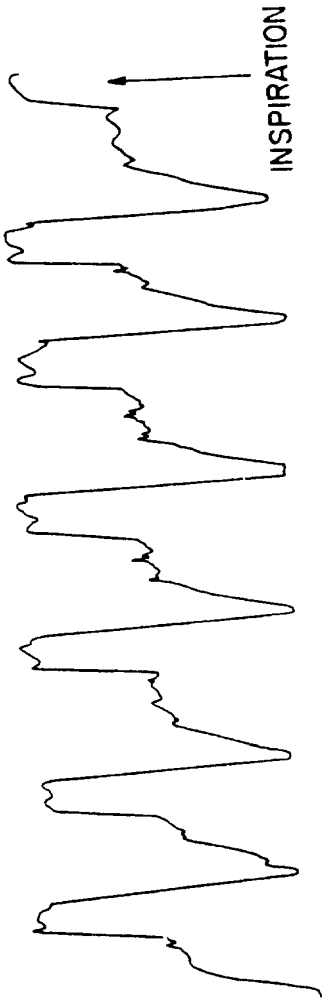


FIG. 2B



FIG. 2C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00412

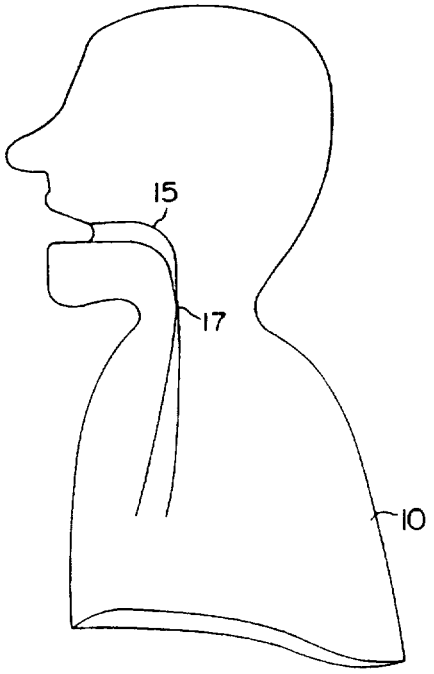


FIG. 3

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00413

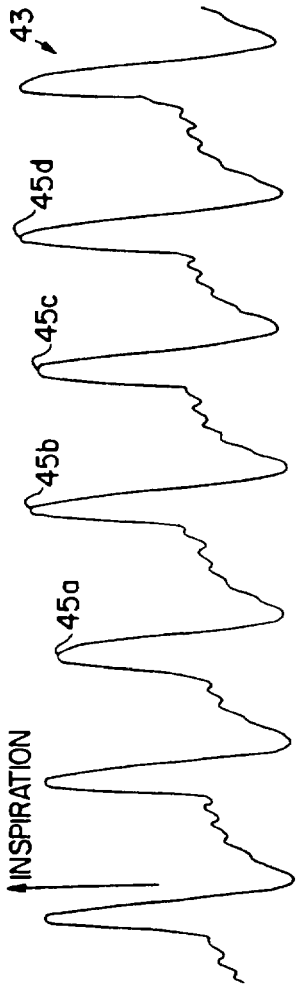


FIG. 4A

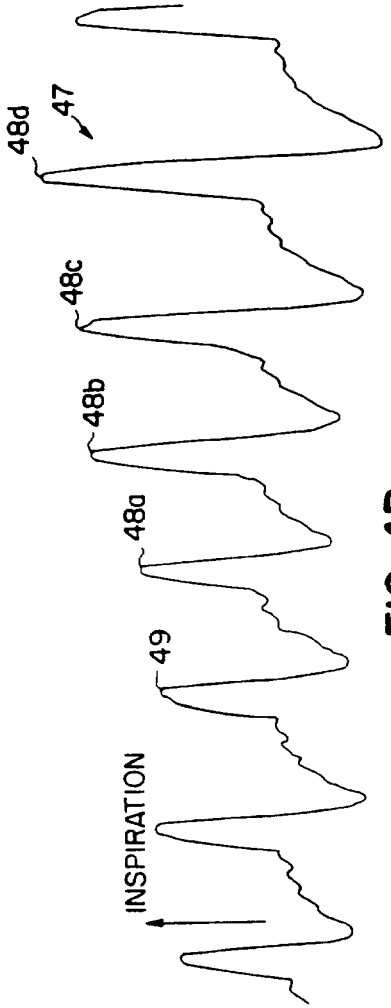


FIG. 4B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00414

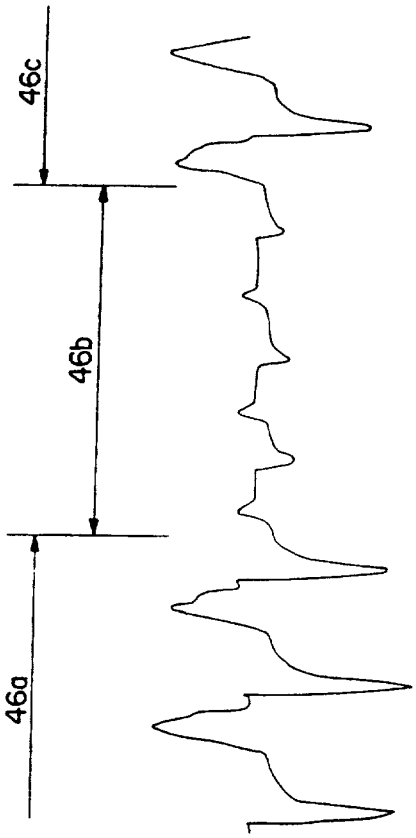


FIG. 4C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00415

6-131

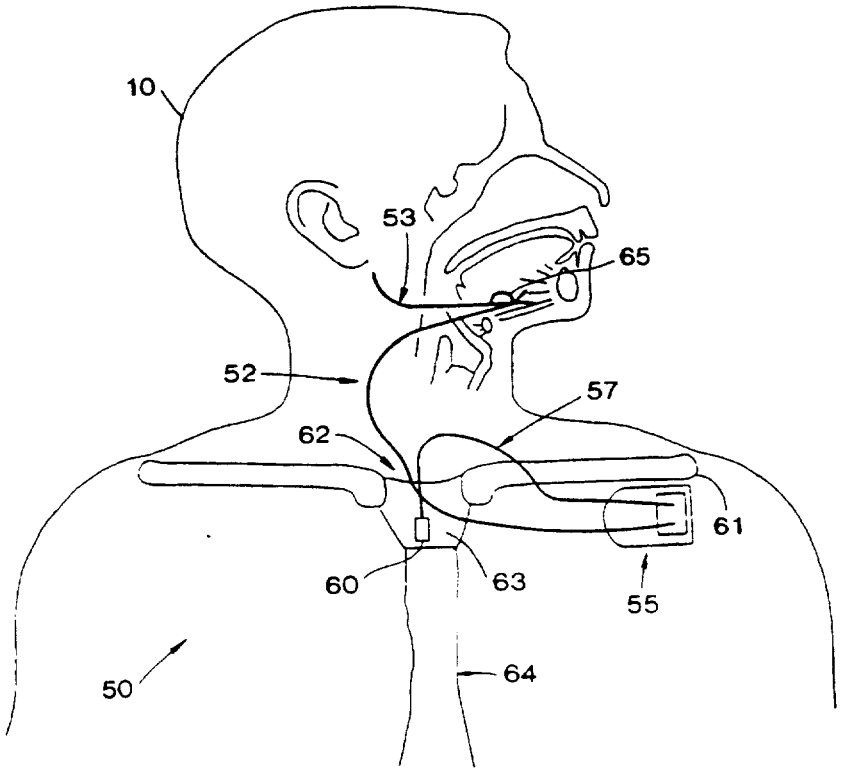


FIG. 5

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00416

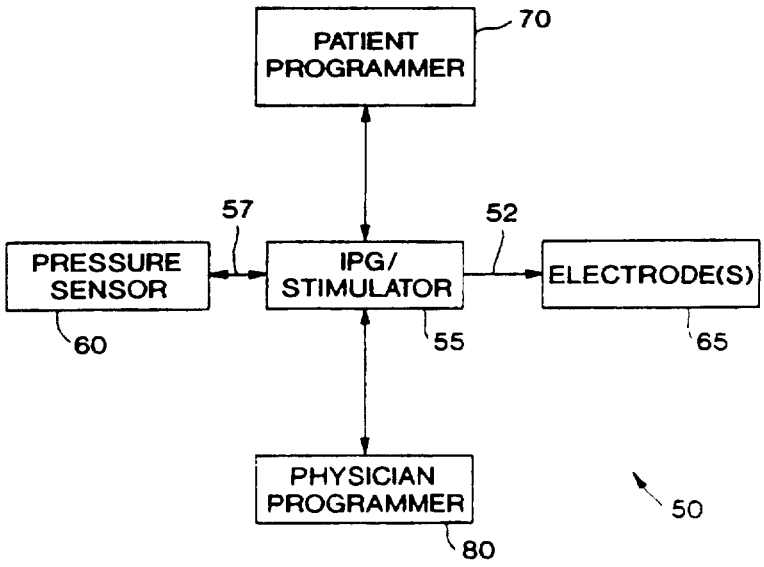


FIG. 6

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00417

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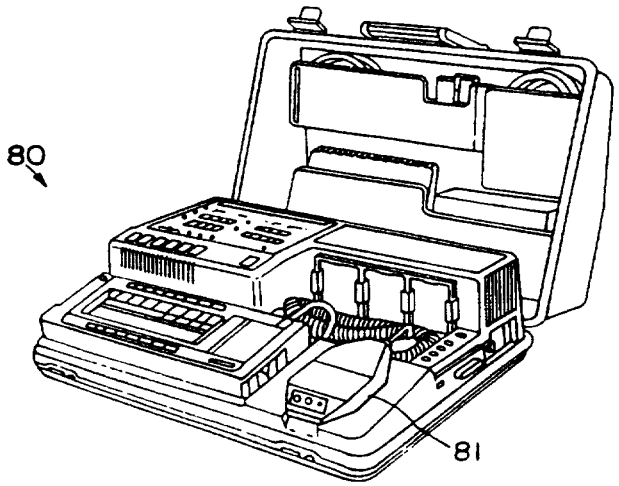


FIG. 7

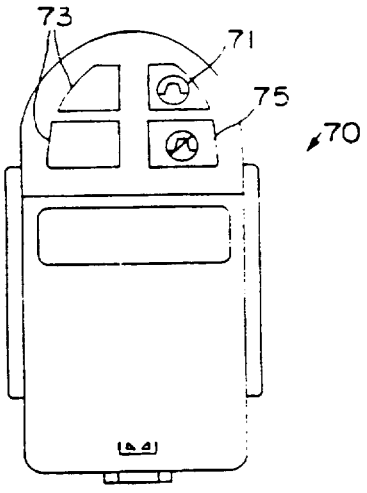


FIG. 8

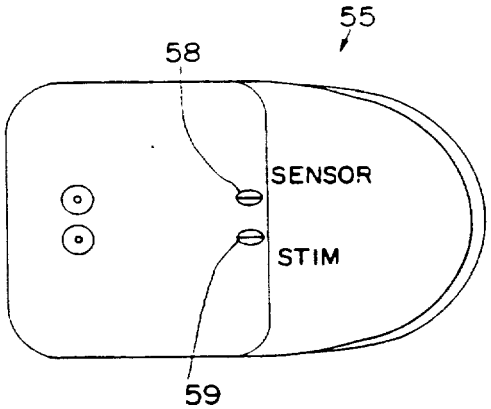


FIG. 9

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00418

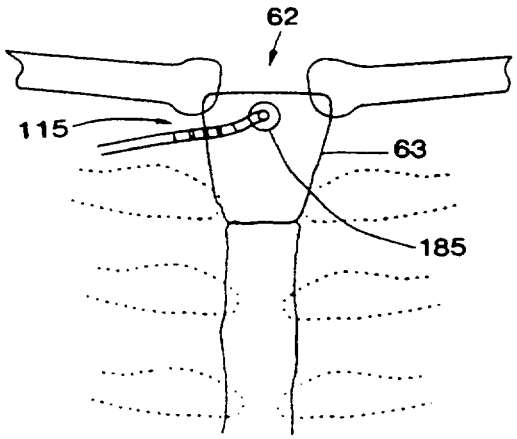


FIG. 10A

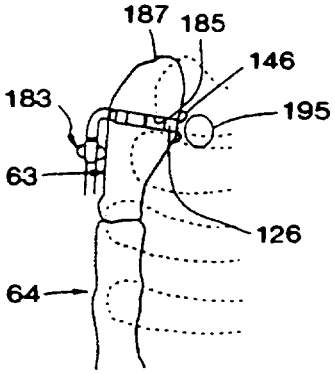


FIG. 10B

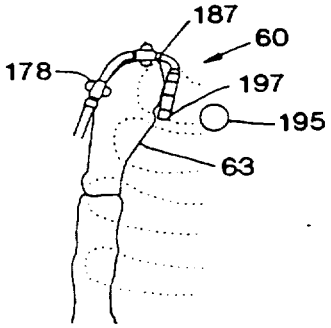


FIG. 10C

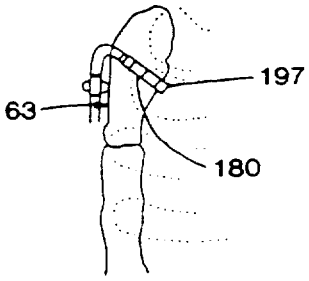


FIG. 10D

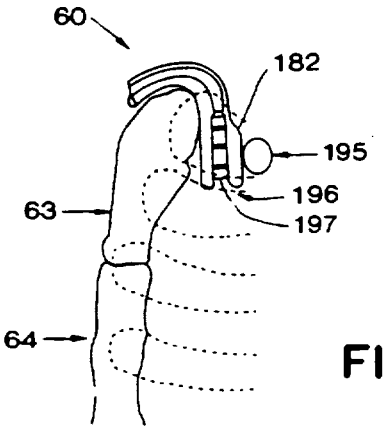


FIG. 10E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00419

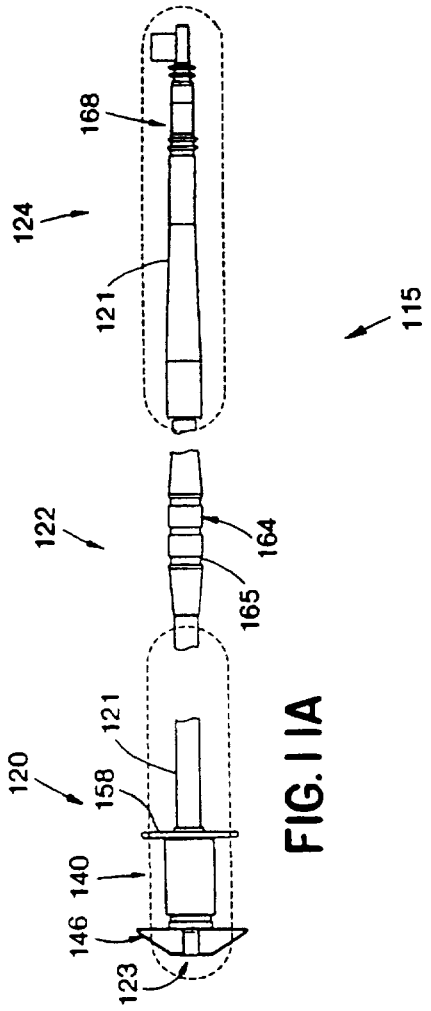


FIG. 1 IA

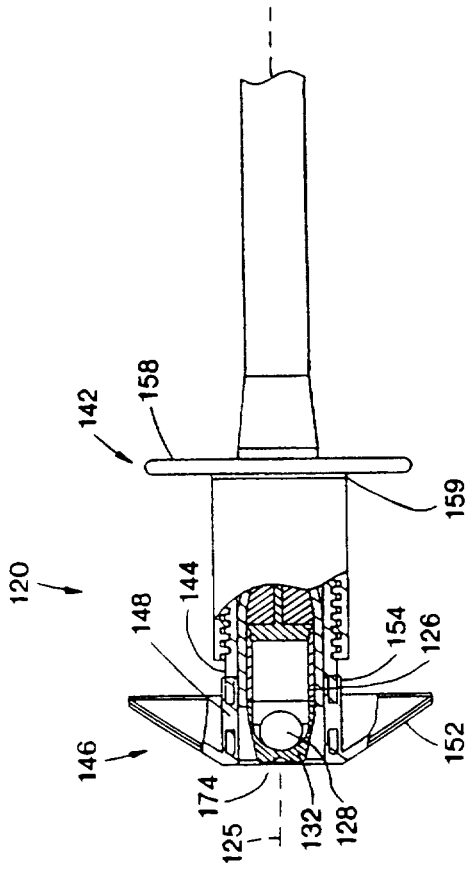


FIG. 1 IB

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00420

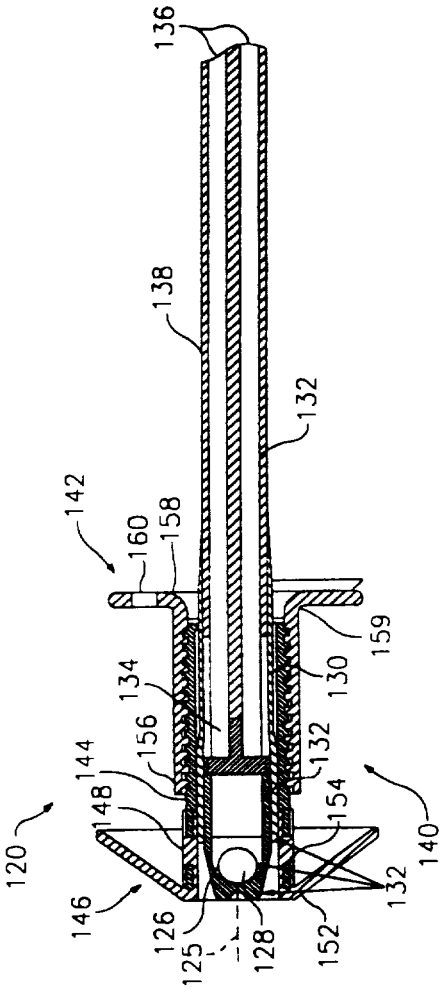


FIG. IIC

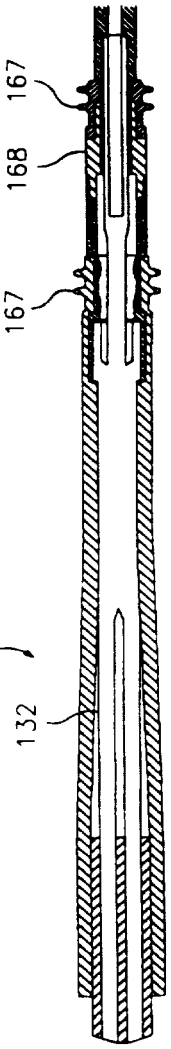


FIG. IID

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00421

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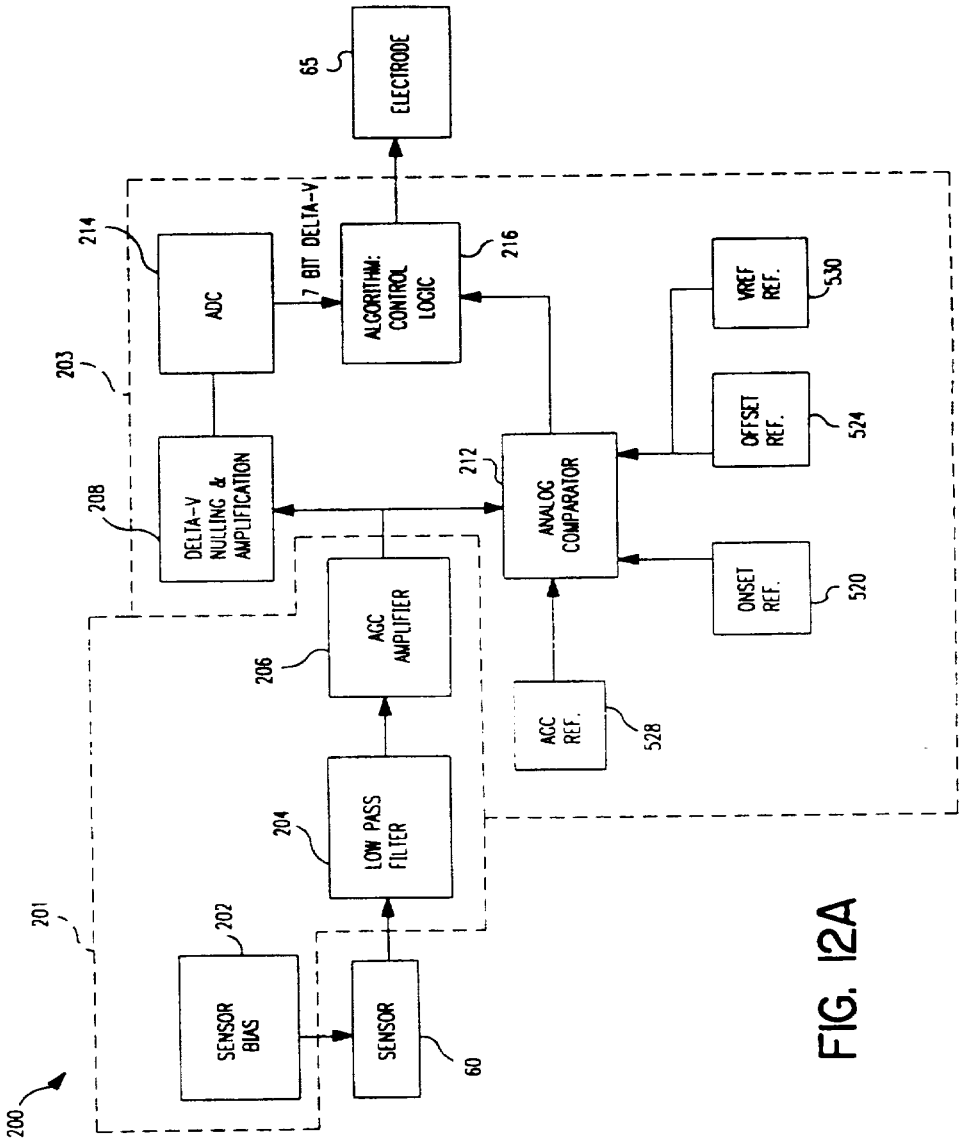


FIG. 12A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00422

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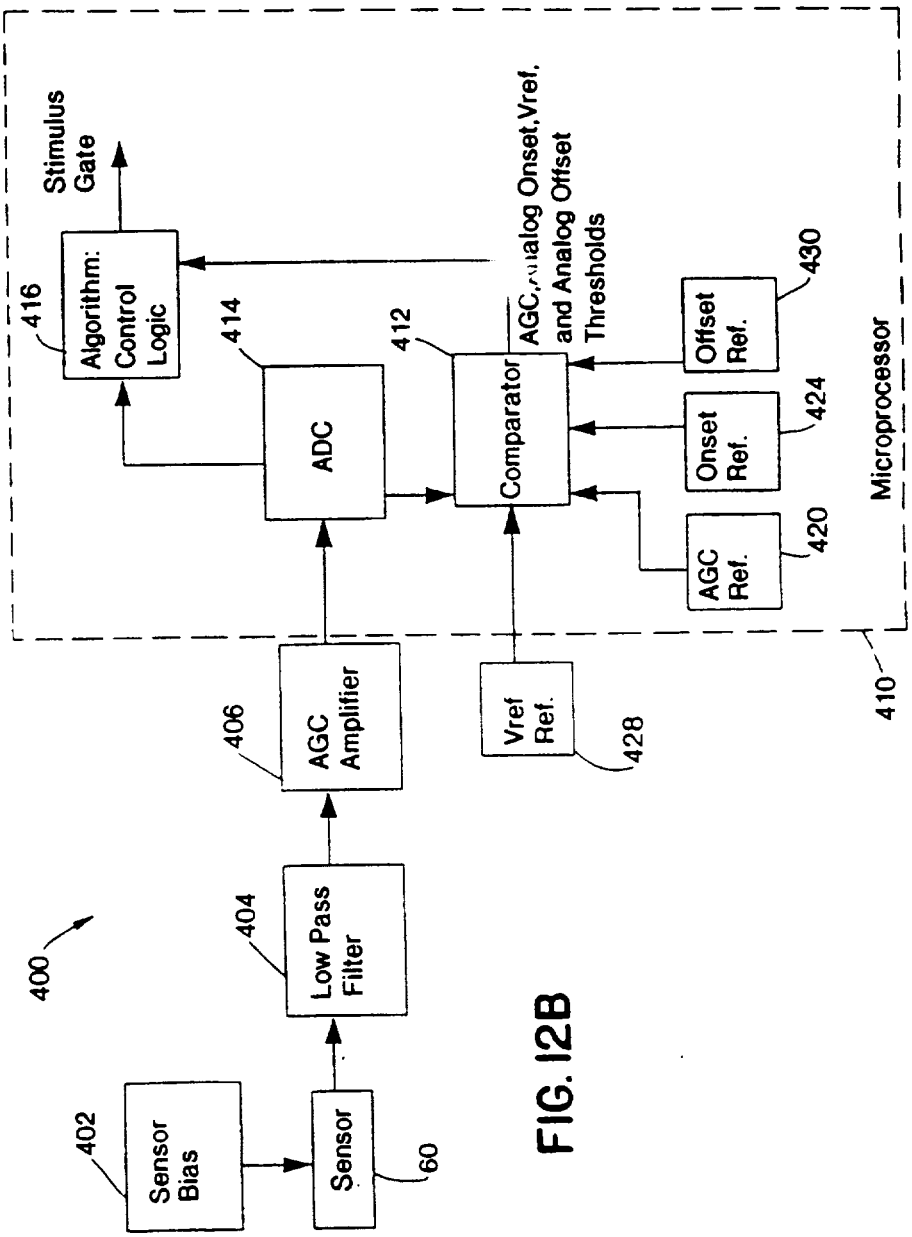


FIG. 12B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00423

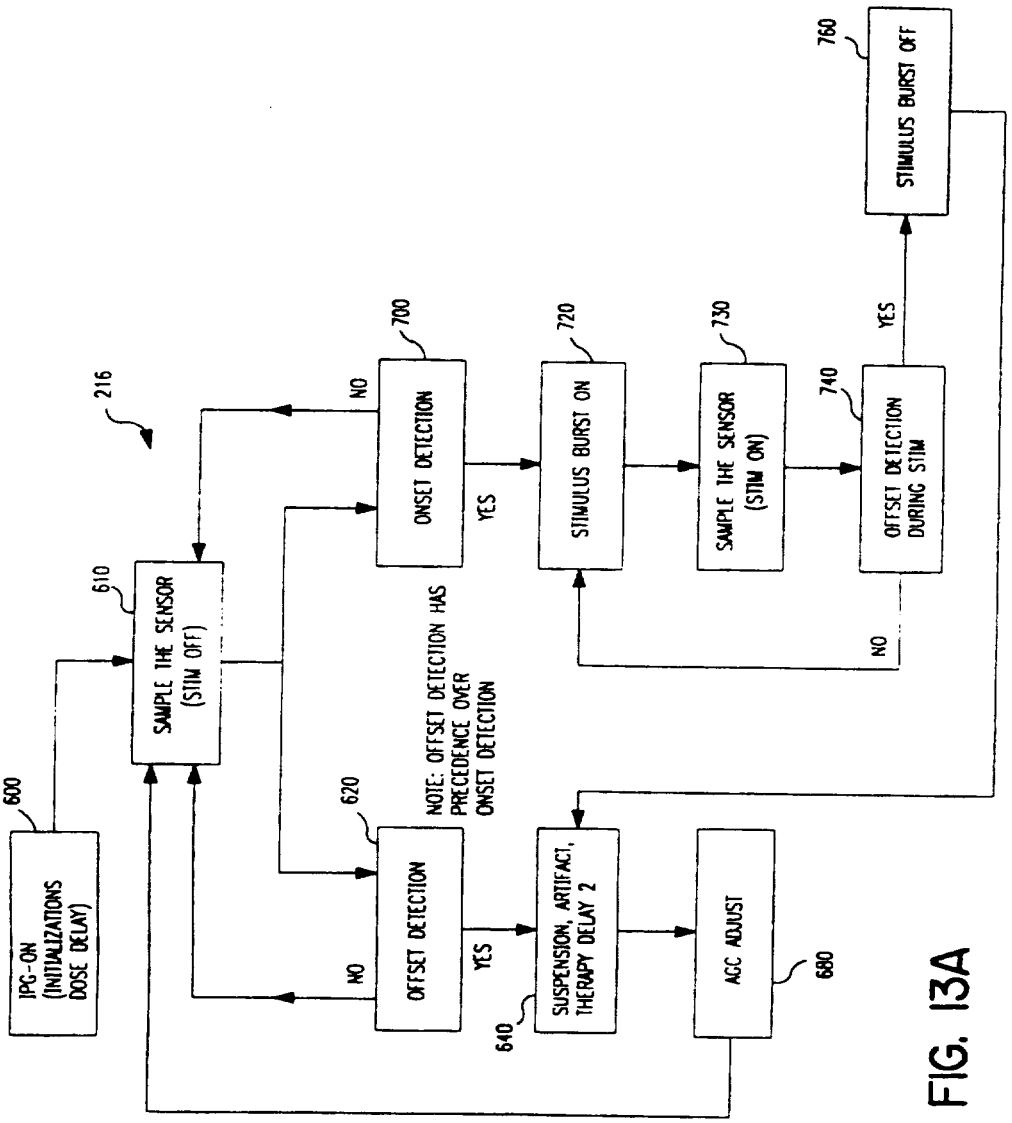


FIG. 13A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00424

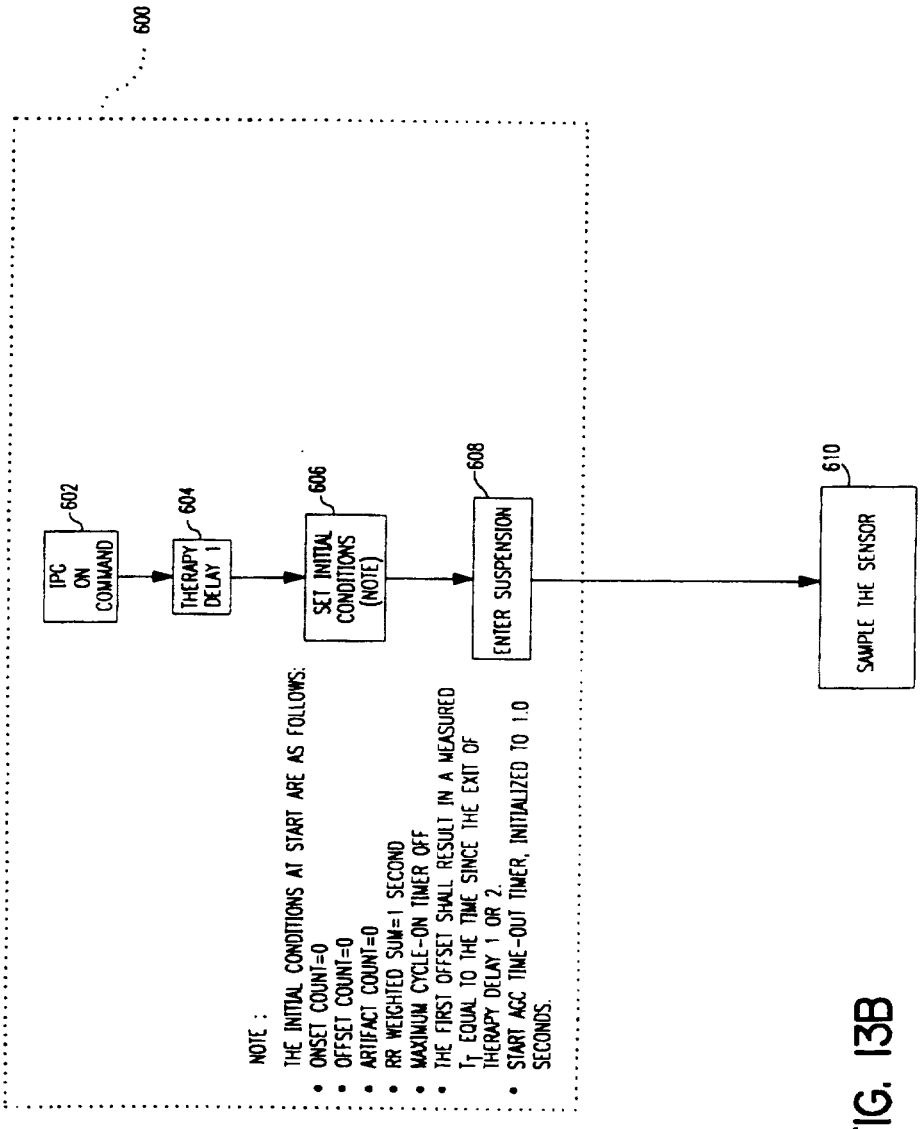


FIG. 13B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00425

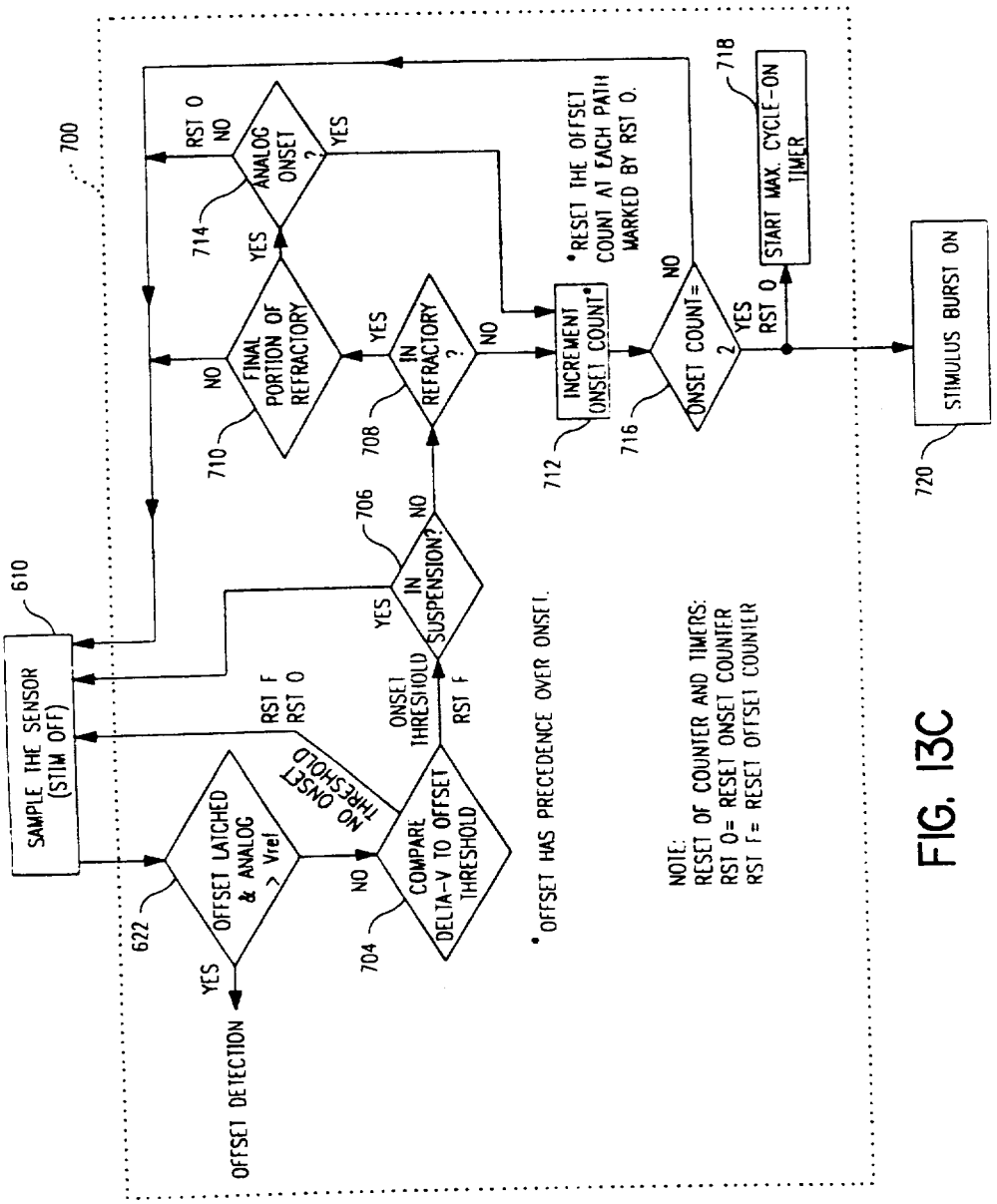


FIG. 13C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00426

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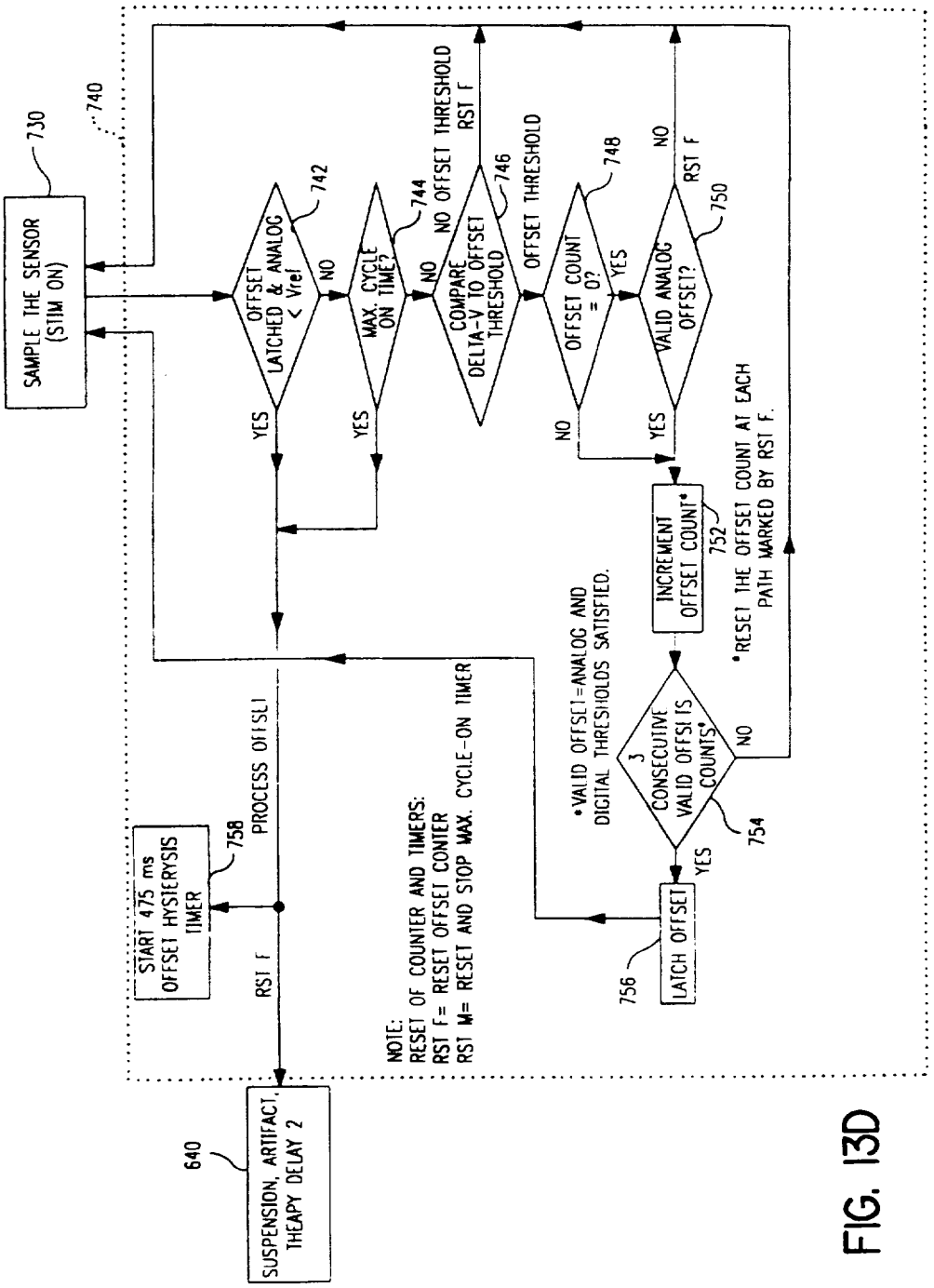


FIG. 13D

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00427

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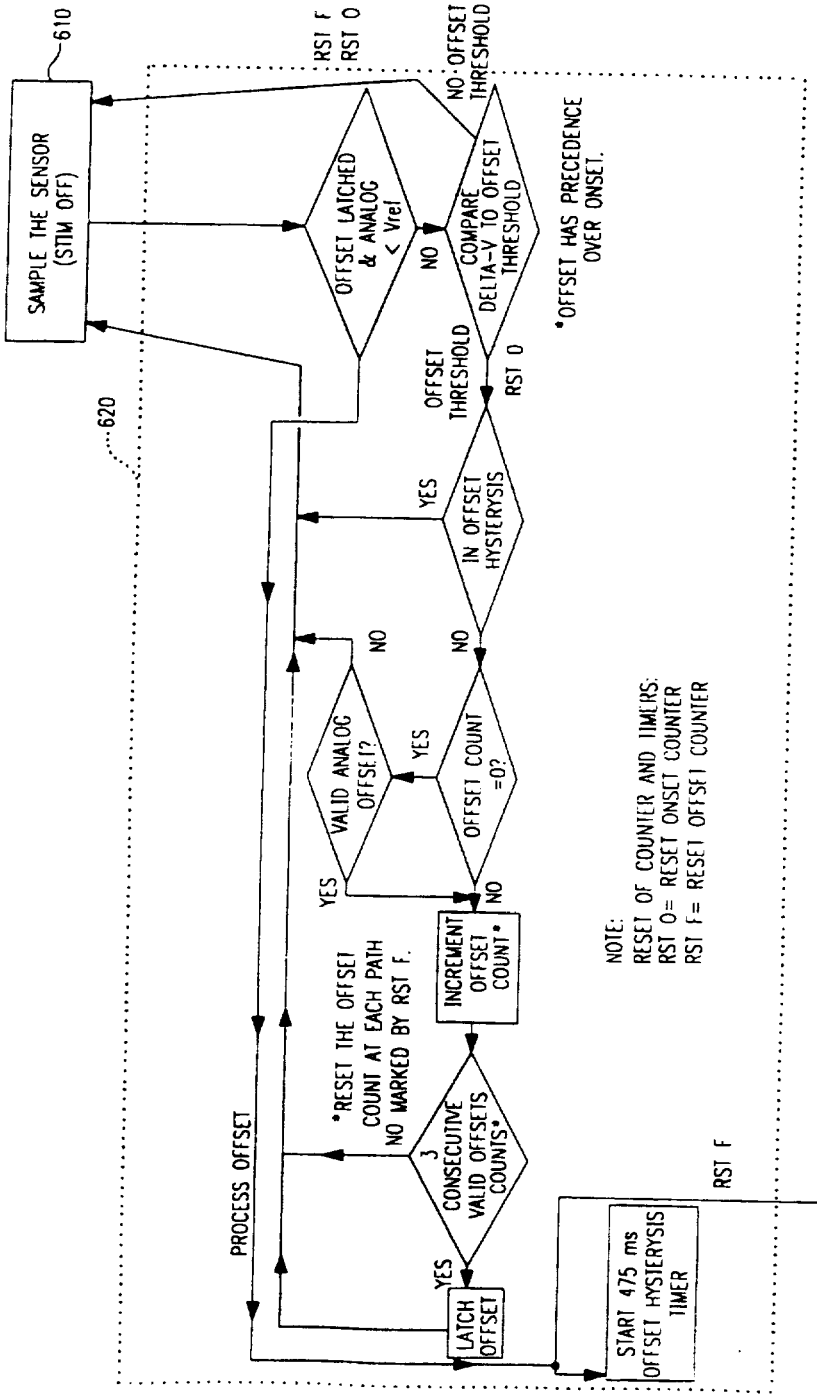


FIG. 13E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00428

FIG. 13F

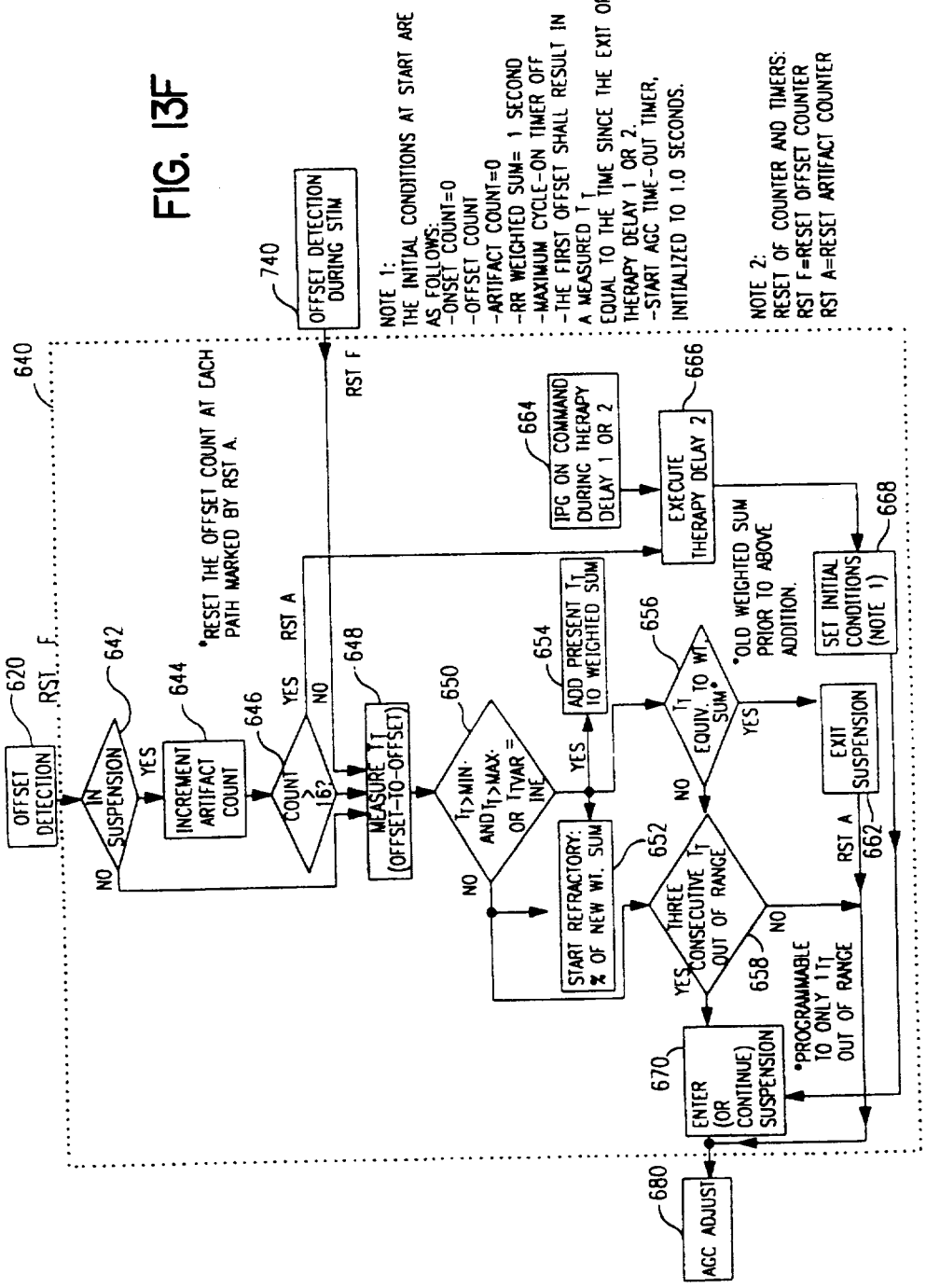


Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00429

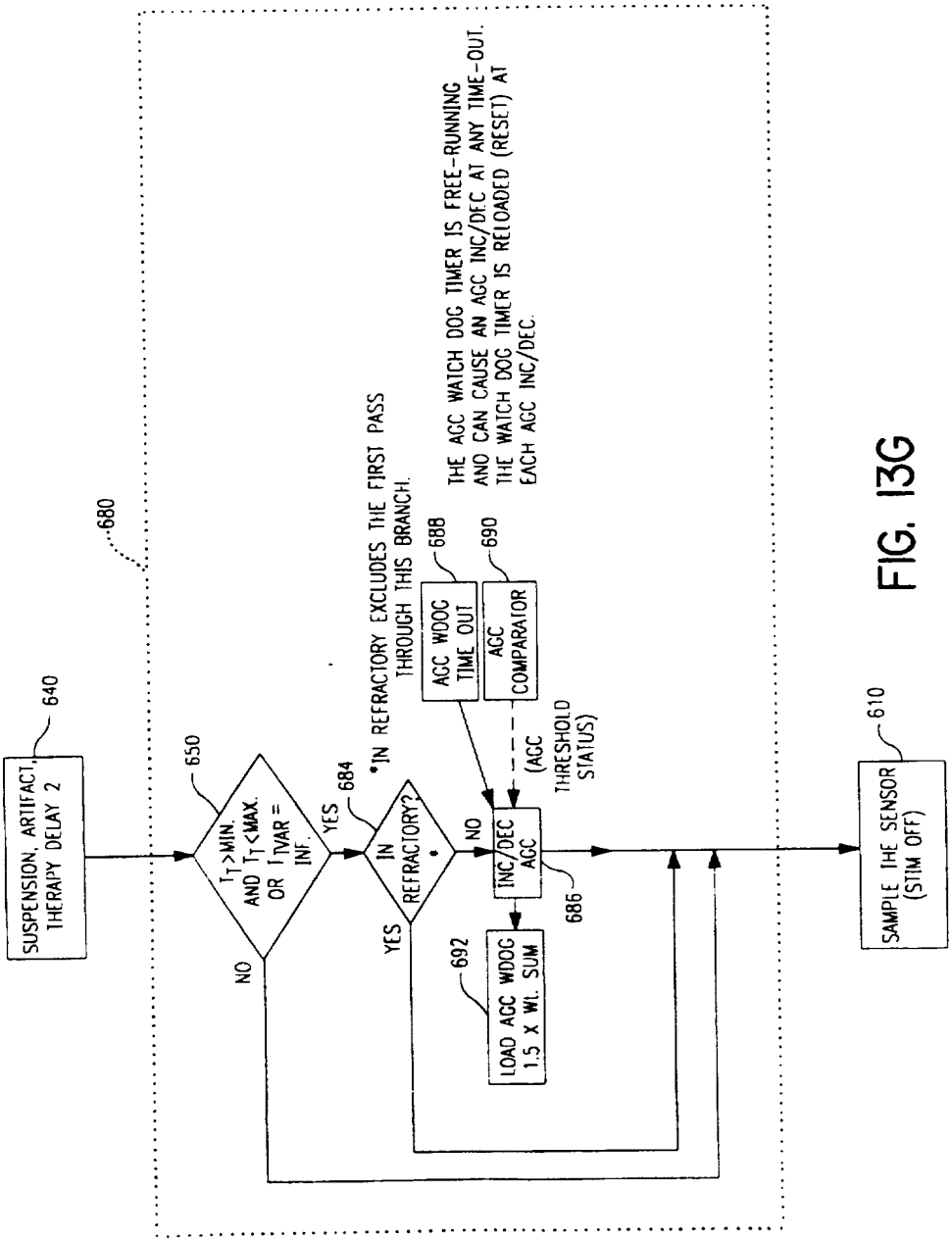


FIG. 13G

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00430

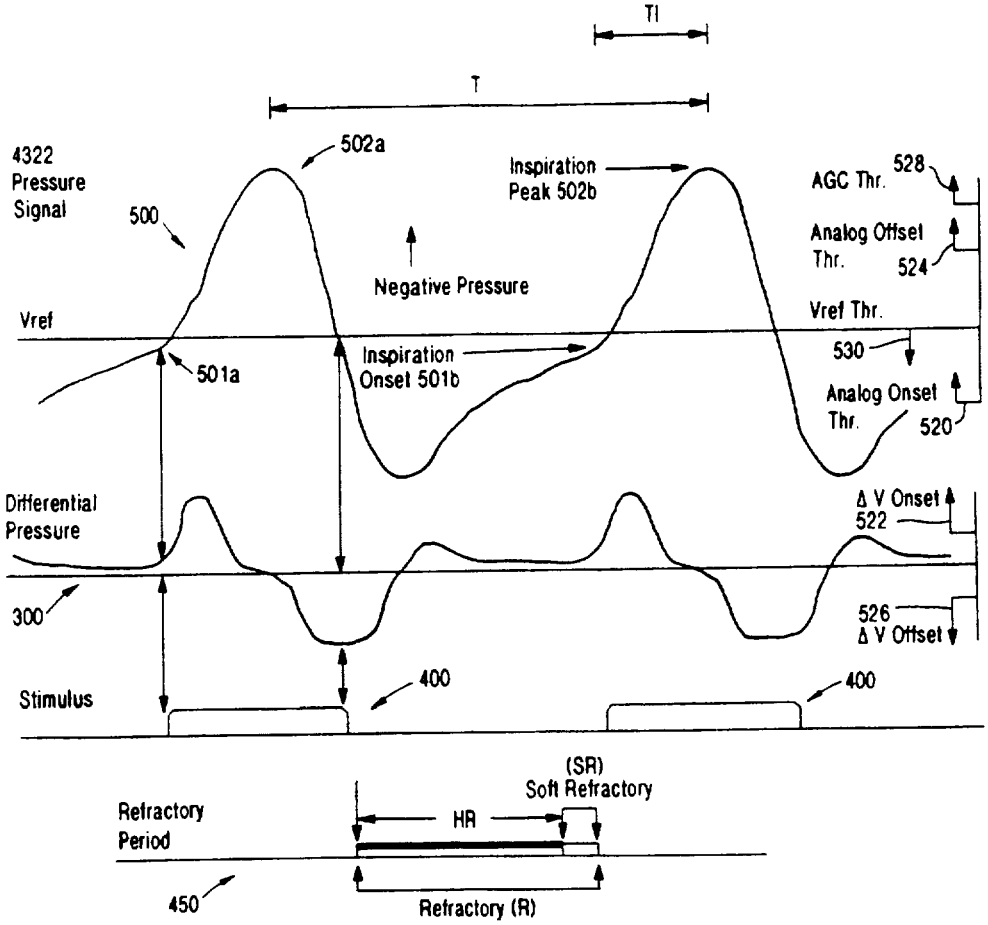


FIG. 14

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00431

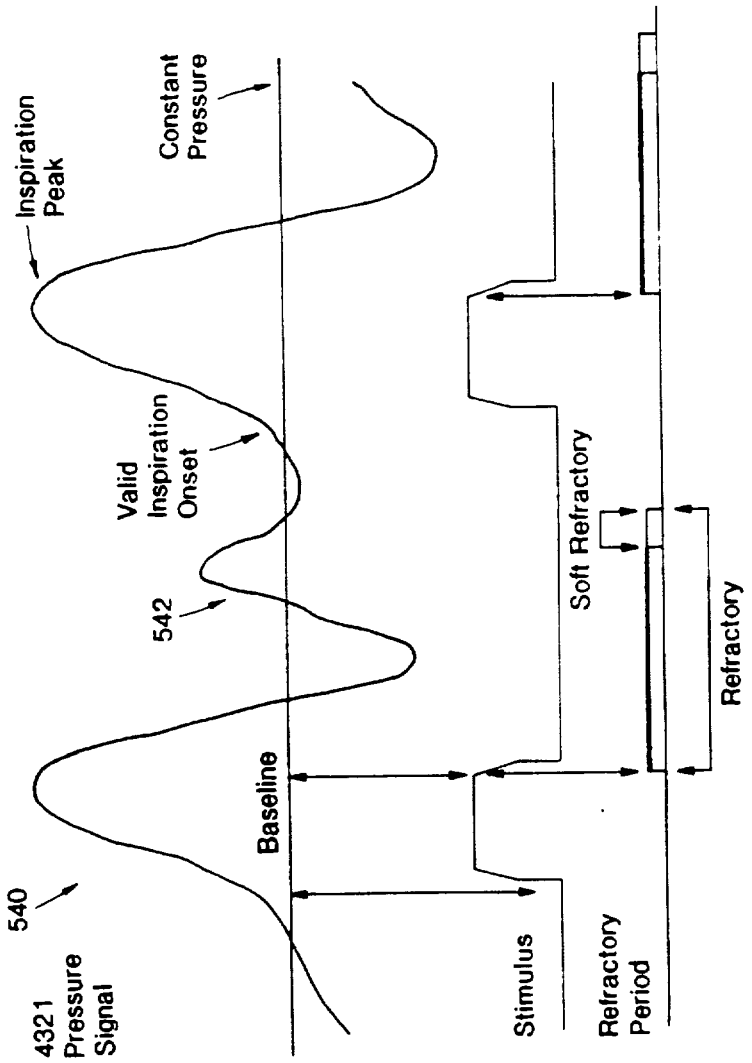


FIG. 15

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00432

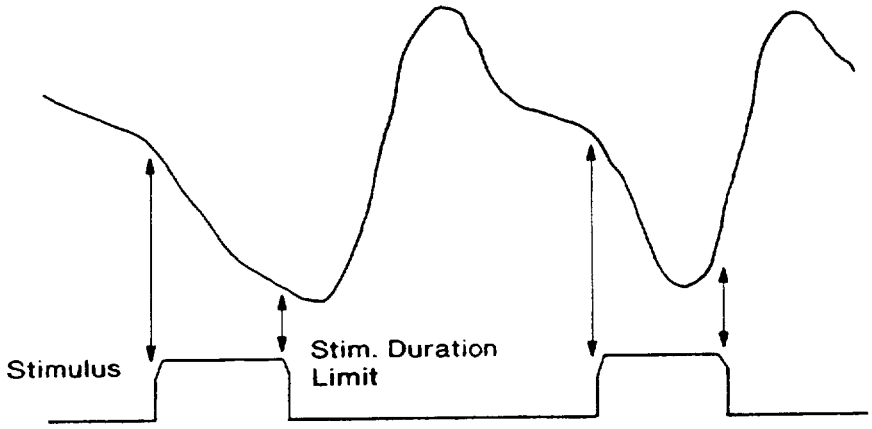


FIG. 16A

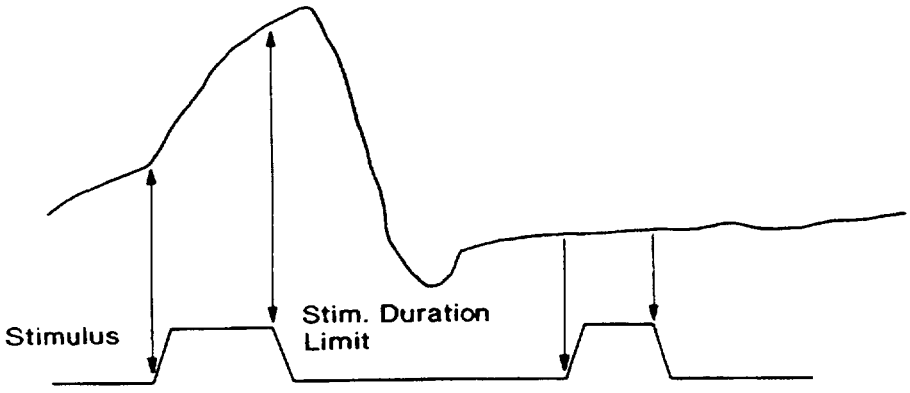


FIG. 16B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00433

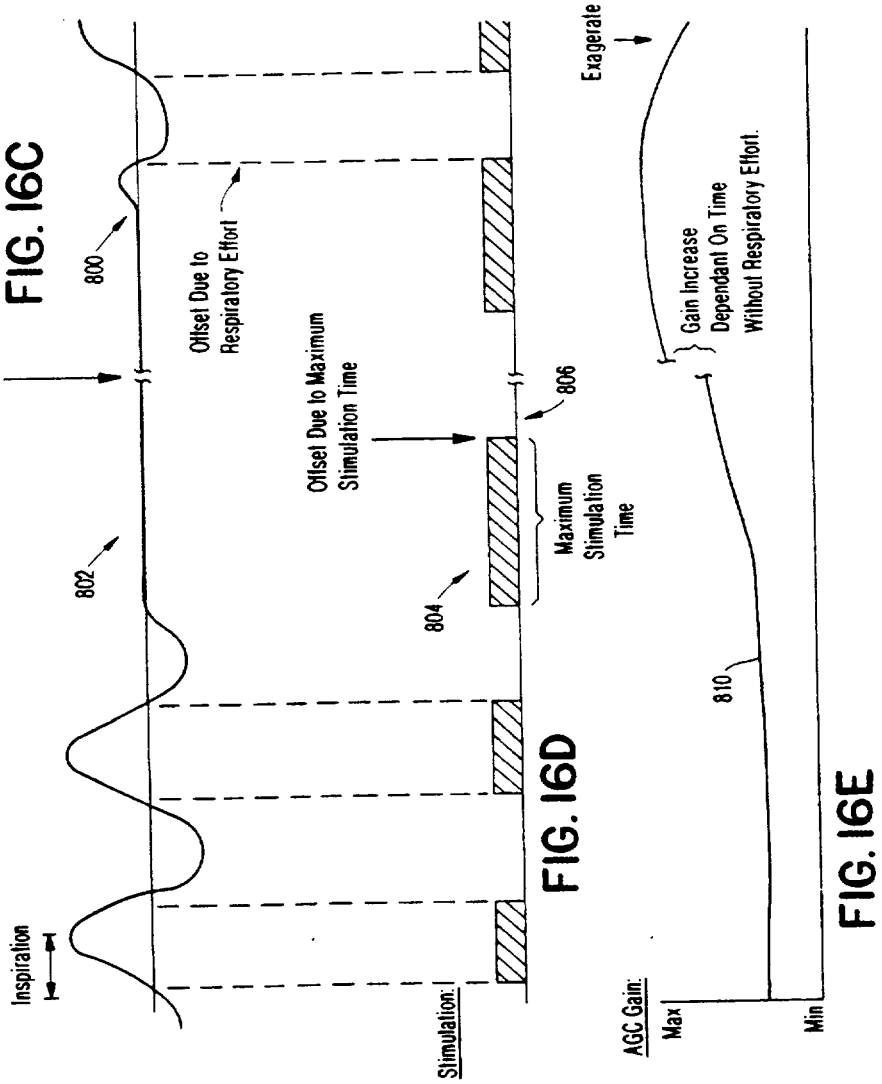


FIG. 16C

FIG. 16D

FIG. 16E

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00434

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FIG. 17A

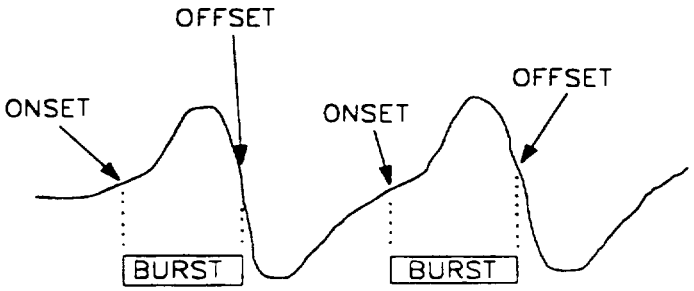


FIG. 17B

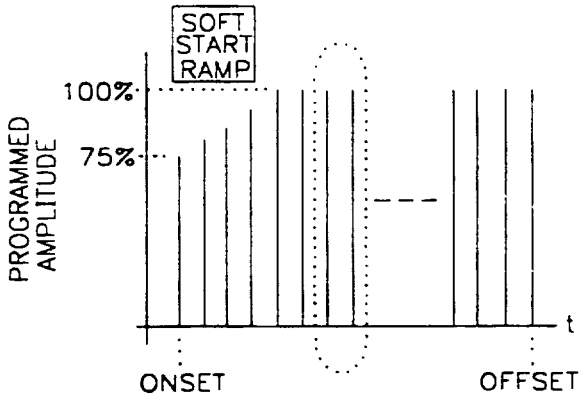


FIG. 17C

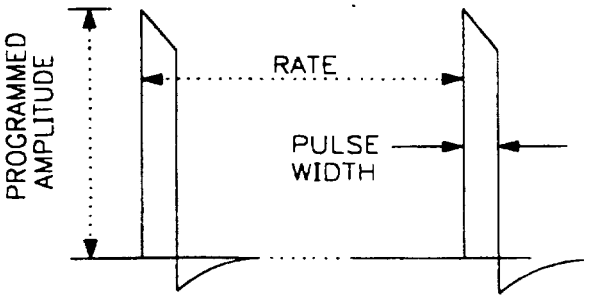


Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00435

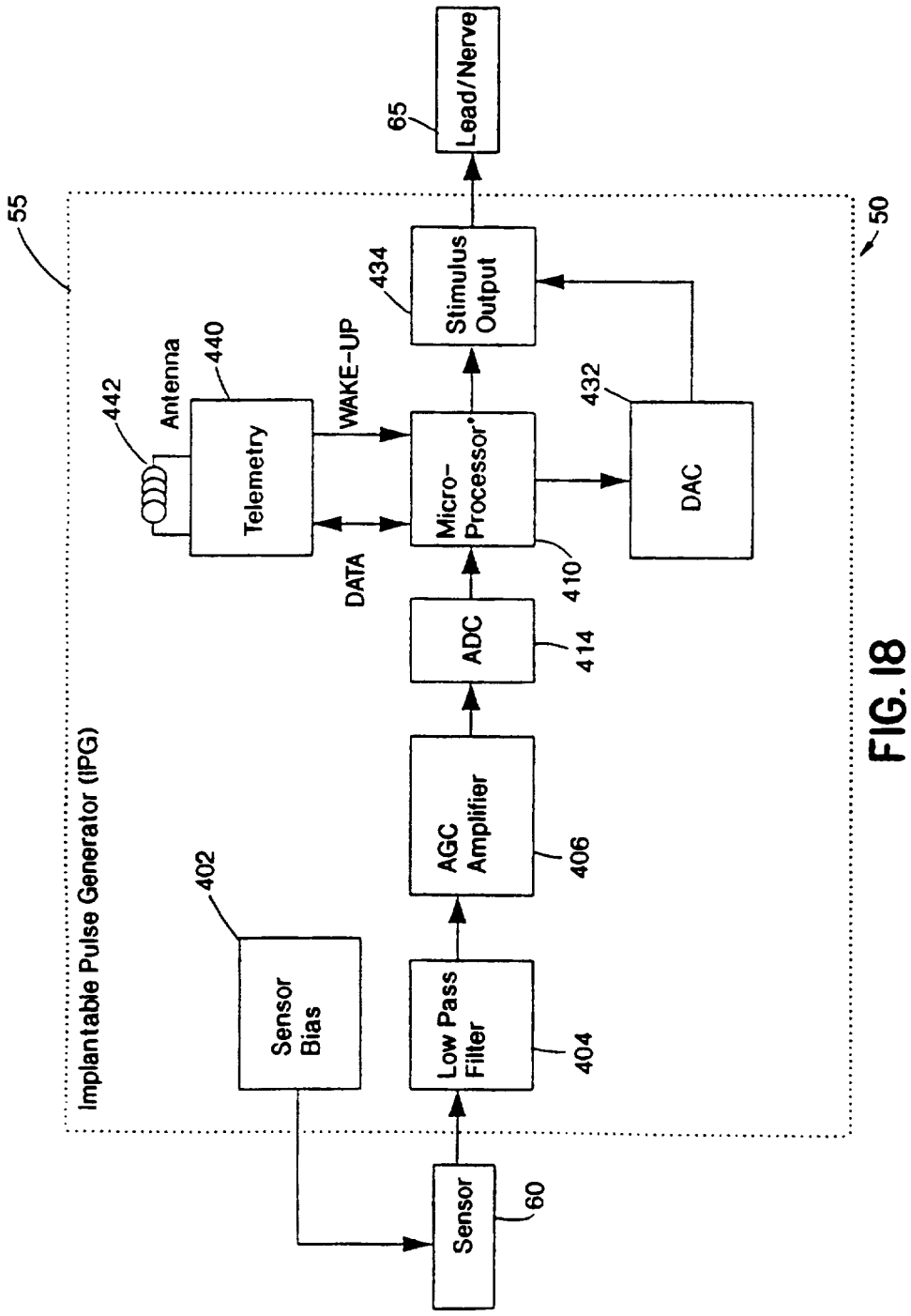


FIG. 18

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00436

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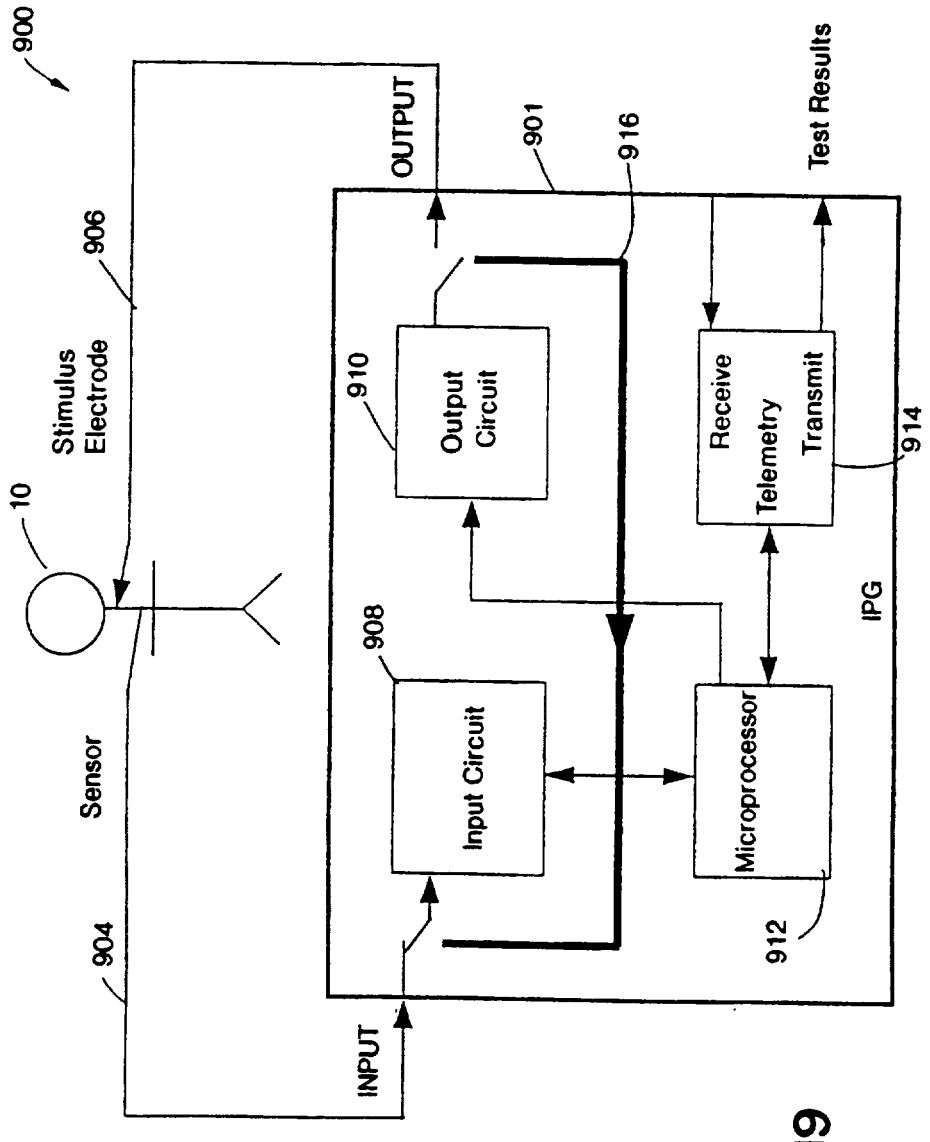


FIG. 19

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00437

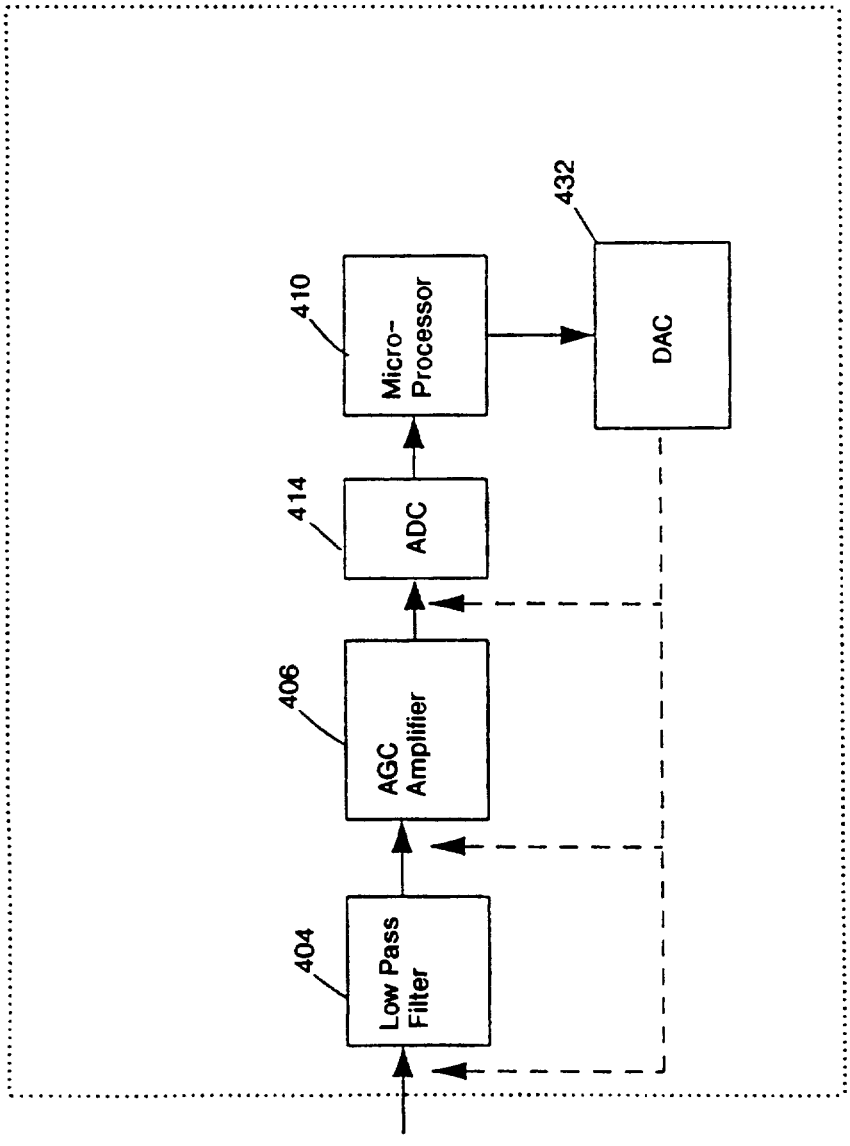


FIG. 20A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00438

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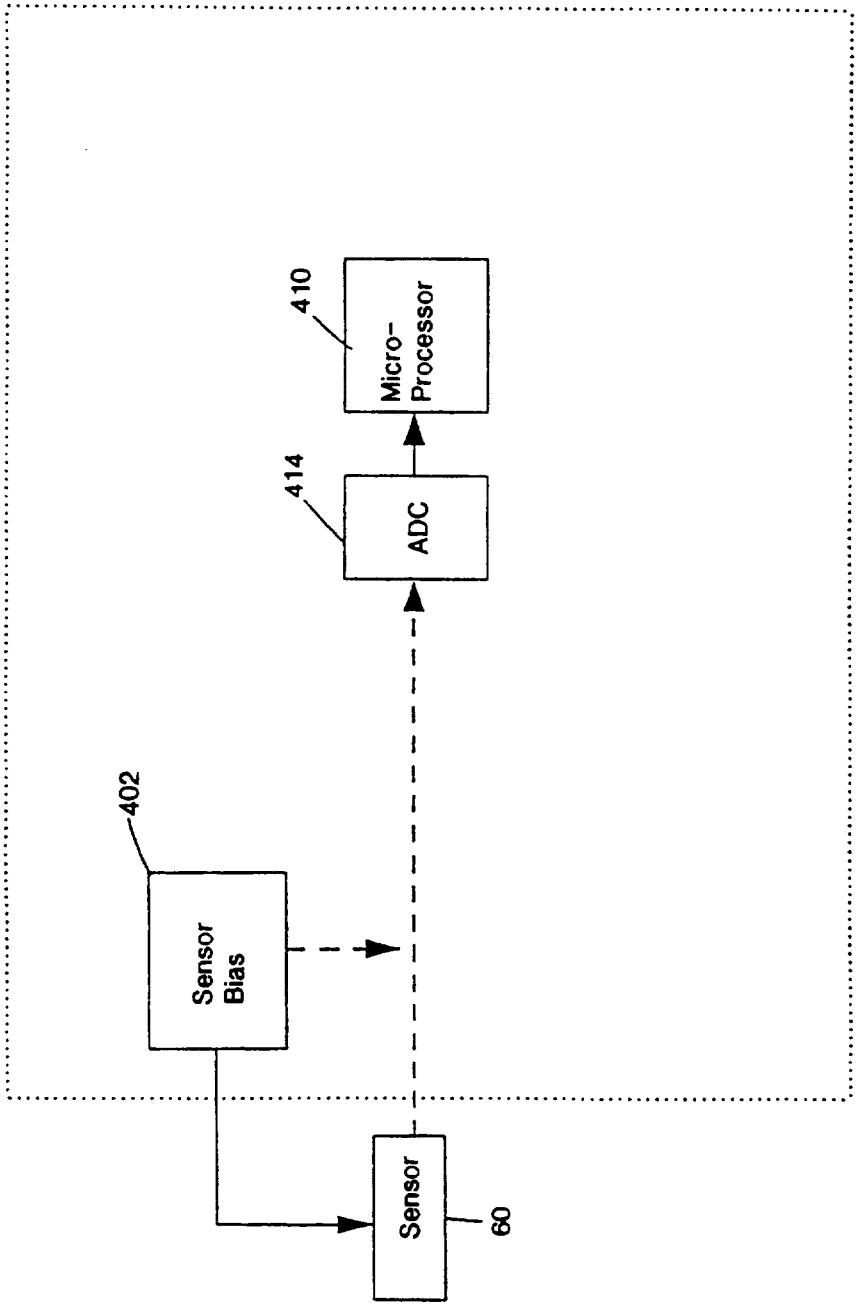


FIG. 20B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00439

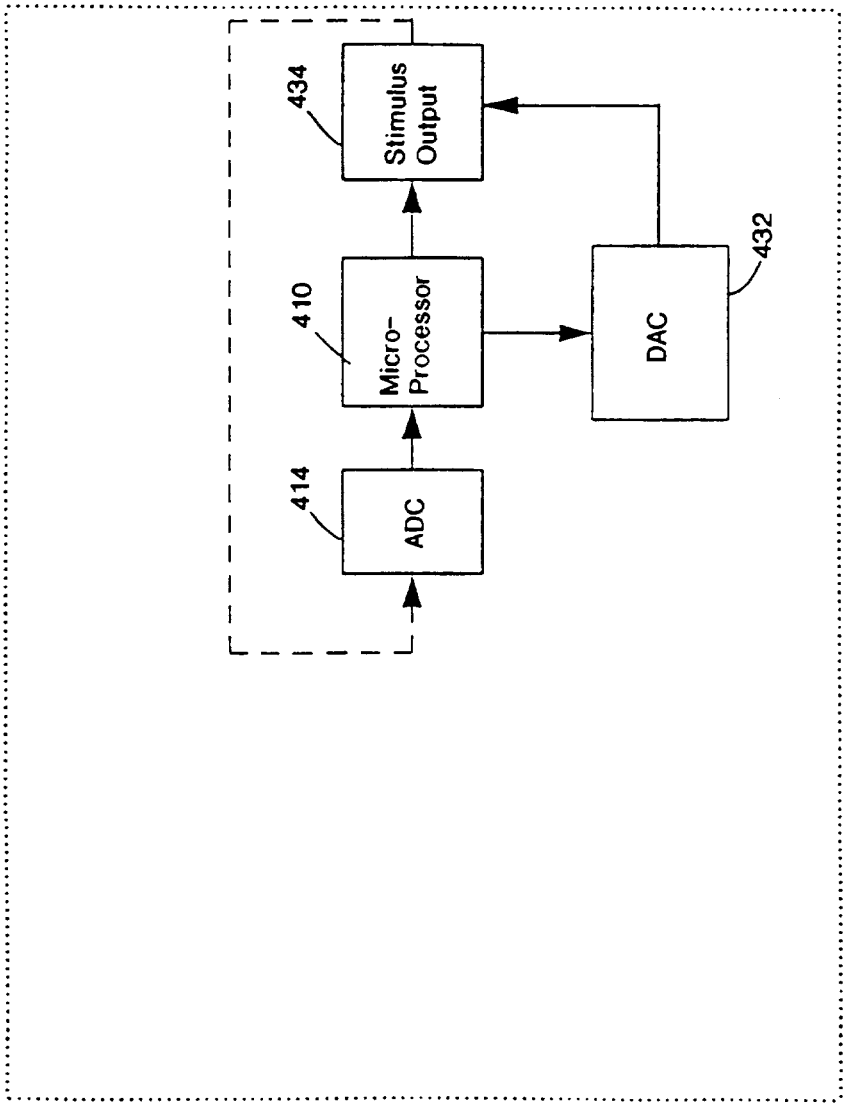


FIG. 20C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00440

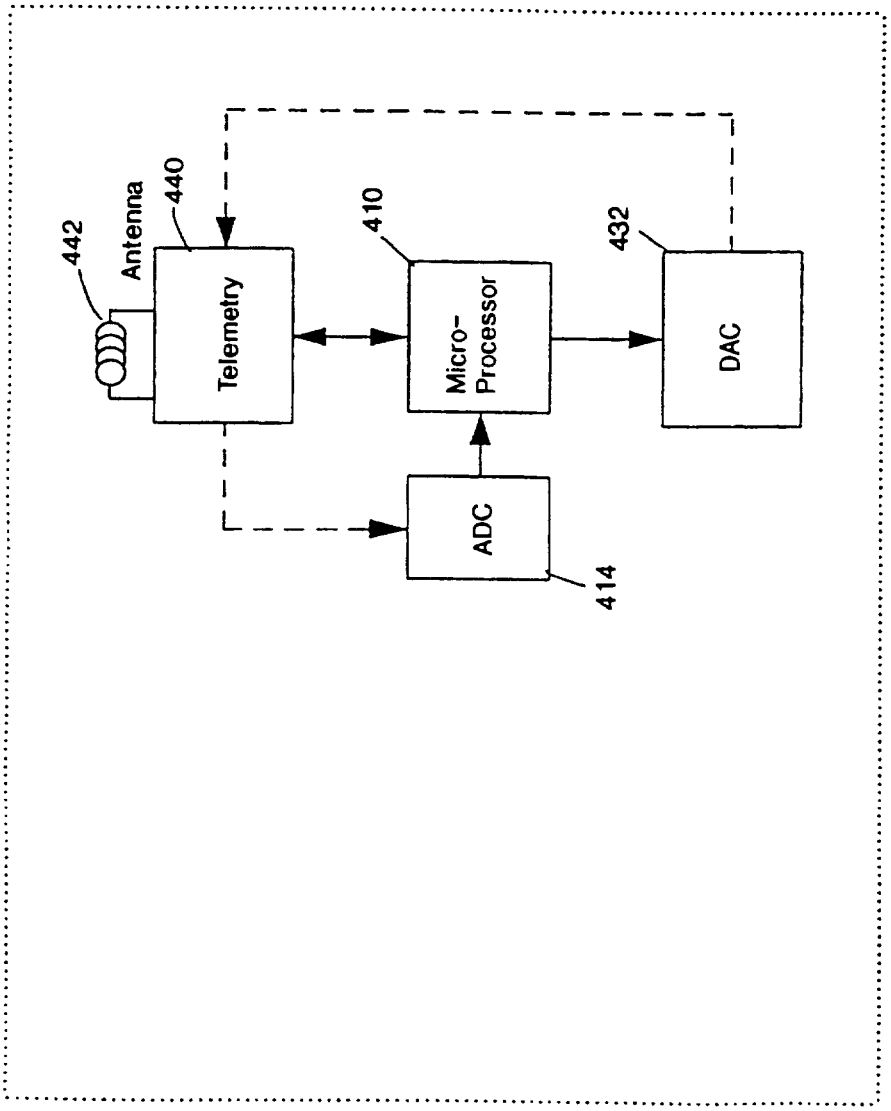


FIG. 20D

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00441

INTERNATIONAL SEARCH REPORT

Int ational Application No
PCT/US 97/11148

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 G06F19/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 G06F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	US 5 540 733 A (TESTERMAN ROY L ET AL) 30 July 1996 see abstract see column 2, line 43 - column 3, line 28 see column 9, line 66 - column 10, line 39; figures 9B-15	1-54
A	US 4 757 824 A (CHAUMET SERGE G J) 19 July 1988 see abstract see column 2, line 57 - column 4, line 29	1-52
P,A	EP 0 765 631 A (SIEMENS MEDICAL SYSTEMS INC) 2 April 1997 see column 2, line 49 - column 3, line 24	1-54

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 1997	08/12/1997

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Gonzalez Ordonez, O

Form PCT/ISA/210 (second sheet) (July 1992)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00442

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 97/11148

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 365 636 A (BARKER KENT R) 28 December 1982 see abstract see column 2, line 37 - column 3, line 10; figures 2,4A,4B	1-52

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00443

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte. onal Application No
PCT/US 97/11148

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5540733 A	30-07-96	NONE	
US 4757824 A	19-07-88	EP 0212370 A	04-03-87
		JP 1680252 C	13-07-92
		JP 3047098 B	18-07-91
		JP 62044265 A	26-02-87
EP 0765631 A	02-04-97	CA 2186706 A	30-03-97
US 4365636 A	28-12-82	NONE	

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00444

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 May 2006 (04.05.2006)

PCT

(10) International Publication Number
WO 2006/047264 A1

(51) International Patent Classification:
A61N 1/36 (2006.01)

(21) International Application Number:
PCT/US2005/037846

(22) International Filing Date: 20 October 2005 (20.10.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/620,827 21 October 2004 (21.10.2004) US
60/631,091 24 November 2004 (24.11.2004) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

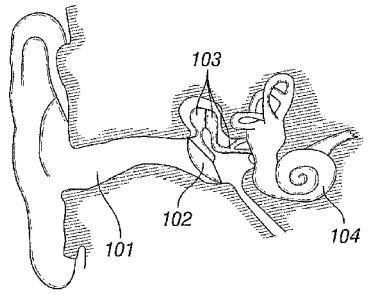
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

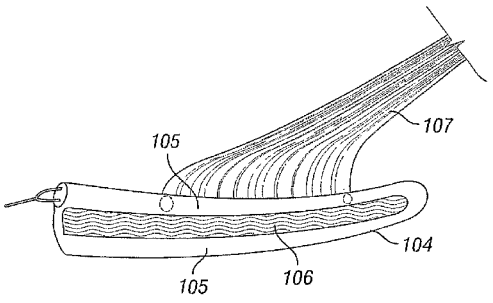
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(54) Title: PERIPHERAL NERVE STIMULATION TO TREAT AUDITORY DYSFUNCTION

(57) Abstract: A system and/or method for treating auditory dysfunction by somatosensory system stimulation. The system and/or method comprises a probe and a device to stimulate the probe. The probe has a stimulation portion implanted in communication with a predetermined peripheral nerve site. The stimulation portion of the probe may be implanted in contact with a peripheral nerve dorsal root ganglia, cranial nerve or dermatome area, for example C2 dermatome area or a trigeminal dermatome area. The stimulation portion may be a laminotomy, paddle, surgical, or multiple electrode lead. The' device to stimulate the probe may be implanted subcutaneously or transcutaneously.



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— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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PERIPHERAL NERVE STIMULATION TO TREAT AUDITORY DYSFUNCTION

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application Nos. 60/620,827 filed October 21, 2004 and 60/631,091 filed November 24, 2004 each of which is incorporated herein by reference in its entirety.

[0002] This application is also related to U.S. Provisional Application Nos. 60/620,762 filed October 21, 2004, 60/631,085 filed November 24, 2004, 60/620,847 filed October 21, 2004, 60/631,089 filed November 24, 2004, and 60/639,365 filed December 27, 2004 each of which is incorporated by reference in its entirety.

TECHNICAL FIELD

[0003] This invention relates to neuronal tissue stimulation for medical treatment, and more particularly to stimulating peripheral nerves to treat auditory dysfunction.

BACKGROUND OF THE INVENTION

[0004] Hearing clarity is taken for granted by most people; however, temporary periods of altered auditory perception are a normal part of existence. Nearly every individual will experience phantom noises such as "ringing in the ears" during their lifetime as a result of exposure to external and/or internal stimuli. Loud noise (reported by Zhang *et al.*, Wallhausser-Franke *et al.*), certain pharmaceuticals, stress, and various physical conditions can all cause altered auditory perception, usually on a temporary basis. However, for some individuals with auditory dysfunction, altered auditory perception can be permanent.

[0005] Auditory dysfunctions are common. For example, in the United States, the prevalence of tinnitus when the whole population is considered is approximately 3%. This prevalence is only 1% under the age of 45 but increases significantly with age, rising to 9% in the population over 65 years (Adams *et al.*, 1999). This roughly translates to 36 million Americans with tinnitus (Heller 2003). Tinnitus is a noise in the ears, often described as ringing, buzzing, roaring, or clicking. Subjective and objective forms of tinnitus exist, with objective tinnitus often caused by muscle contractions or other internal noise sources in

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the area proximal to auditory structures. In certain cases, external observers can hear the sound generated by the internal source of objective tinnitus. In subjective forms, tinnitus is audible only to the subject. Tinnitus varies in perceived amplitude, with some subjects reporting barely audible forms and others essentially deaf to external sounds and/or incapacitated by the intensity of the perceived noise.

[0006] Because auditory dysfunction often occurs secondary to a pathological state, initial treatment may focus on finding an underlying cause. A subject presenting with, for example, tinnitus may be asked for information regarding medications, recent or chronic noise exposure, and home and work environment. Common medications such as aspirin are known to cause tinnitus in some patients or in elevated dosages. Stress can be a direct cause of tinnitus and can aggravate existing cases. A thorough physical exam is typically made of a subject with complaints of tinnitus to eliminate pathologies such as hypertension, tumors, and infections. Objective tinnitus may be diagnosed using a stethoscope if the source of the noise can be localized. For example, hypertension or arterial disorders may produce objective tinnitus, as the carotid arteries pass close to the auditory organs in humans, and excessive pressure or arterial blockage may cause detectible noise to both the subject and to an outside observer.

[0007] If a treatable underlying cause to auditory dysfunction symptoms is identified, treatment may focus on elimination of the cause. For example, hypertensive patients may see a reduction or elimination of tinnitus once anti-hypertensive therapy begins. However, a significant number of patients have untreatable underlying pathologies or have auditory dysfunction in the absence of any identifiable cause. For these patients, treatments for directly reducing or eliminating the auditory dysfunction are desirable.

[0008] Tinnitus research is actively pursued in the hope of finding efficacious treatments. Recently published work has utilized drug delivery systems such as the system described in U.S. Pat. No. 5,713,847, which includes a catheter inserted into a patient's auditory cortex or thalamus for microinfusing drugs.

[0009] Another example of published drug delivery techniques is U.S. Pat. No. 6,656,172, which describes a tinnitus treatment that includes inserting intrathecally a catheter for infusing a drug. Other treatment methods may try to mask the perceived tinnitus noise by

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generating an audible signal of appropriate frequency. WO 01/08617 describes a system with a vibrating probe placed in proximity to the inner ear.

[0010] Nerve stimulation has been shown to be helpful in treating patients with chronic intractable pain. For those patients who prove unresponsive to conservative pain management techniques, peripheral nerve stimulation may be a successful therapy for pain management when the pain is known to result from a specific nerve. Peripheral nerve stimulation is based in part on the Melzack-Wall gate control theory of pain. Sweet and Wespic first used electrical stimulation of peripheral nerves in the 1960s to mask the sensation of pain with a tingling sensation (paresthesia) caused by the electrical stimulation. Subsequent refinements in the technology, surgical technique and patient selection have led to improved long term results.

[0011] The use of certain stimulating electrodes to mask tinnitus has been published. U.S. Patent Nos. 5,735,885 and 5,496,369 describe the placement of an electrode in the primary auditory cortex of a patient. U.S. Patent Nos. 6,456,886 and 5,697,975 also use an electrode placed in the auditory cortex, and further describe placement of an electrode in the medial geniculate body of the thalamus.

BRIEF SUMMARY OF THE INVENTION

[0012] Peripheral nerves carry both motor and sensory information to and from the brain. The present invention comprises a therapeutic system for treating auditory dysfunction having a surgically implanted device in communication with a predetermined peripheral nerve. The device can include a distal probe, such as, for example, an electrode assembly or electrical stimulation lead. The proximal end of the probe is coupled to an electrical signal source, which, in turn, is operated to stimulate the predetermined peripheral nerve.

[0013] The predetermined site can be, for example, but not limited to a dermatome area, for example, C2, C3, C4, C5, C6, C7, C8, as well as any thoracic, lumbar or sacral dermatome. Cervical nerve roots (e.g., C1, C2, C3, C4, C5, C6, C7 and C8) and cranial nerves (e.g., olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and hypoglossal nerve) to provide therapeutic treatments

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according to the instant invention. Other dermatomes that can be included in the present invention include dermatomes associated with cranial nerves having somatosensory function, for example, but not limited to dermatomes associated with the trigeminal nerve, intermediate part of the facial nerve, glossopharyngeal nerve, or vagal nerve. Other peripheral nerves are spinal nerves such as the suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, and the brachial plexus, which branches to form the dorsal scapular nerve, the thoracic nerve, the suprascapular nerve, the lateral pectoral, the musculocutaneous nerve, the axillarily nerve, the radial nerve, the median nerve, the ulnar nerve, and other minor peripheral nerves, as well as sympathetic and parasympathetic nerves. Yet further, other peripheral nerves also includes thoracic nerve roots (e.g., T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12), lumbar nerve roots (L1, L2, L3, L4, L5) sacral nerve roots (e.g., S1, S2, S3, S4, S5) and the coccygeal nerve.

[0014] Embodiments of the invention can operate with various stimulation parameters. One example of stimulation parameters used to treat auditory dysfunctions, such as, for example, tinnitus, may use an amplitude in the range of about 2 mA to about 100 mA, a frequency in the range of about 3 Hz to about 80 Hz, and a pulse width in the range of about 5 microseconds to about 100 microseconds. However, other parameters are used in other embodiments of the invention, such as, for example, higher and lower frequencies, various current amplitudes, and/or pulse width durations. In another embodiment of the invention, a frequency stimulation parameter of about 80 Hz is used. Burst mode stimulation is used in preferred embodiments of the invention. The burst stimulus comprises a frequency in the range of about 1 Hz to about 300 Hz, more particular, in the range of about 1 Hz to about 12 Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4 Hz to about 7 Hz or about 8 Hz to about 12 Hz, 18 Hz to 20 Hz, and 40 Hz. The burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 2 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 50Hz to about 1000 Hz, more particularly, in the range of about 200 Hz to about 500 Hz. The interval between spikes can be about 0.5 milliseconds to about 100 milliseconds. More particularly, the maximum inter-spike interval may be about 5 milliseconds. Those of skill in the art realize that this can vary depending upon the patient and the treatment. The frequency of the spikes within the burst does not need to be constant or regular, in fact,

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typically, the frequency of the spikes is random or variable. In further embodiments, the burst stimulus is followed by an inter-burst interval. The inter-burst interval has a duration in the range of about 5 milliseconds to about 5 seconds, more preferably, in the range of about 10 milliseconds to about 300 milliseconds, or any range therebetween. Preferably, the minimum inter-burst interval may be about 20 milliseconds. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particularly in the range of about 250 milliseconds to 1 second. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (e.g., random or irregular harmonics).

[0015] Embodiments of the invention also comprise methods for treating auditory dysfunction. The method comprises surgically implanting an electrical stimulation lead such as a laminotomy lead, paddle, surgical, or multiple electrode lead. Following implantation, the proximal end of the lead is attached to a signal generator. The signal generator then generates a signal that stimulates a predetermined peripheral nerve. The stimulation of the peripheral nerve modulates components of the somatosensory system that in turn modulate components of the auditory system's extralemniscal pathway.

[0016] In some embodiments of the invention, the stimulation parameters are varied after implantation to optimize treatment of an auditory dysfunction. The parameters varied may include modification of the predetermined implantation site, or modification of, for example, signal amplitude, frequency, pulsewidth or pulse shape of the stimulation signal.

[0017] Other stimulation devices used in certain embodiments are drug pumps which provide chemical stimulation of a predetermined peripheral nerve. Chemical stimulation can be provided by delivery of pharmaceuticals or neuroactive substances that, for example, disrupt, block, stimulate, and/or modulate peripheral nerve activity.

[0018] Magnetic stimulation of predetermined peripheral nerve sites for the treatment of auditory dysfunction is used in certain embodiments of the present invention. Magnetic stimulation can be provided by internally implanted probes or by externally applied directed magnetic fields.

[0019] Yet further, thermal stimulation can be provided via implanted probes that are regulated to heat and/or cold temperatures. In other embodiments, ultrasound

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stimulation is used as a stimulation source, either by itself or in combination with another stimulation source. For example, in certain embodiments of the invention, ultrasound is used to stimulate active tissue by propagating ultrasound in the presence of a magnetic field as described by Norton (2003), herein incorporated by reference in its entirety. Combinations of stimulation sources are used in some embodiments of the invention.

[0020] The foregoing has outlined rather broadly the features and technical advantages of the present invention in order that the detailed description of the invention that follows may be better understood. Additional features and advantages of the invention will be described hereinafter which form the subject of the claims of the invention. It should be appreciated that the conception and specific embodiment disclosed may be readily utilized as a basis for modifying or designing other structures for carrying out the same purposes of the present invention. It should also be realized that such equivalent constructions do not depart from the invention as set forth in the appended claims. The novel features which are believed to be characteristic of the invention, both as to its organization and method of operation, together with further objects and advantages will be better understood from the following description when considered in connection with the accompanying figures. It is to be expressly understood, however, that each of the figures is provided for the purpose of illustration and description only and is not intended as a definition of the limits of the present invention.

BRIEF DESCRIPTION OF THE DRAWING

[0021] For a more complete understanding of the present invention, reference is now made to the following descriptions taken in conjunction with the accompanying drawing, in which:

[0022] FIGURES 1A-1B are illustrations of the human auditory system including neural connections;

[0023] FIGURE 2 is an illustration of connections in the lemniscal auditory pathway;

[0024] FIGURES 3A-3B illustrate example stimulation systems for electrically stimulating peripheral nerves;

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[0025] FIGURES 4A-4I illustrate example electrical stimulation leads that may be used to electrically stimulate peripheral nerves;

[0026] FIGURE 5 illustrates implantation of a single stimulation lead near the spinal cord to stimulate a peripheral nerve;

[0027] FIGURE 6 illustrates an example method of implanting the stimulation system of FIGURES 1A-1B with bilateral leads in communication with peripheral nerves; and

[0028] FIGURES 7A-7B illustrate examples of the C2 dermatome area; FIGURE 7A and FIGURE 7B show the cervical dermatomes, including C2 and C3 dermatome.

[0029] FIGURE 8 shows the anatomy of the occiput or occipital area of a subject's head. Anatomical structures shown include nerves, muscle and the galea.

[0030] FIGURE 9 is a block diagram of processes according to a method for treating auditory dysfunctions such as tinnitus using a peripheral nerve stimulation system.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

[0031] Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. For purposes of the present invention, the following terms are defined below.

[0032] As used herein, the use of the word "a" or "an" when used in conjunction with the term "comprising" in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more", "at least one", and "one or more than one." Still further, the terms "having", "including", "containing" and "comprising" are interchangeable and one of skill in the art is cognizant that these terms are open ended terms.

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[0033] As used herein, the term "auditory dysfunction" refers to conditions or dysfunctions associated with the auditory pathway. Such auditory dysfunctions can include, but are not limited to tinnitus, hyperacousis, phonophobia, misophonia, auditory agnosia in all its forms (verbal and/or non-verbal), auditory spatial dysfunction (localizing sound) and auditory hallucinations, inclusive of musical hallucinosis. Auditory hallucinations can occur in schizophrenia or use of certain drugs (e.g., antimuscarinic agents, antiparkinsonian drugs, antidepressants, beta adrenoceptor antagonists and opiates). Auditory dysfunction can also include hearing loss. Hearing loss can be conductive hearing loss (mechanical transmission of sound into the sensory receptors in the cochlea is impaired), sensorineural hearing loss (a loss of function in the sensory receptors in either the cochlea or the auditory nerve), or central hearing loss (a lesion in the brain stem or auditory cortex).

[0034] As used herein, the terms "auditory nerve" and "cochlear nerve" are interchangeable and refer to the nerve fibers along which the sensory cells of the ear communicate information to the brain. The auditory or cochlear nerve are part of the vestibulocochlear nerve which carries two kinds of sensation, vestibular (balance) and audition (hearing) from sensory receptors in the inner ear. The auditory nerve consists of the vestibular nerve and the cochlear nerve. The vestibulocochlear nerve is also known as the eighth cranial nerve.

[0035] As used herein, the term "in communication" refers to the stimulation lead being adjacent, in the general vicinity, in close proximity, or directly next to or directly on the predetermined stimulation site. Thus, one of skill in the art understands that the lead is "in communication" with the predetermined site if a stimulation signal results in a modulation of neuronal activity. For example, the predetermined site is selected in the present invention such that a stimulation lead in communication with a peripheral nerve will stimulate the peripheral nerve when a stimulation signal is applied to the stimulation lead.

[0036] As used herein, the term "dermatome" refers to the area of skin innervated by a single dorsal root. One of skill in the art realizes that the boundaries of dermatomes are not distinct and in fact overlap because of overlapping innervations by adjacent dorsal roots. Dermatomes are divided into sacral (S), lumbar (L),' thoracic (T) and cervical (C). Yet further, as used herein, the term "dermatome" includes all the neuronal tissues located within the region or adjacent the dermatome area, for example, it may include

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any peripheral nerve, for example, any cervical nerve root (C1, C2, C3, C4, C5, C6, C7 and C8) that may innervate the dermatome, any and cranial nerve (*e.g.*, olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and hypoglossal nerve) that may innervate the dermatome. Other dermatomes that can be included in the present invention include dermatomes associated with cranial nerves having somatosensory function, for example, but not limited to dermatomes associated with the trigeminal nerve, intermediate part of the facial nerve, glossopharyngeal nerve, or vagal nerve. Thus, while to some, dermatomes may have a meaning that relates specifically to sensory neurons, as used herein, this limitation should not be applied, but rather the broader description used herein should be used.

[0037] As used herein, the use of the words "epidural space" or "spinal epidural space" is known to one with skill in the art, and refers to an area in the interval between the dural sheath and the wall of the spinal canal.

[0038] As used herein, the term "C2 dermatome area" refers to the area or the dermatome that covers the occiput or occipital area and the top portion of the neck. Yet further, C2 dermatome area includes the neuronal tissue that is located within this area, for example, the C2 dermatome area and its branches innervate the C2 dermatome, as well as any cervical nerve root and/or cranial nerve that may innervate this area. Thus, the C2 dermatome area may also be referred to as the occiput or occipital area, which refers to the back of the head.

[0039] As used herein the term "modulate" refers to the ability to regulate positively or negatively neuronal activity. Thus, the term modulate can be used to refer to an increase, decrease, masking, altering, overriding or restoring of neuronal activity.

[0040] As used herein, the term "burst firing" or "burst mode" or "burst mode stimulation" refers to an action potential that is a burst of high frequency spikes (300 – 1000 Hz) (Beurrier *et al.*, 1999). Burst firing acts in a non-linear fashion with a summation effect of each spike. One skilled in the art is also aware that burst firing can also be referred to as phasic firing, rhythmic firing (Lee 2001), pulse train firing, oscillatory firing and spike train firing, all of these terms used herein are interchangeable.

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[0041] As used herein, the term "burst" refers to a period in a spike train that has a much higher discharge rate than surrounding periods in the spike train (N. Urbain et al., 2002). Thus, burst can refer to a plurality of groups of spike pulses. A burst is a train of action potentials that occurs during a 'plateau' or 'active phase', followed by a period of relative quiescence called the 'silent phase' (Nunemaker, Cellscience Reviews Vol 2 No.1, 2005.) Thus, a burst comprises spikes having an inter-spike interval in which the spikes are separated by 0.5 milliseconds to about 100 milliseconds. Those of skill in the art realize that the inter-spike interval can be longer or shorter. Yet further, those of skill in the art also realize that the spike rate within the burst does not necessarily occur at a fixed rate; this rate can be variable.

[0042] As used herein, the term "tonic firing" or "tonic mode" refers to an action potential that occurs in a linear fashion.

[0043] As used herein, the term "spike" refers to an action potential. Yet further, a "burst spike" refers to a spike that is preceded or followed by another spike within a short time interval (Matveev, 2000), in otherwords, there is an inter-spike interval, in which this interval is generally about 10 ms but can be shorter or longer, for example 5 milliseconds or 0.5 milliseconds.

[0044] As used herein, the term "neuronal" refers to a neuron which is a morphologic and functional unit of the brain, spinal cord, and peripheral nerves.

[0045] As used herein, the term "peripheral nerve" refers a neuron or a bundle of neurons comprising a part of the peripheral nervous system. The nervous system comprises two general components, the central nervous system, which is composed of the brain and the spinal cord, and the peripheral nervous system, which is composed of ganglia or dorsal root ganglia and the peripheral nerves that lie outside the brain and the spinal cord. One of skill in the art realizes that the nervous system may be separated anatomically, but functionally they are interconnected and interactive. The peripheral nervous system is divided into the autonomic system (parasympathetic and sympathetic), the somatic system and the enteric system. The term peripheral nerve is intended to include both motor and sensory neurons and neuronal bundles of the autonomic system, the somatic system, and the enteric system that reside outside of the spinal cord and the brain. Peripheral nerve ganglia

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and nerves located outside of the brain and spinal cord are also described by the term peripheral nerve.

[0046] As used herein, the term "somatosensory system" refers to the peripheral nervous system division comprising primarily afferent somatic sensory neurons and afferent visceral sensory neurons that receive sensory information from skin and deep tissue, including the 12 cranial and 21 spinal nerves.

[0047] As used herein, "spinal cord," "spinal nervous tissue associated with a vertebral segment," "nervous tissue associated with a vertebral segment" or "spinal cord associated with a vertebral segment or level" includes any spinal nervous tissue associated with a vertebral level or segment. Those of skill in the art are aware that the spinal cord and tissue associated therewith are associated with cervical, thoracic and lumbar vertebrae. As used herein, C1 refers to cervical vertebral segment 1, C2 refers to cervical vertebral segment 2, and so on. T1 refers to thoracic vertebral segment 1, T2 refers to thoracic vertebral segment 2, and so on. L1 refers to lumbar vertebral segment 1, L2 refers to lumbar vertebral segment 2, and so on, unless otherwise specifically noted. In certain cases, spinal cord nerve roots leave the bony spine at a vertebral level different from the vertebral segment with which the root is associated. For example, the T11 nerve root leaves the spinal cord myelum at an area located behind vertebral body T8-T9 but leaves the bony spine between T11 and T12.

[0048] As used herein, the term "stimulate" or "stimulation" refers to electrical, chemical, and/or magnetic stimulation that modulates the predetermined sites in the brain.

[0049] As used herein, the term "treating" and "treatment" refers to modulating certain areas of the brain so that the subject has an improvement in the disease, for example, beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. One of skill in the art realizes that a treatment may improve the disease condition, but may not be a complete cure for the disease.

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II. Auditory Pathways

[0050] The auditory system comprises components that convert sound pressure waves into neural impulses that are ultimately processed by the nervous system. A simplified version of these components as they appear in humans is shown in FIGURE 1B. Auditory canal 101 channels pressure waves to tympanic membrane 102 which moves in response to incoming waves. Movement of the tympanic membrane 102 is transmitted to three ossicles 103 located in the middle ear. The ossicles 103 amplify the movement of the tympanic membrane 102 so that sound vibrations are converted to high pressure sound waves in fluid located in the cochlea 104. In vivo, the cochlea 104 is coiled like a snail shell.

[0051] FIGURE 1B shows the cochlea 104 of FIGURE 1A as it would appear uncoiled. Cochlea 104 is divided into two fluid-filled chambers separated by the organ of Corti 106. Vibrations in the fluid cause mechanical stimulation of sensory receptor cells known as hair cells on the organ of Corti 106. This mechanical stimulation causes ion channels on the hair cells to open, altering their membrane potential and changing the release rate of a synaptic neurotransmitter. Afferent nerve fibers from the auditory nerve 107 take up the neurotransmitter and an action potential in the nerve fibers may be generated depending on the quantity of released neurotransmitter. This is a simplified diagram, and other afferent and efferent nerve fibers are also involved in auditory information collection and processing.

[0052] The auditory nerve connects to two separate pathways after leaving the cochlea. The lemniscal pathway, also known as the classical or specific auditory pathway, is the route taken for signals that humans consciously perceive as sound information. The lemniscal is phylogenetically the youngest of the two pathways. The lemniscal pathway is organized tonotopically, with specific parts of the pathway carrying information specific to received auditory frequencies. It is also linear, such that the impulse rate of lemniscal neurons is related to the amplitude of sound waves detected at the cochlea. The lemniscal pathway is illustrated in simplified form in FIGURE 2. Generally, axons carrying impulses from the cochlea connect to the inferior colliculus 201 and the medial geniculate body 202 in the thalamus to the auditory cortex 203. Specifically, primary axons in synaptic contact with the hair cells of the organ of Corti (106 in FIGURE 1A) have their cell bodies in the spiral ganglion 204 and enter the brainstem at the juncture of the pons and cerebellum. Here, each axon bifurcates and synapses in the dorsal and ventral cochlear nuclei 205, 206 of the

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medulla. Second order axons from the dorsal and ventral cochlear nuclei 205, 206 may synapse in the superior olive 207 or may pass directly to the nucleus of the inferior colliculus 201 via the lateral leminiscus 208. These connections may be made both ipsilaterally (not shown) and contralaterally.

[0053] The second pathway connected to by the auditory nerve is the extralemniscal pathway. This pathway is also known as the non-classical, nonspecific, polysensory, or diffuse auditory pathway, and is used for autonomous reactions to auditory stimuli. Moller and Rollins have found evidence suggesting that this pathway may also be used for hearing in children. The extralemniscal pathway is phylogenetically older than the lemniscal system. Because it is used for autonomous reactions, it is a faster transmission path and is also non-tonotopic and non-linear. Cells of the extralemniscal pathway fire in burst mode and have a slow spontaneous firing rate relative to the lemniscal pathway cells. The auditory extralemniscal pathway makes connections with the somatosensory system at the dorsal cochlear nucleus and the inferior colliculus. Extralemniscal connections at the inferior colliculus occur at the external nucleus and the dorsal cortex. These ascending pathways then connect at all divisions of the medial geniculate bodies, the posterior intralaminar complex, and suprageniculate nuclei at the level of the superior colliculus. Afferent dorsal column neurons connect with the extralemniscal pathway at the external nucleus and the dorsal cortex. Dorsal column neurons may also connect directly with other auditory neurons such as, for example, those in the cochlear nucleus. Peripheral nerve bodies located in the dorsal root ganglia connect to the dorsal column via axonal extensions that may ascend directly to the brain or brain stem, or may connect to ascending pathways via synaptic connections in the spinal cord.

[0054] Connections from the somatosensory system to the auditory system have been explored in the past. Information from the different sensory modalities (sight, hearing, touch, etc.) is known to integrate in most higher organisms, and occurs in the human nervous system. Co-existing cutaneous and auditory responses in neuronal tissue have been observed in the caudomedial auditory cortex, adjacent to the primary auditory cortex (Fu *et al.*, Foxe *et al.*).

[0055] There are also connections between the trigeminal system and the ventral cochlear nucleus. The dorsal cochlear nucleus receives input from the dorsal column

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(proprioception) nuclei and the ventral cochlear nucleus from the trigeminal ganglion (Shore, Vass *et al.* 2000; Shore, El Kashlan *et al.* 2003; Weinberg and Rustioni 1987). The trigeminal ganglion also connects to the superior olivary nucleus (Shore, Vass *et al.* 2000). Electrical stimulation of the somatosensory trigeminal ganglion can influence the activity of central auditory neurons in a manner distinct from acoustic stimulation, suggesting activation of non-classical auditory pathways (El-Kashlan and Shore 2004). Furthermore, the activation seems to be predominantly ipsilateral (El-Kashlan and Shore 2004). These connections may be involved in generating or modulating perceptions of phantom sounds which can be modified by manipulations of somatic regions of the head and neck ("somatic tinnitus")(Levine, Abel *et al.* 2003; Shore, El Kashlan *et al.* 2003). Also, C2 (occipital and greater auricular nerve) innervates the dorsal cochlear nucleus (Kanold and Young 2001) as well as the rest of the body via the cuneate nucleus of the dorsal column (Itoh, Kamiya *et al.* 1987; Wright and Ryugo 1996).

[0056] Thus, it is envisioned that stimulation of the somatosensory system can treat auditory dysfunction, for example, tinnitus by activation of the extralemniscal auditory connections to the somatosensory system.

III. Electrical Stimulation Devices

[0057] FIGURES 3A-3B illustrate example neurological stimulation systems 10 for electrically stimulating a predetermined site, for example, a peripheral nerve, to treat auditory dysfunction. In general terms, stimulation system 10 includes an implantable electrical stimulation source 12 and one or more implantable electrical stimulation leads 14 for applying electrical stimulation pulses to a predetermined site. In operation, one or both of these primary components are implanted in or on a subject's body, as discussed below. In certain embodiments, stimulation source 12 is coupled directly to a connecting portion 16 of stimulation lead 14. In certain other embodiments, stimulation source 12 is incorporated into the stimulation lead 14 and stimulation source 12 instead is embedded within stimulation lead 14. For example, such a stimulation system 10 may be a Bion® stimulation system manufactured by Advanced Bionics Corporation. Whether stimulation source 12 is coupled directly to or embedded within the stimulation lead 14, stimulation source 12 controls the stimulation pulses transmitted to one or more stimulation electrodes 18 located on a stimulating portion 20 of stimulation lead 14, positioned in communication with a

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predetermined site, according to suitable stimulation parameters (e.g., duration, amplitude or intensity, frequency, pulse width, etc.). One example of stimulation parameters used to treat an auditory dysfunction, such as, for example, tinnitus uses an amplitude in the range of about 2 mA to about 100 mA, a frequency in the range of about 3 Hz to about 80 Hz, and a pulse width in the range of about 5 microseconds to about 100 microseconds.

[0058] The predetermined site in communication with the stimulation lead 14 is a peripheral nerve in a preferred embodiment. Peripheral nerves can include cranial nerves for example, olfactory nerve, optic nerve, oculomotor nerve, trochlear nerve, trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear (auditory) nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and the hypoglossal nerve. In addition to cranial nerves, the predetermined site can be a dermatome area, for example, C2, C3, C4, C5, C6, C7, C8, as well as any thoracic, lumbar or sacral dermatome. Other dermatomes that can be included in the present invention include dermatomes associated with cranial nerves having somatosensory function, for example, but not limited to dermatomes associated with the trigeminal nerve, intermediate part of the facial nerve, glossopharyngeal nerve, or vagal nerve. Peripheral nerves also includes spinal nerves, which in general, spinal nerves are named after the vertebral segment of the spinal column above their origin. For example, the spinal nerve originating under the third thoracic vertebra may be termed the third thoracic nerve. Thus, spinal nerves can include, but are limited to cervical nerve roots (e.g., C1, C2, C3, C4, C5, C6, C7 and C8), thoracic nerve roots (e.g., T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12), lumbar nerve roots (L1, L2, L3, L4, L5) sacral nerve roots (e.g., S1, S2, S3, S4, S5) and the coccygeal nerve. Other peripheral nerves are spinal nerves such as the suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, and the brachial plexus, which branches to form the dorsal scapular nerve, the thoracic nerve, the suprascapular nerve, the lateral pectoral, the musculocutaneous nerve, the axillarily nerve, the radial nerve, the median nerve, the ulnar nerve, the intercostal nerves, and other minor peripheral nerves, as well as parasympathetic and/or sympathetic nerves. In certain embodiments, the peripheral nerve stimulated is the trigeminal nerve or the trigeminal dermatome or any peripheral nerve associated with the C2 dermatome area, C3 dermatome area, cranial nerves, the median nerve or any combination thereof. Peripheral nerve ganglia, which are collections of peripheral nerve cell bodies, are predetermined sites in communication with stimulation lead 14 in

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certain embodiments. A doctor, the patient, or another user of stimulation source 12 may directly or indirectly input stimulation parameters to specify or modify the nature of the stimulation provided. In certain embodiments, transcutaneous implantation of stimulation lead 14 is used either permanently or temporarily.

[0059] Some embodiments employ a burst stimulus. Examples of burst stimulus are found in U.S. Application entitled "New Stimulation Design for Neuromodulation", filed October 20, 2005, and incorporated herein by reference. The burst stimulus comprises a frequency in the range of about 1 Hz to about 300 Hz, more particular, in the range of about 1 Hz to about 12 Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4 Hz to about 7 Hz or about 8 Hz to about 12 Hz, 18 Hz to 20 Hz, and 40 Hz. The burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 12 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 50Hz to about 1000 Hz, more particularly, in the range of about 200 Hz to about 500 Hz. The interval between spikes can be about 0.5 milliseconds to about 100 milliseconds. The frequency of the spikes within the burst does not need to be constant or regular, in fact, typically, the frequency of the spikes is random or variable. In further embodiments, the burst stimulus is followed by an inter-burst interval. The inter-burst interval has a duration in the range of about 5 milliseconds to about 5 seconds, more preferably, about 10 milliseconds to about 300 milliseconds, or any range therebetween. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particularly in the range of about 250 milliseconds to 1 second. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (e.g., random or irregular harmonics).

[0060] In one embodiment, as shown in FIGURE 3A, stimulation source 12 includes an implantable pulse generator (IPG). An exemplary IPG may be one incorporated in the Genesis® System manufactured by Advanced Neuromodulation Systems, Inc., part numbers 3604, 3608, 3609, and 3644. In another embodiment, as shown in FIGURE 3B, stimulation source 12 includes an implantable wireless receiver. An example wireless receiver may be one incorporated in the Renew® System manufactured by Advanced Neuromodulation Systems, Inc., part numbers 3408 and 3416. In another embodiment, the IPG can be optimized for high frequency operation as described in U.S. Provisional Application Serial No. 60/685,036, filed May 26, 2005, entitled "SYSTEMS AND

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METHODS FOR USE IN PULSE GENERATION," which is incorporated herein by reference. The wireless receiver is capable of receiving wireless signals from a wireless transmitter 22 located external to the person's body. In some embodiments, the receiver may be stand-alone and no external controller 26 is required. The wireless signals are represented in FIGURE 3B by wireless link symbol 24. A doctor, the patient, or another user of stimulation source 12 may use a controller 26 located external to the person's body to provide control signals for operation of stimulation source 12. Controller 26 provides the control signals to wireless transmitter 22, wireless transmitter 22 transmits the control signals and power to the wireless receiver of stimulation source 12, and stimulation source 12 uses the control signals to vary the stimulation parameters of stimulation pulses transmitted through stimulation lead 14 to the predetermined peripheral nerve. Thus, the external controller 26 can be for example, a handheld programmer, to provide a means for programming the IPG. An example wireless transmitter 122 may be one manufactured by Advanced Neuromodulation Systems, Inc., such as the Renew® System, part numbers 3508 and 3516.

[0061] Conventional neuromodulation devices can be modified to apply burst stimulation to nerve tissue of a patient by modifying the software instructions stored in the devices. Specifically, conventional neuromodulation devices typically include a microprocessor and a pulse generation module. The pulse generation module generates the electrical pulses according to a defined pulse width and pulse amplitude and applies the electrical pulses to defined electrodes. The microprocessor controls the operations of the pulse generation module according to software instructions stored in the device.

[0062] These conventional neuromodulation devices can be adapted by programming the microprocessor to deliver a number of spikes (relatively short pulse width pulses) that are separated by an appropriate inter-spike interval. Thereafter, the programming of the microprocessor causes the pulse generation module to cease pulse generation operations for an inter-burst interval. The programming of the microprocessor also causes a repetition of the spike generation and cessation of operations for a predetermined number of times. After the predetermined number of repetitions have been completed, the microprocessor can cause burst stimulation to cease for an amount of time (and resume thereafter). Also, in some embodiments, the microprocessor could be programmed to cause the pulse generation module to deliver a hyperpolarizing pulse before the first spike of each group of multiple spikes.

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[0063] The microprocessor can be programmed to allow the various characteristics of the burst stimulus to be set by a physician to allow the burst stimulus to be optimized for a particular pathology of a patient. For example, the spike amplitude, the inter-spike interval, the inter-burst interval, the number of bursts to be repeated in succession, the amplitude of the hyperpolarizing pulse, and other such characteristics could be controlled using respective parameters accessed by the microprocessor during burst stimulus operations. These parameters could be set to desired values by an external programming device via wireless communication with the implantable neuromodulation device.

[0064] In another embodiment, a neuromodulation device can be implemented to apply burst stimulation using a digital signal processor and one or several digital-to-analog converters. The burst stimulus waveform could be defined in memory and applied to the digital-to-analog converter(s) for application through electrodes of the medical lead. The digital signal processor could scale the various portions of the waveform in amplitude and within the time domain (e.g., for the various intervals) according to the various burst parameters.

[0065] FIGURES 4A-4I illustrate example stimulation leads 14 that may be used for electrically stimulating a predetermined peripheral nerve for treating auditory dysfunction. As described above, each of the one or more stimulation leads 14 incorporated in stimulation system 10 includes one or more stimulation electrodes 18 adapted to be positioned in communication with the predetermined peripheral nerve and used to deliver to the stimulation pulses received from stimulation source 12. A percutaneous stimulation lead 14, such as example stimulation leads 14a-d, includes one or more circumferential electrodes 18 spaced apart from one another along the length of stimulating portion 20 of stimulation lead 14. Circumferential electrodes 18 emit electrical stimulation energy generally radially (i.e., generally perpendicular to the axis of stimulation lead 14) in all directions. A laminotomy, paddle, or surgical stimulation lead 14, such as example stimulation leads 14e-i, includes one or more directional stimulation electrodes 18 spaced apart from one another along one surface of stimulation lead 14. Directional stimulation electrodes 18 emit electrical stimulation energy in a direction generally perpendicular to the surface of stimulation lead 14 on which they are located. Although various types of stimulation leads 14 are shown as examples, the present invention contemplates stimulation system 10 including any suitable type of stimulation lead 14 in any suitable number. In addition, stimulation leads 14 may be

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used alone or in combination. For example, unilateral stimulation of a peripheral nerve may be accomplished using a single electrical stimulation lead 14 implanted in communication with the nerve on one side of the subject's body, while bilateral electrical stimulation of the peripheral nerve may be accomplished using two stimulation leads 14 implanted in communication with the peripheral nerve on both sides of the subject's body. Multi-nerve implantation of stimulation leads can be used.

[0066] In one embodiment, the stimulation source is transcutaneously in communication with the electrical stimulation lead. In "transcutaneous", electrical nerve stimulation (TENS) the stimulation source is external to the patient's body, and may be worn in an appropriate fanny pack or belt, and the electrical stimulation lead is in communication with the stimulation source, either remotely or directly. In another embodiment, the stimulation is percutaneous. In "percutaneous" electrical nerve stimulation (PENS), needles are inserted to an appropriate depth around or immediately adjacent to a predetermined stimulation site, and then stimulated.

[0067] In addition to electrical stimulation, other forms of stimulation can be used, for example magnetic. Magnetic stimulation can be provided by internally implanted probes or by externally applied directed magnetic fields, for example, U.S. Patent Nos. 6,592,509; 6,132,361; 5,752,911; and 6,425,852, each of which is incorporated herein in its entirety. Quick pulses of magnetic stimulation can be applied externally or transcranially, for example repetitive transcranially magnetic stimulation (rTMS).

[0068] Whether using percutaneous leads, laminotomy leads, or some combination of both, the leads are coupled to one or more conventional neurostimulation devices, or signal generators. The devices can be totally implanted systems and/or radio frequency (RF) systems. An example of an RF system is a MNT/MNR-916CC system manufactured by Advanced Neuromodulation Systems, Inc.

[0069] The preferred neurostimulation devices should allow each electrode of each lead to be defined as a positive, a negative, or a neutral polarity. For each electrode combination (*e.g.,* the defined polarity of at least two electrodes having at least one cathode and at least one anode), an electrical signal can have at least a definable amplitude (*e.g.,* voltage), pulse width, and frequency, where these variables may be independently adjusted to finely select the sensory transmitting nerve tissue required to inhibit transmission of neuronal

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signals. Generally, amplitudes, pulse widths, and frequencies are determinable by the capabilities of the neurostimulation systems, which are known by those of skill in the art. Voltages that may be used can include, for example about 0.5 to about 10 volts, more preferably about 1 to about 10 volts.

[0070] It is envisaged that the patient will require intermittent assessment with regard to patterns of stimulation. Different electrodes on the lead can be selected by suitable computer programming, such as that described in U.S. Pat. No. 5,938,690, which is incorporated by reference here in full. Utilizing such a program allows an optimal stimulation pattern to be obtained at minimal voltages. This ensures a longer battery life for the implanted systems.

IV. Implantation of Electrical Devices

[0071] FIGURE 5 illustrates example placement of a single stimulation lead 14 for medial electrical stimulation of a peripheral nerve dorsal root ganglia by a stimulation electrode 18. Those of skill in the art are aware that the peripheral nerves can be stimulated anywhere along the nerve. Thus, it is not necessary to stimulate the dorsal root ganglia. Multiple stimulation leads 14 and electrodes 18 are used in other embodiments of the invention.

[0072] FIGURE 6 is an illustration of an implantable pulse generator with a single simulation lead 14 that is employed with two stimulation electrodes 18 for bilateral stimulation of peripheral nerve dorsal root ganglia 20. As indicated above, those of skill in the art realize that the peripheral nerve can be stimulated anywhere along the nerve.

[0073] FIGURE 4 illustrate examples of one or more stimulation leads 14 implanted subcutaneously such that one or more stimulation electrodes 18 of each stimulation lead 14 are positioned in communication with the a dermatome (e.g., C2-C8, T1-T12, L1-L5, S1-S5), cervical nerve roots (*e.g.,* C1, C2, C3, C4, C5, C6, C7 and C8) cranial nerves (*e.g.,* olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and hypoglossal nerve), thoracic nerve roots (e.g., T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12), lumbar nerve roots (e.g.,L1, L2, L3, L4, L5), sacral nerve roots (S1, S2, S3, S4, S5), as well as any other spinal or peripheral nerve. Other dermatomes that can be

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included in the present invention include dermatomes associated with cranial nerves having somatosensory function, for example, but not limited to dermatomes associated with the trigeminal nerve, intermediate part of the facial nerve, glossopharyngeal nerve, or vagal nerve. FIGURES 7 and 8 illustrate example placement of a single stimulation lead 14 for medial electrical stimulation of a dermatome area. FIGURE 8 illustrates example placement of an electrode in the occipital area or C2/C3 dermatome area. In certain embodiments one or more stimulation electrodes 18 are positioned in the C2 dermatome area, subcutaneously, but superior to the galea. Within certain areas of the C2 dermatome area, there is little or no muscle, this area primarily consists of fat, fascia, periostium, and neurovascular structures (*e.g.,* galea). Thus, the advantage implanting a stimulation lead in this area is that there will be no to little muscular contraction. One of skill in the art is aware that stimulation of the C2 dermatome area may result in stimulation of various neuronal structures, for example, but not limited to the C2 dermatome area, C3 dermatome, trigeminal dermatome, trigeminal nerve, olfactory nerve, other cranial nerves, or other cervical nerve roots.

[0074] Different numbers of stimulation leads 14 and stimulation electrodes 18 may be used in other embodiments of the invention. Additionally, other peripheral nerves or peripheral nerve branches are stimulated by stimulation electrodes 18 in certain embodiments.

[0075] FIGURE 9 illustrates an example method of treating auditory dysfunction using stimulation system 10, described above, implanted into a person's body with stimulation lead 14 located in communication with a peripheral nerve for treating auditory dysfunction. At process 800, one or more stimulation leads 14 are implanted such that one or more stimulation electrodes 18 of each stimulation lead 14 are positioned in communication with a peripheral nerve (for the purposes described herein and as those skilled in the art will recognize, when an embedded stimulation system, such as the Bion®, is used, it is positioned similar to positioning the lead 14). Techniques for implanting stimulation leads such as stimulation lead 14 are known to those skilled in the art. In certain embodiments, as described above, one or more stimulation electrodes 18 are positioned in communication with a peripheral nerve. Stimulation electrodes 18 are commonly positioned in communication with the peripheral nerve by electrodes applied cutaneously to the dermatome area of a peripheral nerve. Stimulation electrodes 18 can also be positioned subcutaneously in communication with the peripheral nerve or on the nerve root ganglion.

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The electrodes are carried by two primary vehicles: percutaneous leads and a laminotomy lead. Percutaneous leads commonly have two or more, equally-spaced electrodes, which are placed subcutaneously in communication with the peripheral nerve. For unilateral auditory dysfunction, percutaneous leads are positioned on the peripheral nerve on the contralateral side of the body corresponding to the "afflicted" side of the body, and for bilateral auditory dysfunction, a single percutaneous lead with two or more leads is positioned with each lead in communication with a peripheral nerve. An example of an eight-electrode percutaneous lead is an OCTRODE® lead manufactured by Advanced Neuromodulation Systems, Inc. Use of a Bion® stimulation system manufactured by Advanced Bionics Corporation is also contemplated in certain embodiments.

[0076] In contrast to the percutaneous leads, laminotomy leads have a paddle configuration and typically possess a plurality of electrodes (for example, two, four, eight, or sixteen) arranged in one or more columns. An example of a sixteen-electrode laminotomy lead is shown in FIG. 4H. Another example of a laminotomy lead is an eight-electrode, two column laminotomy lead called the LAMITRODE® 44, which is manufactured by Advanced Neuromodulation Systems, Inc. Implanted laminotomy leads are commonly transversely centered over the physiological midline of a patient. In such position, multiple columns of electrodes are well suited to address bilateral auditory dysfunction, where electrical energy may be administered bilaterally near peripheral nerve ganglia around the spinal cord via a single laminotomy lead. A multi-column laminotomy lead enables reliable positioning of a plurality of electrodes, and in particular, a plurality of electrode columns that do not readily deviate from an initial implantation position.

[0077] Laminotomy leads require a surgical procedure for implantation. The surgical procedure, or partial laminectomy, requires the resection and removal of certain vertebral tissue to properly position the laminotomy lead. The laminotomy lead offers a more stable platform, which is further capable of being sutured in place, that tends to migrate less in the operating environment of the human body. Depending on the position of insertion, however, access to the peripheral nerve or nerve ganglia may only require a partial removal of the ligamentum flavum at the insertion site. In some embodiments, two or more laminotomy leads may be positioned to treat multiple peripheral nerves or multiple branch points of a single nerve.

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[0078] In addition to stimulation of peripheral nerve ganglia, the laminotomy or percutaneous leads can be implanted subcutaneously in the dermatome area as shown in FIGURES 7 and 8 to stimulate any cranial and/or cervical nerve root associated with the C2 dermatome area. The leads can also be implanted subcutaneously at other dermatomes such as C3, trigeminal nerve dermatome, etc.

[0079] At process 802, if necessary, stimulation source 12 may be coupled directly to connecting portion 16 of stimulation lead 14. Alternatively, as described above and if necessary, stimulation source 12 may not be coupled directly to stimulation lead 14 and may instead be coupled to stimulation lead 14 via an appropriate wireless link. Of course, as those skilled in the art know, an embedded stimulation system will not need to be so coupled.

[0080] Intra-implantation trial stimulation may be conducted at processes 804 through 808. These processes may be used to optimize the effect of the treatment on auditory dysfunction. In certain embodiments, the intra-implantation trial stimulation is not performed, and the method proceeds from process 802 to 810. At process 804, stimulation source 12 is activated to generate and transmit stimulation pulses via one or more stimulation electrodes 18. At process 806, informal subjective questioning of the person, formal subjective testing and analysis according to one or more audiology tests and/or other analyses (such as the Goebel tinnitus questionnaire or other validated tinnitus questionnaires, audiometry, tinnitus matching, impedence, BAEP, and OAE) may be performed to determine whether the subject's auditory dysfunction has sufficiently improved through the intra-implantation trial stimulation. If the subject's auditory dysfunction has not sufficiently improved, one or more stimulation parameters may be adjusted, stimulation lead 14 may be moved incrementally or even re-implanted, or both of these modifications may be made at process 808 and the trial stimulation and analysis repeated until the auditory dysfunction has sufficiently improved. Once the stimulation parameters have been properly set and stimulation lead 14 has been properly positioned such that subject's auditory dysfunction has improved, intra-implantation trial stimulation is complete. One of skill in the art is aware that other types of intra-implantation trailing methods or stimulation trails can be used in the present invention, for example, but not limited to transcutaneous electrical nerve stimulation (TENS), transmagnetic stimulation (TMS), nerve blocks, etc.

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[0081] Once stimulation lead 14 has been properly implanted and secured, and any trial stimulation completed, if necessary, stimulation source 12 is implanted at process 810. Techniques for implanting stimulation sources such as stimulation source 12 are known to those skilled in the art. For non-embedded systems, the implant site is typically a subcutaneous pocket formed to receive and house stimulation source 12. The implant site is usually located some distance away from the insertion site, such as in or near the lower back or buttocks. Where stimulation lead 14 includes connecting portion 16, connecting portion 16 may be tunneled, at least in part, subcutaneously to the implant site of stimulation source 12 at process 812. Some embodiments of the invention may use a non-implantable stimulation source. At process 814, a doctor, the patient, or another user of stimulation source 12 may directly or indirectly input stimulation parameters for controlling the nature of the electrical stimulation provided to the peripheral nerve, if not already set during any intra-implantation trial stimulation period. Where appropriate, post-implantation trial stimulation may be conducted, over one or more weeks or months for example, and any necessary modifications made accordingly.

[0082] Although example processes are illustrated and described, the present invention contemplates two or more processes taking place substantially simultaneously or in a different order. In addition, the present invention contemplates using methods with additional processes, fewer processes, or different processes, so long as the processes remain appropriate for implanting stimulation system 10 into a person for electrical stimulation of the predetermined site, such as, for example the C2 dermatome area, C3 dermatome area, a cervical (e.g., C1, C2, C3, etc) or other spinal nerve or any cranial nerve (e.g., trigeminal, olfactory, etc) to treat auditory dysfunction.

[0083] One technique that offers the ability to affect neuronal function is the delivery of electrical stimulation for neuromodulation directly to target tissues via an implanted device having a probe. The probe is a stimulation lead or electrode in certain embodiments. The electrode assembly may be one electrode, multiple electrodes, or an array of electrodes in or around the target area. The proximal end of the probe is coupled to system to operate the device to stimulate the target site. Thus, the probe is coupled to an electrical signal source which, in turn, is operated to stimulate the predetermined treatment site.

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V. Infusion pumps

[0084] In further embodiments, it may be desirable to use a drug delivery system independently or in combination with electrical stimulation to result in the stimulation parameters of the present invention. Drug delivery may be used independent of or in combination with a lead/electrode to provide electrical stimulation and chemical stimulation. When used, the drug delivery catheter is implanted such that the proximal end of the catheter is coupled to a pump and a discharge portion for infusing a dosage of a pharmaceutical or drug. Implantation of the catheter can be achieved by combining data from a number of sources including CT, MRI or conventional and/or magnetic resonance angiography into the stereotactic targeting model. Thus, implantation of the catheter can be achieved using similar techniques as discussed above for implantation of electrical leads, which is incorporated herein. The distal portion of the catheter can have multiple orifices to maximize delivery of the pharmaceutical while minimizing mechanical occlusion. The proximal portion of the catheter can be connected directly to a pump or via a metal, plastic, or other hollow connector, to an extending catheter.

[0085] Implantable infusion pumps are used with certain embodiments of the invention to provide chemical stimulation. Further details of implantable infusion pumps that may be used with the invention are found in pending U.S. Application No. 10/755,985 "Actuation System and Method for an Implantable Infusion Pump" herein incorporated by reference.

[0086] In further embodiments, "active pumping" devices or so-called peristaltic pumps can be used as described in U.S. Pat. Nos. 4,692,147, 5,840,069, and 6,036,459, which are incorporated herein by reference in their entirety. Peristaltic pumps are used to provide a metered amount of a drug in response to an electronic pulse generated by control circuitry associated within the device. An example of a commercially available peristaltic pump is SynchroMed® implantable pump from Medtronic, Inc., Minneapolis, Minn.

[0087] Other pumps that may be used in the present invention include accumulator-type pumps, for example certain external infusion pumps from Minimed, Inc., Northridge, Calif. and Infusaid® implantable pump from Strato/Infusaid, Inc., Norwood, Mass. Passive pumping mechanisms can be used to release an agent in a constant flow or

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intermittently or in a bolus release. Passive type pumps include, for example, but are not limited to gas-driven pumps described in U.S. Pat. Nos. 3,731,681 and 3,951,147; and drive-spring diaphragm pumps described in U.S. Pat. Nos. 4,772,263, 6,666,845, 6,620,151 all of which are incorporated by reference in their entirety. Pumps of this type are commercially available, for example, Model 3000® from Arrow International, Reading, Penn. and IsoMed® from Medtronic, Inc., Minneapolis, Minn.; AccuRx® pump from Advanced Neuromodulation Systems, Inc., Plano, TX.

[0088] Instances in which chemical and electrical stimulation will be administered to the subject, a catheter having electrical leads may be used, similar to the ones described in U.S. Patent 6,176,242; 5,423,877; 5,458,631 and 5,119,832, each of which are incorporated herein by reference in its entirety.

[0089] Still further, the present invention can comprise a chemical stimulation system that comprises a system to control release of neurotransmitters (e.g., glutamate, acetylcholine, norepinephrine, epinephrine), chemicals (e.g., zinc, magnesium, lithium) and/or pharmaceuticals that are known to alter the activity of neuronal tissue. For example, infusion formulation delivery system can utilize a control system having an input-response relationship. A sensor generates a sensor signal representative of a system parameter input (such as levels of neurotransmitters), and provides the sensor signal to a controller . The controller receives the sensor signal and generates commands that are communicated to the infusion formulation delivery device . The infusion formulation delivery device then delivers the infusion formulation output to the predetermined site at a determined rate and amount in order to control the system parameter.

[0090] Sensor may comprise a sensor, sensor electrical components for providing power to the sensor and generating the sensor signal, a sensor communication system for carrying the sensor signal to controller, and a sensor housing for enclosing the electrical components and the communication system. Controller may include one or more programmable processors, logic circuits, or other hardware, firmware or software components configured for implementing the control functions described herein, a controller communication system for receiving the sensor signal from the sensor, and a controller housing for enclosing the controller communication system and the one or more programmable processors, logic circuits, or other hardware, firmware or software

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components. The infusion formulation delivery device may include a suitable infusion pump, infusion pump electrical components for powering and activating the infusion pump, an infusion pump communication system for receiving commands from the controller, and an infusion pump housing for enclosing the infusion pump, infusion pump electrical components, and infusion pump communication system. Such systems are described in US Patent No. 6,740,072, which is incorporated herein by reference in its entirety.

[0091] In certain embodiments, the sensor can be an electrode that senses a hyperactive burst pattern of activity, which in turns stimulates the infusion pump to release a chemical or stimulating drug or agent to modify the neuronal activity. The chemical or stimulating agent can be either an inhibiting agent or stimulating agent.

[0092] Herein, stimulating drugs comprise medications, anesthetic agents, synthetic or natural peptides or hormones, neurotransmitters, cytokines and other intracellular and intercellular chemical signals and messengers, other agents such as zinc and the like. In addition, certain neurotransmitters, hormones, and other drugs are excitatory for some tissues, yet are inhibitory to other tissues. Therefore, where, herein, a drug is referred to as an "excitatory" drug, this means that the drug is acting in an excitatory manner, although it may act in an inhibitory manner in other circumstances and/or locations. Similarly, where an "inhibitory" drug is mentioned, this drug is acting in an inhibitory manner, although in other circumstances and/or locations, it may be an "excitatory" drug. In addition, stimulation of an area herein includes stimulation of cell bodies and axons in the area.

[0093] Similarly, excitatory neurotransmitter agonists (e.g., norepinephrine, epinephrine, glutamate, acetylcholine, serotonin, dopamine), agonists thereof, and agents that act to increase levels of an excitatory neurotransmitter(s) (e.g., edrophonium; Mestinon; trazodone; SSRIs (e.g., flouxetine, paroxetine, sertraline, citalopram and fluvoxamine); tricyclic antidepressants (e.g., imipramine, amitriptyline, doxepin, desipramine, trimipramine and nortriptyline), monoamine oxidase inhibitors (e.g., phenelzine, tranylcypromine, isocarboxasid)), generally have an excitatory effect on neural tissue, while inhibitory neurotransmitters (e.g., dopamine, glycine, and gamma-aminobutyric acid (GABA)), agonists thereof, and agents that act to increase levels of an inhibitory neurotransmitter(s) generally have an inhibitory effect (e.g., benzodiasepine (e.g., chlordiazepoxide, clonazepam, diazepam, lorazepam, oxazepam, prazepam alprazolam); flurazepam, temazepam, or

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triazolam). (Dopamine acts as an excitatory neurotransmitter in some locations and circumstances, and as an inhibitory neurotransmitter in other locations and circumstances.) However, antagonists of inhibitory neurotransmitters (e.g., bicuculline) and agents that act to decrease levels of an inhibitory neurotransmitter(s) have been demonstrated to excite neural tissue, leading to increased neural activity. Similarly, excitatory neurotransmitter antagonists (e.g., prazosin, and metoprolol) and agents that decrease levels of excitatory neurotransmitters may inhibit neural activity. Yet further, lithium salts, anesthetics (e.g., lidocane), and magnesium may also be used in combination with electrical stimulation.

VI. Treatment of Auditory Dysfunction

[0094] The present method acts to stimulate nerve afferents which in turn stimulate the brain and cause/allow the brain to act in the best interest of the host through use of the brain's natural mechanisms. The prior art fails to recognize that stimulation of a patient's peripheral nerves can provide the therapeutic treatments for auditory dysfunction according to the instant invention.

[0095] The present invention is particularly useful in the treatment of auditory dysfunction in humans. However, one skilled in the art appreciates that the present invention is applicable to other animals which experience auditory dysfunction. This may include, for example, primates, canines, felines, horses, elephants, dolphins, etc. Utilizing the various embodiments of the present invention, one skilled in the art may be able to modulate the auditory system via peripheral nerve stimulation to achieve a desirable result.

[0096] One technique that offers the ability to affect neuronal function is the delivery of electrical, chemical, and/or magnetic stimulation for neuromodulation directly to target tissues via an implanted device having a probe. The probe is, for example, a stimulation lead, electrode assembly, or a catheter in certain embodiments of the invention. An electrode assembly may be one electrode, multiple electrodes, or an array of electrodes in or around the target area. The proximal end of the probe is coupled to system to operate the device to stimulate the target site. Thus, the probe is coupled to an electrical signal source, which, in turn, is operated to stimulate the predetermined treatment site of a peripheral nerve or nerves. In the case of unilateral auditory dysfunction, contralateral peripheral nerve stimulation may be more effective than ipsilateral stimulation. However, as the auditory system crosses over at numerous points, effective auditory dysfunction treatment may require

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bilateral stimulation. Stimulation of the predetermined site is performed to modulate neuronal extralemniscal pathways of the auditory system. Modulation of this neuronal tissue may result in efficacious treatment of auditory dysfunction in a subject. While optimal results from the treatment may result in the complete cessation of auditory dysfunction in a subject, any lessening of the amplitude of a subject's auditory dysfunction may be considered successful according to the present invention.

[0097] The predetermined site can be, for example, but not limited to a dermatome area, for example, C2, C3, C4, C5, C6, C7, C8, as well as any thoracic, lumbar or sacral dermatome. Cervical nerve roots (*e.g.*, C1, C2, C3, C4, C5, C6, C7 and C8) and cranial nerves (*e.g.*, olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and hypoglossal nerve) to provide therapeutic treatments according to the instant invention. Other dermatomes that can be included in the present invention include dermatomes associated with cranial nerves having somatosensory function, for example, but not limited to dermatomes associated with the trigeminal nerve, intermediate part of the facial nerve, glossopharyngeal nerve, or vagal nerve. Other peripheral nerves are spinal nerves such as the suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, and the brachial plexus, which branches to form the dorsal scapular nerve, the thoracic nerve, the suprascapular nerve, the lateral pectoral, the musculocutaneous nerve, the axillarily nerve, the radial nerve, the median nerve, the ulnar nerve, and other minor peripheral nerves, as well as sympathetic and parasympathetic nerves. Yet further, other peripheral nerves also includes thoracic nerve roots (e.g., T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12), lumbar nerve roots (L1, L2, L3, L4, L5) sacral nerve roots (e.g., S1, S2, S3, S4, S5) and the coccygeal nerve.

[0098] One example of stimulation parameters that can be used in the present invention is a parameter set with an amplitude in the range of about 2 mA to about 100 mA, a frequency in the range of about 1 Hz to about 80 Hz, and a pulse width in the range of about 5 microseconds to about 100 microseconds.

[0099] One of skill in the art is aware that stimulation parameters can be varied to achieve the desired result. One such parameter that may be varied in the present invention

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is signal frequency. Altering the frequency signal can result in the generation of a bursting type rhythm or burst stimulus frequency or burst mode stimulation, as described in "New Stimulation Design for Neuromodulation", filed October 20, 2005 incorporated by reference herein.

[0100] In certain embodiments, the burst stimulus frequency may be in the range of about 1 Hz to about 100 Hz, more particular, in the range of about 1 Hz to about 12Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4Hz to about 7Hz or about 8Hz to about 12Hz for each burst. One skilled in the art will further realize that each burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 2 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 5OHz to about 1000Hz, more particularly, in the range of about 200Hz to about 500Hz. One of skill in the art is aware that the frequency for each spike within a burst can be variable, thus it is not necessary for each spike to contain similar frequencies, e.g., the frequencies can vary in each spike. The inter-spike interval can be also vary, for example, the inter-spike interval, can be about 0.5 milliseconds to about 100 milliseconds or any range therebetween. The burst stimulus is followed by an inter-burst interval a duration in the range of about 5 milliseconds to about 5 seconds, preferably, about 10 milliseconds to about 300 milliseconds. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particular, in the range of about 250 msec to 1000 msec (1-4 Hz burst firing), 145 msec to about 250 msec (4-7 Hz,), 145 msec to about 80 msec (8-12 Hz) or 1 to 5 seconds in plateau potential firing. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (e.g., random or irregular harmonics).

[0101] In the auditory system, tonic firing the contents of auditory information, while burst firing may transmit the change in the auditory environment and valence or importance attached to that sound (Lisman 1997; Sherman 2001; Swadlow and Gusev 2001). Repetitive stimulus presentation results in decreased neuronal response to that stimulus, known as auditory habituation at the single cell level (Ulanovsky *et al.*, 2003), auditory mismatch negativity at multiple cell level (Naatanen *et al.*, 1993; Ulanovsky *et al.*, 2003).

[0102] Many auditory dysfunctions are constantly present. For example, tinnitus is usually constantly present, e.g., a non-rational valence is attached to the internally

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generated sound, and there is no auditory habituation to this specific sound, at this specific frequency. Thus, tinnitus is the result of hyperactivity of lesion-edge frequencies, and auditory mismatch negativity in tinnitus patients is specific for frequencies located at the audiometrically normal lesion edge (Weisz 2004).

[0103] As pathological valence of the tinnitus sound is mediated by burst firing, burst firing is increased in tinnitus in the extralemniscal system (Chen and Jastreboff 1995; Eggermont and Kenmochi 1998; Eggermont 2003), in the inner hair cells (Puel 1995; Puel *et al.*, 2002), the auditory nerve (Moller 1984), the dorsal and external inferior colliculus (Chen and Jastreboff 1995), the thalamus (Jeanmonod, Magnin *et al.*, 1996) and the secondary auditory cortex (Eggermont and Kenmochi 1998; Eggermont 2003). Furthermore, quinine, known to generate tinnitus, induces an increased regularity in burst firing, at the level of the auditory cortex, inferior colliculus and frontal cortex (Gopal and Gross 2004). It is contemplated that tinnitus can only become conscious if an increased tonic firing rate is present in the lemniscal system, generating the sound. This increased firing activity has been demonstrated in the lemniscal dorsal cochlear nucleus (Kaltenbach, Godfrey *et al.*, 1998; Zhang and Kaltenbach 1998; Kaltenbach and Afman 2000; Brozoski, Bauer *et al.*, 2002; Zacharek *et al.*, 2002; Kaltenbach *et al.*, 2004), inferior colliculus (Jastreboff and Sasaki 1986; Jastreboff, Brennan *et al.*, 1988; Jastreboff 1990) (Gerken 1996) and primary auditory cortex (Komiya, 2000). Interestingly, not only tonic firing is increased generating the tinnitus sound, but also the burst firing (Ochi and Eggermont 1997) (keeping it conscious) at a regular basis. Repetitive burst firing is known to generate tonic gamma band activity (Gray and Singer 1989; Brumberg, 2000). Thus, it is envisioned that the present invention can be used to modify burst firing, thus modifying tonic gamma activity. However, other pathways may be employed by embodiments of the invention that potentially contribute to the treatment efficacy.

[0104] Burst mode firing boosts the gain of neural signaling of important or novel events by enhancing transmitter release and enhancing dendritic depolarization, thereby increasing synaptic potentiation. Conversely, single spiking mode may be used to dampen neuronal signaling and may be associated with habituation to unimportant events (Cooper 2002). It is believed that the main problem in tinnitus is that the internally generated stimulus does not decay due to the presence of regular bursting activity telling the cortex this signal is important and has to remain conscious.

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[0105] Thus, in the present invention, it is envisioned that a burst mode type stimulation can attack either of these two pathways: slowing down tonic firing in the lemniscal system (below 40 Hz) or removing the valence attached to it by the extralemniscal system by suppressing the bursting rhythm, thereby treating auditory dysfunctions such as tinnitus. Yet further, the system of the present invention can also make the auditory dysfunction disappear via auditory habituation. Suppressing the burst firing in the frontal cortex may alter the emotional effect of tinnitus, with the tinnitus persisting, but without much influence on the daily life of a tinnitus sufferer.

[0106] Thus, using the therapeutic stimulation system of the present invention, the predetermined site is stimulated in an effective amount or effective treatment regimen to decrease, reduce, modulate or abrogate the neurological disorder. Thus, a subject is administered a therapeutically effective stimulation so that the subject has an improvement in the parameters relating to tinnitus including the Goebel tinnitus questionnaire or other validated tinnitus questionnaires, audiometry, tinnitus matching, impedence, BAEP, and OAE. The improvement is any observable or measurable improvement. Thus, one of skill in the art realizes that a treatment may improve the patient condition, but may not be a complete cure of the disease.

[0107] In certain embodiments, in connection with improvement the electrical stimulation may have a "brightening" effect on the person such that the person looks better, feels better, moves better, thinks better, and otherwise experiences an overall improvement in quality of life.

[0108] Treatment regimens may vary as well, and often depend on the health and age of the patient. Obviously, certain types of disease will require more aggressive treatment, while at the same time, certain patients cannot tolerate more taxing regimens. The clinician will be best suited to make such decisions based on the known subject's history.

[0109] For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, improvement of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether objective or subjective. The improvement is any

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observable or measurable improvement. Thus, one of skill in the art realizes that a treatment may improve the patient condition, but may not be a complete cure of the disease.

VII. Examples

[0110] The following example is included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the example which follows represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

Example 1
Treatment of Tinnitus

[0111] Thirteen patients with tinnitus were treated by stimulating at least one peripheral nerve. 200 Hz, 250 microsecond pulse width pulses were used with amplitude dependent on an individual threshold. Of these, four noted a decrease in tinnitus, one noted an increase and eight had no alteration in tinnitus. Tinnitus was evaluated using TMS, TENS, the Goebel tinnitus questionnaire, audiometry, tinnitus matching, impedence, BAEP, and OAE.

Example 2
Treatment of Auditory Agnosia and Tinnitus

[0112] Auditory agnosia is characterized by a relatively isolated deficit in auditory comprehension despite normal hearing. When only verbal material is not understood, it is often called word deafness; when the deficit is in recognizing environmental sounds, it is often termed nonverbal auditory agnosia (Saygin, Dick et al. 2003).

[0113] In a patient suffering word deafness with associated complete auditory agnosia (verbal and non-verbal) and bilateral tinnitus, TENS stimulation was capable of attenuating the tinnitus and improving auditory agnosia during stimulation. In order to obtain a permanent suppression a bilateral subcutaneous occipital nerve stimulation was implanted leading to a continuous improvement of both tinnitus and auditory agnosia.

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Patient History:

[0114] After a flu like syndrome a patient became comatose due to a bilateral herpes encephalitis, from which she recovered. Initially she presented with a complete cortical deafness, however after 3 to 4 weeks the patient recovered partially, with almost normalized pure tone perception, but leaving her with a complete auditory agnosia and bilateral tinnitus. Language function per se is intact, with normal language comprehension and (motor) speech, but speech comprehension is 0%. The patient can communicate via lipreading and reading. Her auditory agnosia was complete, inclusive of a pure word deafness (=auditory verbal agnosia). She does not recognize the sound of a barking dog, the sound of a car, she does not recognize the voice of her husband, she only hears sounds, perceived as a lot of chaotic noise.

Audiologic Evaluation:

[0115] Pure tone audiometry: in the right ear an average perception loss of 40 dB is noted, in the left ear an average hearing loss of 50 dB

[0116] Speech audiometry : 0% for all intensities

[0117] Language analysis : normal reading, writing and language testing

Tinnitus Evaluation :

[0118] Visual Analoge Scale (intensity) rating of her tinnitus : 10/10 left side, 5/10 right side

[0119] Tinnitus matching : polyphonic tinnitus centered around 250 dB, 40 dB above sensorineural hearing level. Tinnitus worsens on talking, chewing and head movement (somatic tinnitus), as well as on exertion, tinnitus improves slightly when resting. The perceived sound is described as if 10 airplanes are taking off at the same time.

[0120] Tinnitus Questionnaire (Goebel and Hiller)(grade 0-4): grade 4, i.e., a decompensated severe tinnitus.

MRI Evaluation:

[0121] MRI with and without Gadolineum demonstrates thickened meninges at the temporal lobe and contrast enhancement of the internal auditory meatus.

[0122] Functional MRI resulted in absent activation of Wernicke's area with auditory word presentation, but activation of Wernicke's area with visual word presentation.

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Treatment

[0123] The patient received transcranial magnetic stimulation at 1, 5, 10 and 20 Hz. This type of stimulation did not improve the tinnitus.

[0124] Next, transcutaneous electrical nerve stimulation (TENS) was used. TENS had a beneficial effect on her tinnitus, decreasing the tinnitus intensity to 7/10 on the left side and removing the aggressivity of the sound, as well as stabilizing the tinnitus. TENS at 6 and 40 Hz, 50 μs pulse width have the best effect. The patient described that the tinnitus sounds less chaotic, less fluctuating. Stress or fatigue however kept worsening the tinnitus, but the spontaneous variability in the tinnitus has disappeared. After three months of TENS, the patients first noticed she can recognize the sound of a car and a dog barking, but only when the TENS is on. One month later she can recognize her husbands voice, and after one year of TENS she can recognize some words, but also only when the TENS is on.

[0125] Next, a bilateral subcutaneous occipital electrode was implanted (quatrode, ANS Medical) and connected to an internal pulse generator (Genesis, ANS Medical). This improved the tinnitus even more at stimulation settings 6 Hz, 5 μs pulse width and intensities between 2 and 6 mAmp, however without auditory agnosia improvement. Stimulation at 18 Hz has better effects, with even better tinnitus suppression and immediate auditory agnosia and word deafness improvement.

[0126] Thus, electrical stimulation of the somatosensory system can be used to treat tinnitus, as well as improve auditory perception, such as auditory agnosia and word deafness by activation of the extralemniscal auditory connections to the somatosensory system.

REFERENCES

[0127] All patents and publications mentioned in the specification are indicative of the levels of those skilled in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

Foxe *et al.*, Cognitive Brain Research 10:77-83 (2000)

Fu *et al.*, The Journal of Neuroscience 23(20):7510-7515 (2003)

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Jones, Trends in Neuroscience, Vol. 24, No. 10:595-601 (2001)

Moller et al., (1992), Laryngoscope. 102(10):1165-71

Moller and Rollins, Neuroscience Letters 319:41-44 (2002)

Moller *et al.*, Laryngoscope 102:1165-1171 (1992)

Mirz *et al.*, Hearing Research 134:133-144 (1999)

Norton, BioMedical Engineering OnLine 2:6 (2003)

Tardif *et al.*, Neuroscience 116:1111-1121 (2003)

Wallhausser-Franke *et al.*, Experimental Brain Research 153:649-654 (2003)

Zhang *et al.*, Experimental Brain Research 153:655-660 (2003)

U.S. Patent No. 5,496,369

U.S. Patent No. 5,697,975

U.S. Patent No. 5,713,847

U.S. Patent No. 5,735,885

U.S. Patent No. 5,788,656

U.S. Patent No. 6,210,321

U.S. Patent No. 6,456,886

U.S. Patent No. 6,656,172

International Pub. No. WO 01/08617

[0128] Although the present invention and its advantages have been described in detail, it should be understood that various changes, substitutions and alterations can be made herein without departing from the invention as defined by the appended claims. Moreover, the scope of the present application is not intended to be limited to the particular embodiments of the process, machine, manufacture, composition of matter, means, methods and steps described in the specification. As one will readily appreciate from the disclosure, processes, machines, manufacture, compositions of matter, means, methods, or steps, presently existing or later to be developed that perform substantially the same function or achieve substantially the same result as the corresponding embodiments described herein may

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be utilized. Accordingly, the appended claims are intended to include within their scope such processes, machines, manufacture, compositions of matter, means, methods, or steps.

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CLAIMS

What is claimed is:

1. A method of treating auditory dysfunction comprising the steps of:

implanting at least an electrical lead within a patient such that at least one electrode of the electrical lead is disposed adjacent to nerve tissue associated with a C2 dermatome area or a C3 dermatome area;

selecting a plurality of operating parameters for an electrical stimulation system that are effective for treating auditory dysfunction;

programming the electrical stimulation system according to the plurality of operating parameters; and

activating the electrical stimulation system to deliver electrical pulses to the electrode adjacent to the nerve tissue associated with a C2 dermatome area or a C3 dermatome area thereby treating the patient's auditory dysfunction.

2. The method of claim 1 wherein the nerve tissue associated with the C2 dermatome area or C3 dermatome area comprises cranial nerves.

3. The method of claim 1, wherein the nerve tissue associated with the C2 dermatome area or C3 dermatome area comprises the occipital nerve.

4. The method of claim 1 wherein the auditory dysfunction is tinnitus, hyperacousis, phonophobia, misophonia, auditory agnosia, auditory spatial dysfunction or auditory hallucinations.

5. The method of claim 1 wherein the auditory dysfunction is tinnitus.

6. The method of claim 1 wherein the auditory dysfunction is uditory agnosia.

7. A method of treating auditory dysfunction comprising the steps of:

implanting at least an electrical lead within a patient such that at least one electrode of the electrical lead is disposed adjacent to nerve tissue associated with a peripheral nerve selected from the group of cranial nerves consisting of olfactory nerve, optic, nerve,

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oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, hypoglossal nerve, and a combination thereof;

selecting a plurality of operating parameters for an electrical stimulation system that are effective for treating auditory dysfunction;

programming the electrical stimulation system according to the plurality of operating parameters; and

activating the electrical stimulation system to deliver electrical pulses to the electrode adjacent to the nerve tissue associated with the peripheral nerve thereby treating the patient's auditory dysfunction.

8. The method of claim 7 wherein the electrical stimulation delivers electrical pulses on a substantially continuous basis.

9. The method of claim 7 wherein the plurality of operating parameters include a pulse amplitude parameter, a pulse width parameter, and a pulse frequency parameter.

10. The method of claim 7 wherein the pulse frequency parameter is within the range of about 3 to about 80 Hz.

11. The method of claim 7 wherein the electrical stimulation delivers electrical pulses on a temporary basis in response to receiving an initiation signal from an external control device operated by the patient.

12. The method of claim 7 wherein the selecting comprises:

temporarily delivering electrical pulses according to the plurality of operating parameters to the electrode adjacent to the nerve tissue associated with a peripheral nerve; and

monitoring the auditory dysfunction while the temporarily delivering is performed.

13. The method of claim 12 wherein the monitoring comprises:

determining an improvement in the auditory dysfunction.

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14. The method of claim 7 wherein the auditory dysfunction is tinnitus, hyperacousis, phonophobia, misophonia, auditory agnosia, auditory spatial dysfunction or auditory hallucinations.

15. The method of claim 7 wherein the lead comprises a plurality of electrodes and the plurality of operating parameters include an electrode configuration.

16. The method of claim 7 further comprising adjusting stimulation parameters to optimize auditory dysfunction treatment.

17. A system for treating auditory dysfunction by somatosensory system stimulation comprising:

a probe implanted into a subject, wherein the probe is adjacent to nerve tissue associated a C2 or C3 dermatome area;

a pulse generator source operable to generate a stimulation pulse; and

a means of programming the pulse generator source such that the pulse generator source stimulates the nerve tissue thereby treating the auditory dysfunction.

18. The system of claim 17 wherein said probe is an electrical stimulation lead selected from the group consisting of laminotomy lead, paddle lead, surgical lead, and multiple electrode lead.

19. The system of claim 17 wherein the auditory dysfunction is tinnitus, hyperacousis, phonophobia, misophonia, auditory agnosia, auditory spatial dysfunction or auditory hallucinations.

20. A system for treating auditory dysfunction by somatosensory system stimulation comprising:

a probe implanted into a subject, wherein the probe is adjacent to nerve tissue associated with a peripheral nerve is a cranial nerve selected from the group consisting of olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, hypoglossal nerve, and a combination thereof;

a pulse generator source operable to generate a stimulation pulse; and

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a means of programming the pulse generator source such that the pulse generator source stimulates the nerve tissue associated with a peripheral nerve thereby treating the auditory dysfunction.

21. The system of claim 20 wherein said probe is an electrical stimulation lead selected from the group consisting of laminotomy lead, paddle lead, surgical lead, and multiple electrode lead.

22. The system of claim 20 wherein the auditory dysfunction is tinnitus, hyperacousis, phonophobia, misophonia, auditory agnosia, auditory spatial dysfunction or auditory hallucinations.

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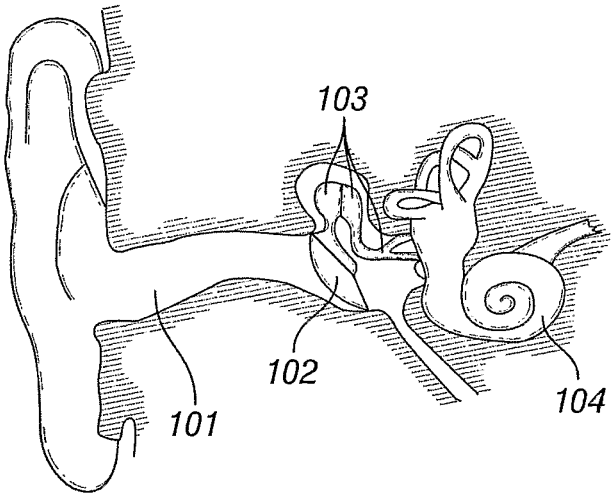


FIG. 1A

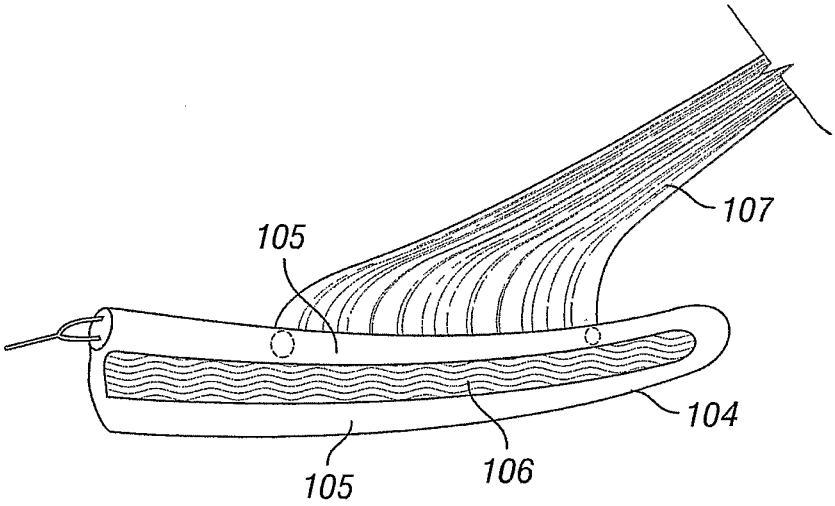


FIG. 1B

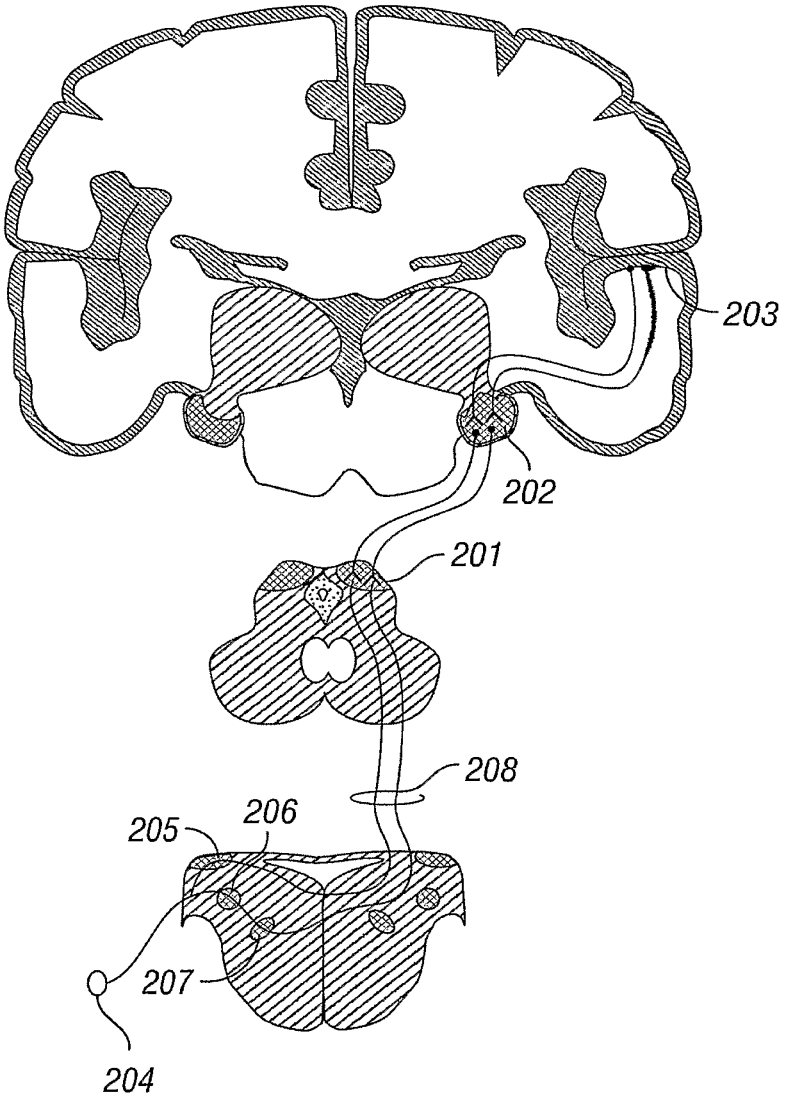


FIG. 2

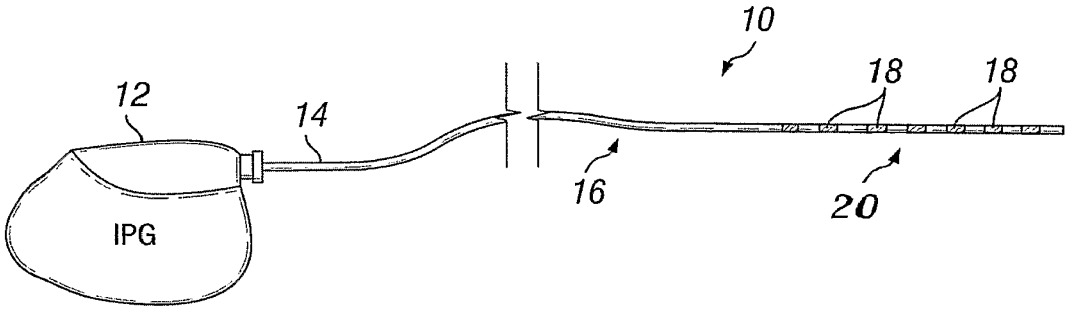

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IPG

FIG. 3A

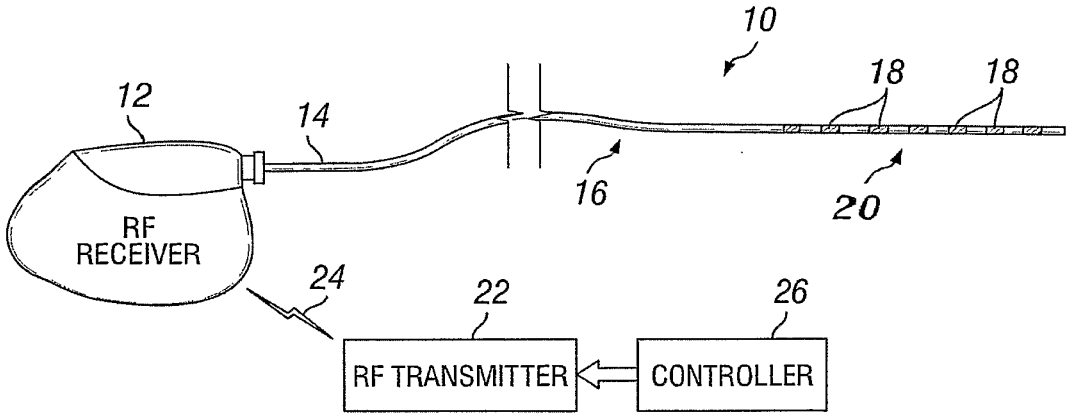

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18
18
16
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RF
RECEIVER
24
22
26
RF TRANSMITTER
CONTROLLER

FIG. 3B

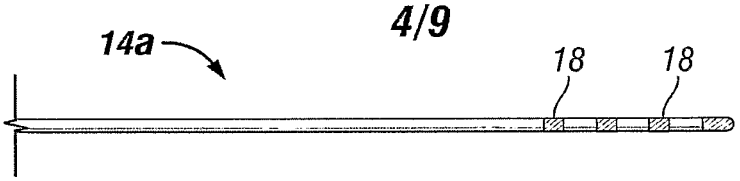


FIG. 4A

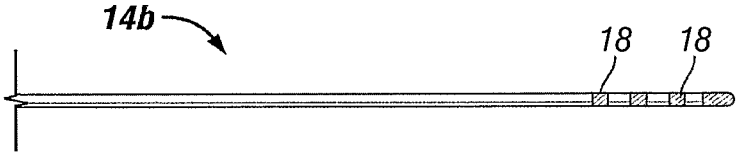


FIG. 4B

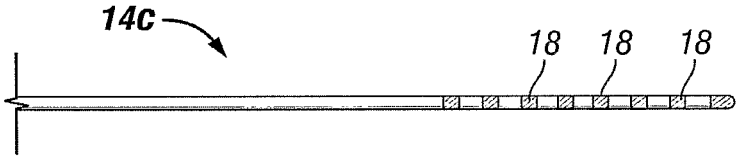


FIG. 4C

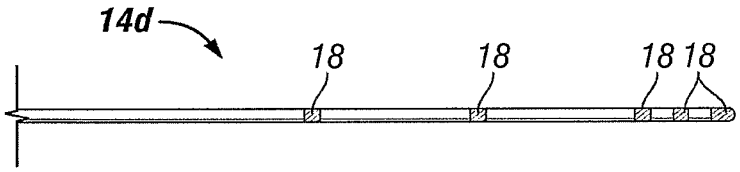


FIG. 4D

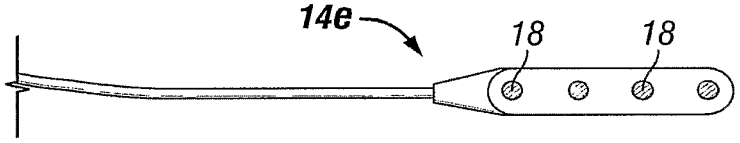


FIG. 4E

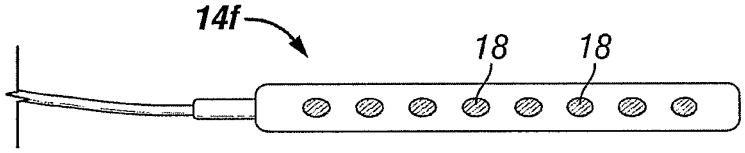


FIG. 4F

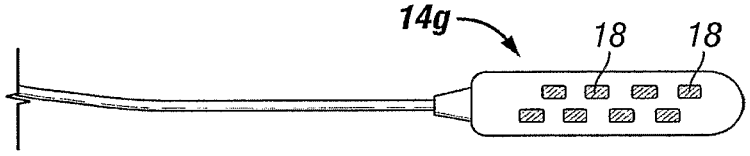


FIG. 4G

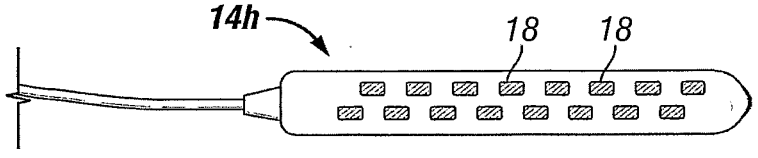


FIG. 4H

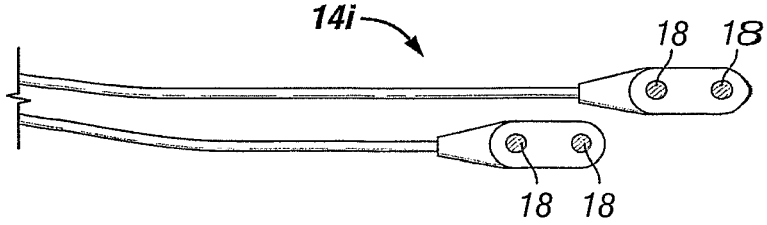


FIG. 4I

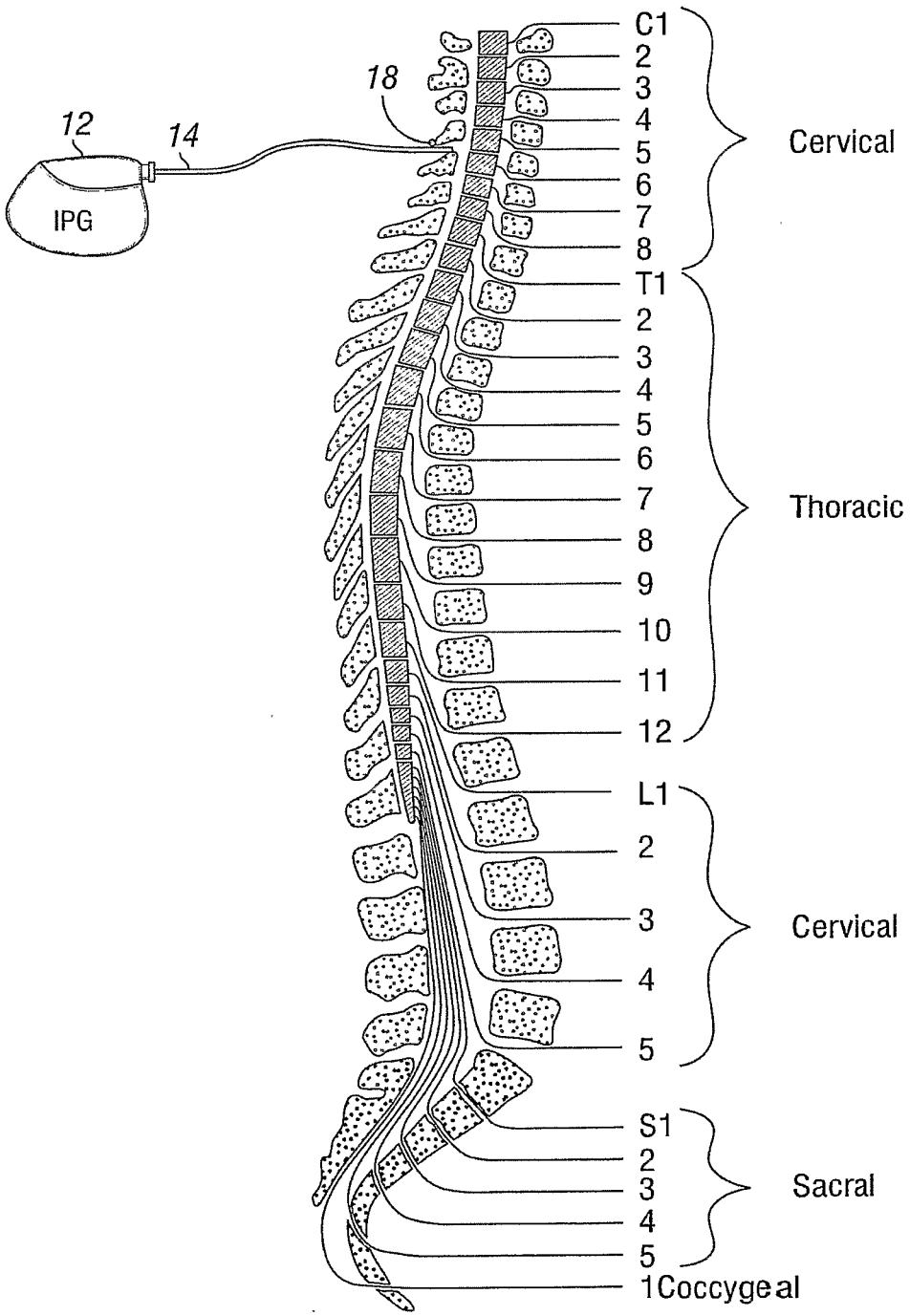

12
14
18
IPG
C1
2
3
4
5
6
7
8
T1
2
3
4
5
6
7
8
9
10
11
12
L1
2
3
4
5
S1
2
3
4
5
1Coccygeal
Cervical
Thoracic
Cervical
Sacral

FIG. 5

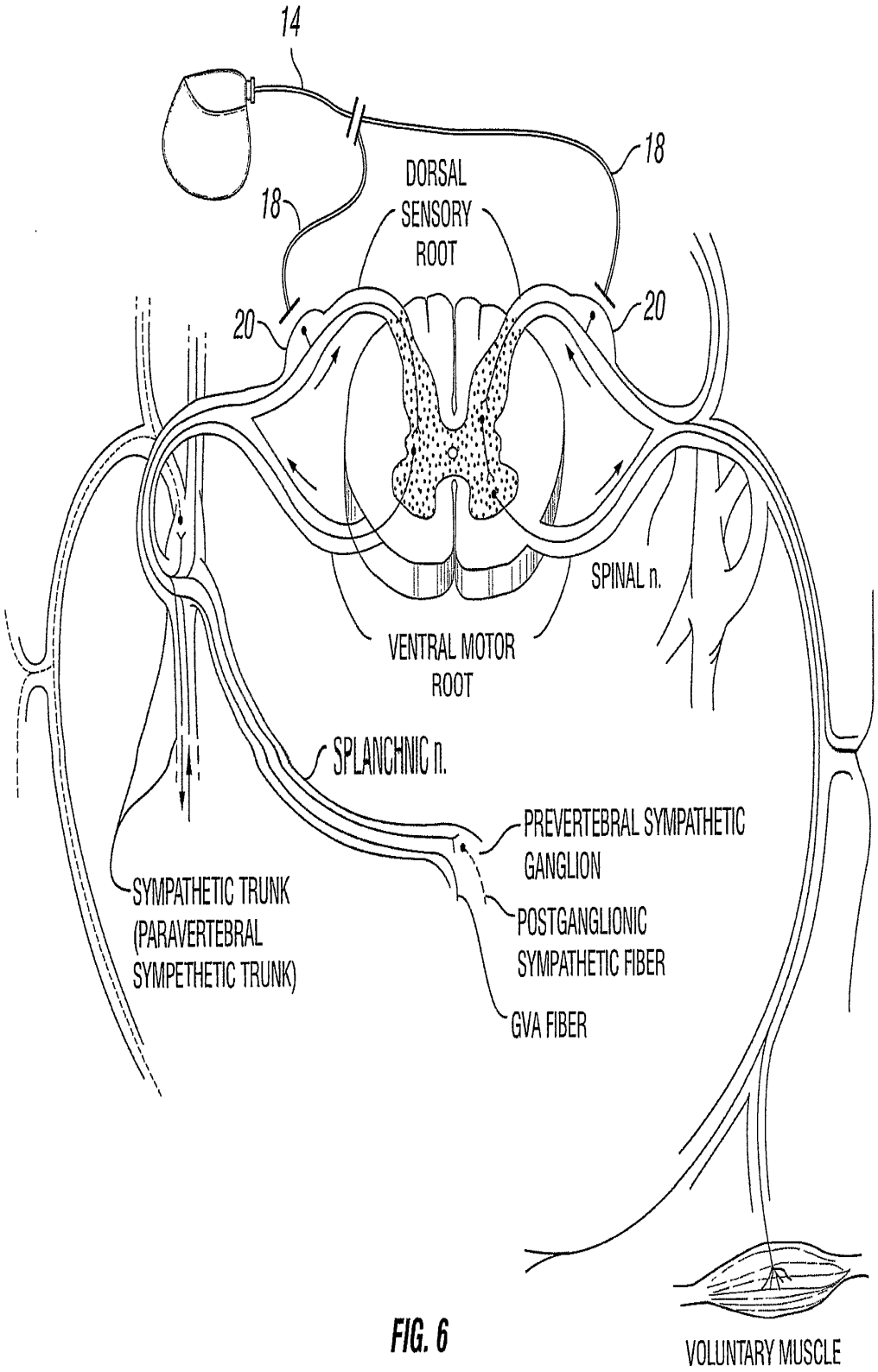

14
18
18
DORSAL
SENSORY
ROOT
20
20
SPINAL n.
VENTRAL MOTOR
ROOT
SPLANCHNIC n.
PREVERTEBRAL SYMPATHETIC
GANGLION
SYMPATHETIC TRUNK
(PARAVERTEBRAL
SYMPETHETIC TRUNK)
POSTGANGLIONIC
SYMPATHETIC FIBER
GVA FIBER
VOLUNTARY MUSCLE

FIG. 6

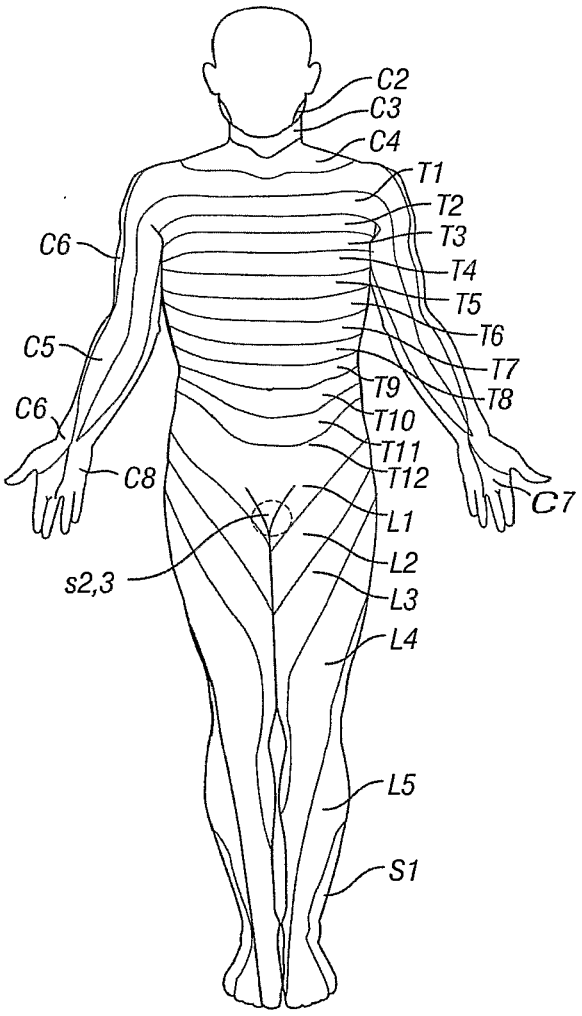

C2
C3
C4
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
L5
S1
C6
C5
C6
C8
C7
s2,3

FIG. 7A

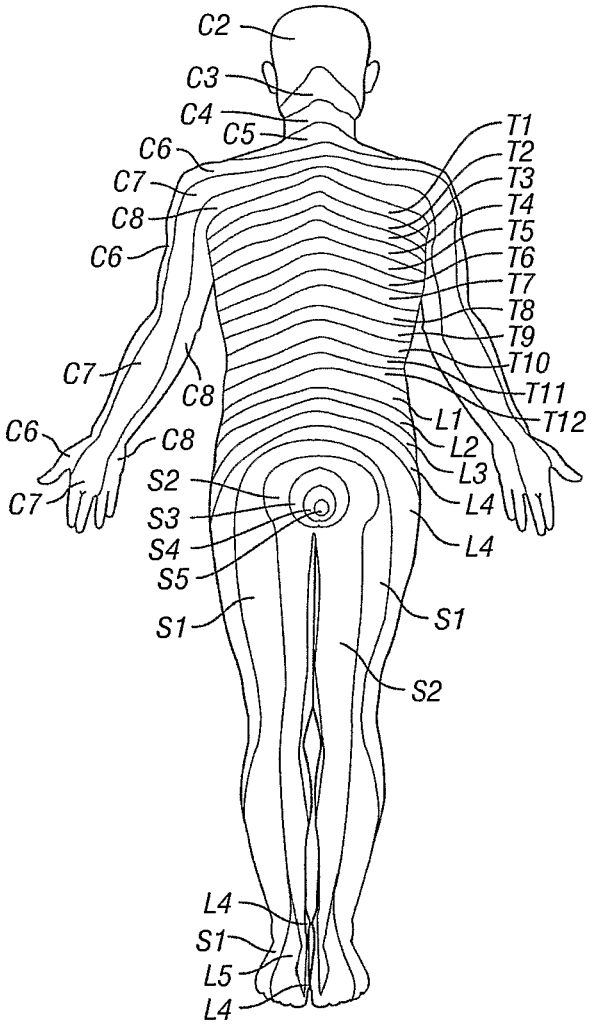

C2
C3
C4
C5
C6
C7
C8
C6
C7
C8
C6
C8
C7
T1
T2
T3
T4
T5
T6
T7
T8
T9
T10
T11
T12
L1
L2
L3
L4
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S2
S2
S3
S4
S5
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L4
S1
L5
L4

FIG. 7B

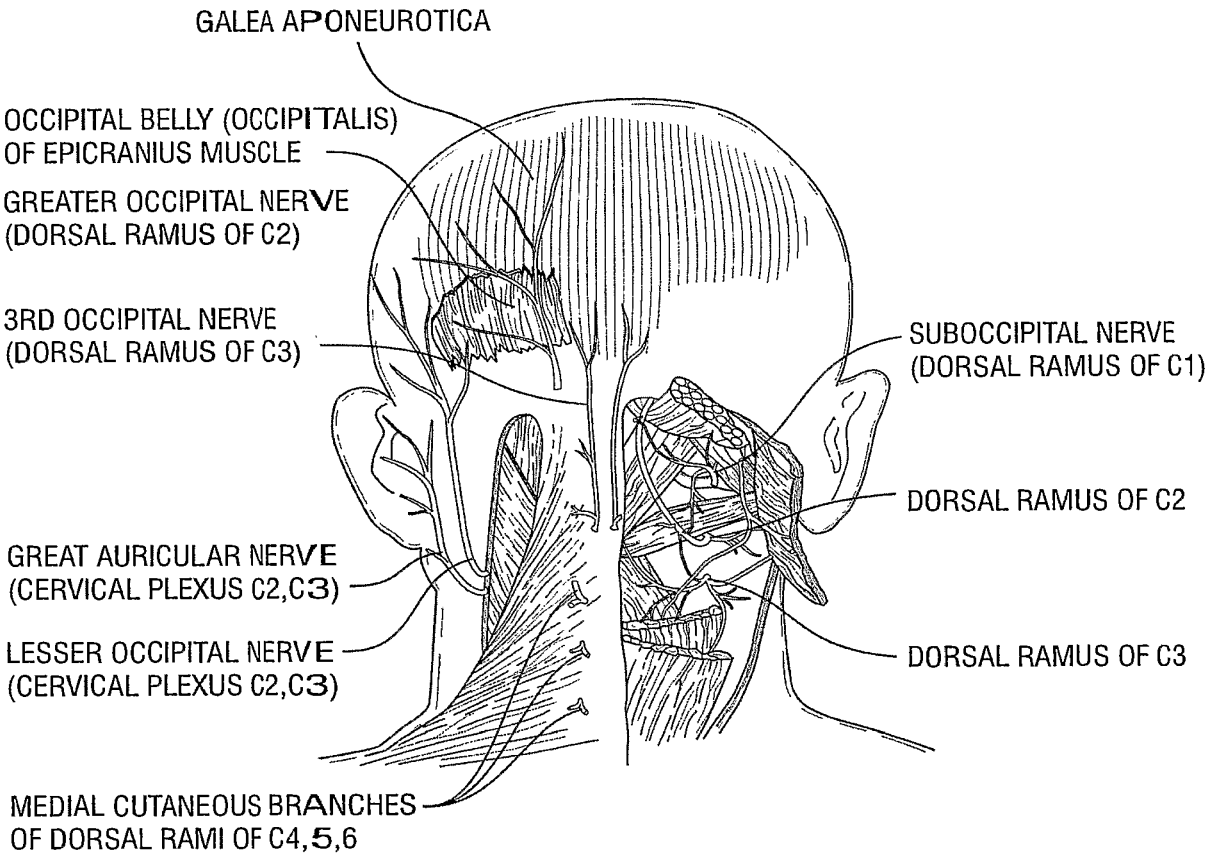

GALEA APONEUROTICA
OCCIPITAL BELLY (OCCIPITALIS) OF EPICRANIUS MUSCLE
GREATER OCCIPITAL NERVE (DORSAL RAMUS OF C2)
3RD OCCIPITAL NERVE (DORSAL RAMUS OF C3)
GREAT AURICULAR NERVE (CERVICAL PLEXUS C2,C3)
LESSER OCCIPITAL NERVE (CERVICAL PLEXUS C2,C3)
MEDIAL CUTANEOUS BRANCHES OF DORSAL RAMI OF C4,5,6
SUBOCCIPITAL NERVE (DORSAL RAMUS OF C1)
DORSAL RAMUS OF C2
DORSAL RAMUS OF C3

FIG. 8

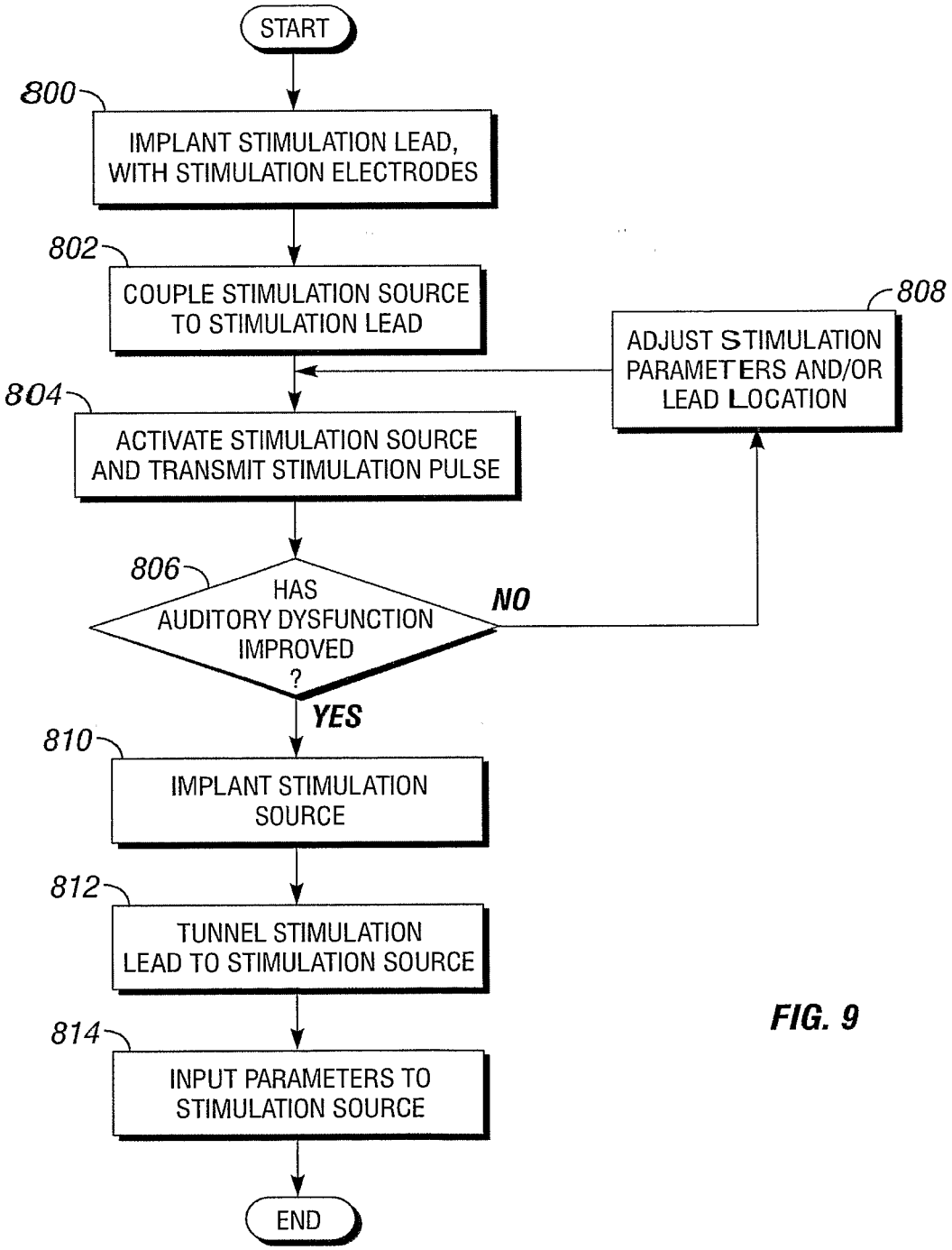

START
800
IMPLANT STIMULATION LEAD, WITH STIMULATION ELECTRODES
802
COUPLE STIMULATION SOURCE TO STIMULATION LEAD
808
ADJUST STIMULATION PARAMETERS AND/OR LEAD LOCATION
804
ACTIVATE STIMULATION SOURCE AND TRANSMIT STIMULATION PULSE
806
HAS AUDITORY DYSFUNCTION IMPROVED ?
NO
YES
810
IMPLANT STIMULATION SOURCE
812
TUNNEL STIMULATION LEAD TO STIMULATION SOURCE
814
INPUT PARAMETERS TO STIMULATION SOURCE
END

FIG. 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2005/037846

A. CLASSIFICATION OF SUBJECT MATTER
A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/045242 A (BRAINSGATE LTD; SHALEV, ALON; GROSS, YOSSI) 27 May 2004 (2004-05-27) page 10, line 11 - page 19, line 23; figures 1a,b,2,3	17,19, 21-24
X	US 6 735 475 B1 (WHITEHURST TODD K ET AL) 11 May 2004 (2004-05-11) column 16, lines 26-64; figures 4,5	17,22
X	US 5 697 975 A (M A HOWARD III, ET AL) 16 December 1997 (1997-12-16) cited in the application the whole document	17,19, 22,23
A	US 5 603 726 A (SCHULMAN ET AL) 18 February 1997 (1997-02-18) the whole document	17-24

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 February 2006	27/02/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Schoeffmann, H

3

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/037846

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-16
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
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00498

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2005/037846

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004045242 A	27-05-2004	AU 2003279513 A1	03-06-2004
US 6735475 B1	11-05-2004	NONE	
US 5697975 A	16-12-1997	US 5496369 A US 5800535 A	05-03-1996 01-09-1998
US 5603726 A	18-02-1997	NONE	

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00499

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 June 2006 (01.06.2006)

PCT

(10) International Publication Number
WO 2006/057734 A1

(51) International Patent Classification:
A61N 1/05 (2006.01) *A61N 1/36* (2006.01)

(21) International Application Number:
PCT/US2005/037736

(22) International Filing Date: 20 October 2005 (20.10.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/620,781 21 October 2004 (21.10.2004) US

(71) Applicant *(for all designated States except US)*: **ADVANCED NEUROMODULATION SYSTEMS, INC.** [US/US]; 6901 Preston Road, Plano, TX 75024 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **DE RIDDER, Dirk** [BE/BE]; Poelstraat 3, B-9060 Zelzate (BE).

(74) Agent: **ACOSTA, Melissa, W.**; Fulbright & Jaworski L.L.P., Fulbright Tower, 2200 Ross Avenue, Suite 2800, Dallas, TX 75201-2784 (US).

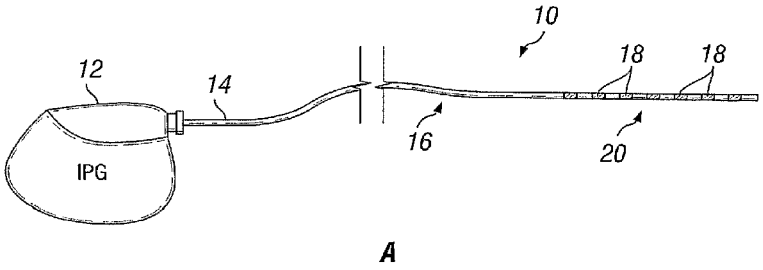
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

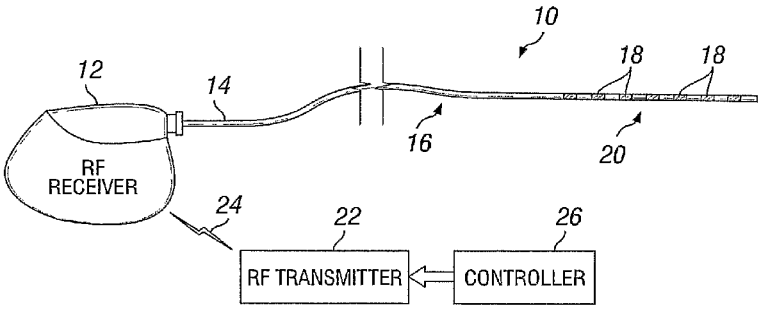
Published:
— *with international search report*

[Continued on next page]

(54) Title: NEW STIMULATION DESIGN FOR NEUROMODULATION



A



B

(57) Abstract: The stimulation system for treating a neurological disorder comprising: an implantable pulse generator that is programmable to generate a burst stimulus that comprises a plurality of groups of spike pulses, wherein the burst stimulus is substantially quiescent between the plurality of groups, wherein each spike within each group is separated by a minimum inter-group interval, wherein the maximum inter-spike interval is 5 milliseconds and the minimum inter-group interval is 20 milliseconds; and a medical lead for delivering the burst stimulus form the implantable pulse generator to a patient via one or several electrodes.

WO 2006/057734 A1

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

NEW STIMULATION DESIGN FOR NEUROMODULATION

RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 60/620,781 filed October 21, 2004 which is incorporated herein by reference in its entirety.

[0002] This application is also related to U.S. Provisional Application Nos. 60/620,762 filed, October 21, 2004, 60/631,085 filed November 24, 2004, 60/620,827 filed October 21, 2004, 60/631,091 filed November 24, 2004, 60/631,089 filed November 24, 2004, 60/620,847 filed October 21, 2004, and 60/638,365, filed December 27, 2004 each of which is incorporated by reference in its entirety.

TECHNICAL FIELD

[0003] The present application relates to a new stimulation system and method which can be utilized to treat neurological conditions and/or disorders.

BACKGROUND OF THE INVENTION

[0004] Different firing modes or frequencies occur in the brain and/or other neuronal tissue, for example tonic firing and burst firing (irregular or regular burst firing). Such firing modes can be utilized for normal processing of information, however, alteration of the firing modes, may also lead to pathology.

[0005] For example, certain neurological conditions are associated with hyperactivity of the brain and can be traced to a rhythmic burst firing or high frequency tonic firing (*e.g.*, tinnitus, pain, and epilepsy). Other conditions can be associated with an arrhythmic burst firing or a desynchronized form of tonic and burst firing (*e.g.*, movement disorders and hallucinations).

[0006] During the past decade, neuromodulation systems have been used to modulate various areas of the brain, spinal cord, or peripheral nerves (See, for example, U.S. Patent Nos. 6,671,555; 6,690,974). These types of systems utilize tonic forms of electrical stimulation. The disadvantage to these systems is that the neurological condition is related to a high frequency tonic rhythm or bursting type rhythm, it may be difficult for a second tonic stimulation to alter the diseased stimulation to actually result in treatment.

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[0007] Thus, the present invention is the first to describe a neuromodulation design or stimulation parameters in which the stimulation parameters produce burst stimulation to override or alter the pathological and/or physiological stimulation to treat a neurological condition.

BRIEF SUMMARY OF THE INVENTION

[0008] The present invention is directed to a method and/or system of stimulating nerve tissue of a patient using an implantable pulse generator. The method comprises generating, by the implantable pulse generator, a burst stimulus that comprises a plurality of groups of spike pulses, wherein the burst stimulus is substantially quiescent between the plurality of groups, wherein each spike within each group is separated by a maximum inter-spike interval and each group of spikes is separated by a minimum inter-group interval, wherein the maximum inter-spike interval is 100 milliseconds and the minimum inter-group interval is 5 seconds; providing the burst stimulus from the implantable pulse generator to a medical lead; and applying the burst stimulus to nerve tissue of the patient via one or several electrodes of the medical lead. More particularly, each spike in each group occurs from a plateau potential, which is controllable by a parameter stored in the implantable pulse generator..

[0009] In certain embodiments, the method of stimulating nerve tissue comprises controlling a number of spikes within a group of spikes of the burst stimulus according to a parameter stored in the implantable pulse generator. The pulse generator is also capable of controlling a spike amplitude according to a parameter stored in the implantable pulse generator. In certain embodiments, the method comprises an amplitude of the hyperpolarizing pulse is controllable by a parameter stored in the implantable pulse generator.

[0010] Yet further, the method of stimulating nerve tissue comprises controlling an inter-spike interval according to a parameter stored in the implantable pulse generator and/or controlling an inter-group interval according to a parameter stored in the implantable pulse generator and/or controlling a number of groups within the burst stimulus according to a parameter stored in the implantable pulse generator.

[0011] In another embodiment, the method further comprises detecting, by the implantable pulse generator, hyperactivity within neural tissue using a sensor in the implantable

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pulse generator, wherein the generating the burst stimulus occurs in response to the detecting. The sensor is coupled to one or several electrodes of the medical lead.

[0012] The present invention is directed to a method and a system of neuromodulation by providing a burst mode stimulus to either central or peripheral neuronal tissue in which the burst mode stimulus alters the activity of the neuronal tissue. It is envisioned that this method of neuromodulation can be used to treat various neurological disorders or neurologically mediated disorders. Stimulation can be in the form of electrical and/or chemical stimulation. In certain embodiments, the invention uses electrical stimulation and/or chemical stimulation (*e.g.,* one or more pharmaceuticals) to treat the neurological condition. In addition to electrical and/or chemical stimulation, magnetic stimulation and/or thermal as well as sound stimulation can also be used. Magnetic stimulation can be provided by internally implanted probes or by externally applied directed magnetic fields. Thermal stimulation can be provided by using implanted probes that are regulated to produce or emit heat and/or cold temperatures.

[0013] In certain embodiments, the present invention comprises a therapeutic stimulation system for treating neurological conditions or disorders having a surgically implanted device in communication with a predetermined site, which can be either a central neuronal or peripheral neuronal tissue site. The device can include an electrode, for example an electrode assembly or electrical stimulation lead. The electrode is coupled to a signal source (e.g., an electrical signal source), which, in turn, is operated to stimulate the predetermined site.

[0014] In certain embodiments, it is envisioned that the present invention comprises a method of treating a neurological disorder comprising the step of providing an electrical burst stimulus to a predetermined neuronal tissue site whereby the stimulus alters neuronal activity thereby treating the disorder.

[0015] The burst stimulus comprises a frequency in the range of about 1 Hz to about 300 Hz, more particular, in the range of about 1 Hz to about 18 Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4 Hz to about 7 Hz or about 8 Hz to about 12 Hz, 18 Hz to 20 Hz, and 40 Hz. The burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 2 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 50 to 1000Hz, more preferably in a range of 200 to 500Hz. The interval between spikes (e.g., inter-spike interval) can be about 0.5 milliseconds to about 100 milliseconds. Preferably, the maximum inter-spike interval is 5

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milliseconds. The frequency of the spikes within the burst does not need to be constant or regular, in fact, typically, the frequency of the spikes is random or variable.

[0016] In further embodiments, the burst stimulus is followed by an inter-burst interval or inter-group interval. The inter-burst interval has duration in the range of about 5 milliseconds to about 5 seconds, more preferably, about 10 milliseconds to about 300 milliseconds. Preferably, the minimum inter-group interval is 20 milliseconds. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particular, in the range of about 250 msec to 1000 msec (1-4 Hz burst firing), 145 msec to about 250 msec (4-7 Hz,), 145 msec to about 80 msec (8-12 Hz) or 1 to 5 seconds in plateau potential firing. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (*e.g.,* random or irregular harmonics).

[0017] In certain embodiments, the neuromodulation method can be used to treat neurological disorders or diseases that result from incorrect central nervous system control in which the disorder comprises a regular bursting rhythm. Such disorders having a regular bursting rhythm include, but are not limited to movement disorders such as Parkinson's Disease, epilepsy, tinnitus, central pain including phantom pain or other forms of deafferentation or central pain.

[0018] Still further, the neuromodulation method of the present invention can be used to treat neurological disorders or diseases that result from incorrect central nervous system control in which the disorder comprises an irregular bursting rhythm. Such disorders can include, but are not limited to dystonia or chorea. Still further, the neuromodulation method of the present invention can be used to treat neurological disorders or diseases that result from incorrect central nervous system control, and in which the methods corrects neuronal inbalances (inhibitory vs excitatory, high frequency vs low frequency (e.g., thalamocortical dysrhythmia), sympathetic vs parasympathetic).

[0019] The neuromodulation method of the present invention can also be used to alter a physiological and/or pathological signaling pattern. Those of skill in the art are aware that a physiological and/or pathological signaling pattern can be either regular or irregular. Thus, it is envisioned that the stimulation method as used herein can alter such patterns to alleviate the neurological condition or disease.

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[0020] The neuromodulation method of the present invention can be used to modulate neuronal activity of any neuronal tissue within a patient. In certain embodiments, a device is surgically implanted in the patient such that the device is in communication with a predetermined neuronal tissue site, and the device is operated to stimulate the predetermined site. The device can include a probe, for example, electrode assembly (*e.g.,* electrical stimulation lead). The proximal end of the probe is coupled to an electrical signal source, which, in turn, is operated to stimulate the predetermined treatment site.

[0021] Neuronal tissue includes any tissue associated with the peripheral nervous system or the central nervous system. Peripheral neuronal tissue can include a nerve root, root ganglion or other nerves, for example the median nerve, sympathetic nerve or vagal nerve, etc. Central neuronal tissue includes brain tissue, spinal tissue or brainstem tissue. Brain tissue can include thalamus/sub-thalamus, basal ganglia, hippocampus, amygdala, hypothalamus, mammilary bodies, substantia nigra or cortex or white matter tracts afferent to or efferent from the abovementioned brain tissue, inclusive of the corpus callosum. Spinal tissue can include the ascending and descending tracts of the spinal cord, more specifically, the ascending tracts of the spinal cord that comprise intralaminar neurons or the dorsal column. The brainstem tissue can include the medulla oblongata, pons or mesencephalon, more particular the posterior pons or posterior mesencephalon, Lushka's foramen, and ventrolateral part of the medulla oblongata.

[0022] The foregoing has outlined rather broadly the features and technical advantages of the present invention in order that the detailed description of the invention that follows may be better understood. Additional features and advantages of the invention will be described hereinafter which form the subject of the claims of the invention. It should be appreciated that the conception and specific embodiment disclosed may be readily utilized as a basis for modifying or designing other structures for carrying out the same purposes of the present invention. It should also be realized that such equivalent constructions do not depart from the invention as set forth in the appended claims. The novel features which are believed to be characteristic of the invention, both as to its organization and method of operation, together with further objects and advantages will be better understood from the following description when considered in connection with the accompanying figures. It is to be expressly understood, however, that each of the figures is provided for the purpose of illustration and description only and is not intended as a definition of the limits of the present invention.

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BRIEF DESCRIPTION OF THE DRAWINGS

[0023] For a more complete understanding of the present invention, reference is now made to the following descriptions taken in conjunction with the accompanying drawing, in which:

[0024] FIGURES 1A-1B illustrate example stimulation systems for electrically stimulating neuronal tissue.

[0025] FIGURES 2A-2I illustrate example electrical stimulation leads that may be used to electrically stimulate neuronal tissue.

[0026] FIGURES 3A-3B illustrate example neuronal firings. FIGURE 3A illustrates an example of regular neuronal firing. FIGURE 3B illustrates an example of a neuronal burst firing.

[0027] FIGURE 4A-4B illustrate examples of burst firing. FIGURE 4A illustrate an example of an regular burst firing pattern. FIGURE 4B illustrate an example of a irregular burst firing pattern.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

[0028] Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. For purposes of the present invention, the following terms are defined below.

[0029] As used herein, the use of the word "a" or "an" when used in conjunction with the term "comprising" in the claims and/or the specification may mean "one," but it is also consistent with the meaning of "one or more," "at least one," and "one or more than one." Still further, the terms "having", "including", "containing" and "comprising" are interchangeable and one of skill in the art is cognizant that these terms are open ended terms.

[0030] As used herein, the term "in communication" refers to the stimulation lead being adjacent, in the general vicinity, in close proximity, or directly next to or directly on the predetermined stimulation site. Thus, one of skill in the art understands that the lead is "in communication" with the predetermined site if the stimulation results in a modulation of

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neuronal activity. The predetermined site may be selected from the group consisting of the peripheral neuronal tissue or central neuronal tissue. Central neuronal tissue includes, but is not limited to brain tissue, brainstem, spinal tissue. Spinal tissue includes, the spinal cord, or the dorsal column of the spinal cord which may include the spinal cord area corresponding to cervical vertebral segments C1 to C8, thoracic vertebral segments T1 to T12, lumbar vertebral segments L1 and L2. One of ordinary skill in the art will understand that the spinal cord normally terminates at the second lumbar vertebrae L2. However, in certain subjects the spinal cord may terminate before or after the L2 vertebrae segment and that the present invention is intended for use along the entire length of the spinal cord.

[0031] As used herein, the use of the term "dorsal column" refers to conducting pathways in the spinal cord that are located in the dorsal portion of the spinal cord between the posterior horns, and which comprises afferent somatosensory neurons. The dorsal column is also known as the posterior funiculus.

[0032] As used herein, the use of the words "epidural space" or "spinal epidural space" is known to one with skill in the art, and refers to an area in the interval between the dural sheath and the wall of the spinal canal.

[0033] As used herein the term "modulate" refers to the ability to regulate positively or negatively neuronal activity. Thus, the term modulate can be used to refer to an increase, decrease, masking, altering, overriding or restoring of neuronal activity.

[0034] As used herein, the term "burst firing" or "burst mode" refers to an action potential that is a burst of high frequency spikes (300 – 1000 Hz) (Beurrier *et al.,* 1999). Burst firing acts in a non-linear fashion with a summation effect of each spike. One skilled in the art is also aware that burst firing can also be referred to as phasic firing, rhythmic firing (Lee 2001), pulse train firing, oscillatory firing and spike train firing, all of these terms used herein are interchangeable.

[0035] As used herein, the term "tonic firing" or "tonic mode" refers to an action potential that occurs in a linear fashion.

[0036] As used herein, the term "burst" refers to a period in a spike train that has a much higher discharge rate than surrounding periods in the spike train (N. Urbain et al., 2002). Thus, burst can refer to a plurality of groups of spike pulses. A burst is a train of action

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potentials that, possibly, occurs during a 'plateau' or 'active phase', followed by a period of relative quiescence called the 'silent phase' (Nunemaker, Cellscience Reviews Vol 2 No.1, 2005.) Thus, a burst comprises spikes having an inter-spike interval in which the spikes are separated by 0.5 milliseconds to about 100 milliseconds. Those of skill in the art realize that the inter-spike interval can be longer or shorter. Yet further, those of skill in the art also realize that the spike rate within the burst does not necessarily occur at a fixed rate; this rate can be variable.

[0037] As used herein, the term "spike" refers to an action potential. Yet further, a "burst spike" refers to a spike that is preceded or followed by another spike within a short time interval (Matveev, 2000), in otherwords, there is an inter-spike interval, in which this interval is generally about 100 ms but can be shorter or longer, for example 0.5 milliseconds.

[0038] As used herein, the term "neuronal" refers to a cell which is a morphologic and functional unit of the brain, brainstem, spinal cord, and peripheral nerves.

[0039] As used herein, the term "peripheral neuronal tissue" refers to any neuronal tissue associated with a nerve root, root ganglion, or peripheral nerve that is outside the brain and the spinal cord. It includes the autonomous nervous system, inclusive of (ortho-)sympathetic and parasympathetic system.

[0040] As used herein, the term "central neuronal tissue" refers to neuronal tissue associated with the brain, spinal cord or brainstem.

[0041] As used herein, the term "neurology" or "neurological" refers to conditions, disorders, and/or diseases that are associated with the nervous system. The nervous system comprises two components, the central nervous system, which is composed of the brain and the spinal cord, and the peripheral nervous system, which is composed of ganglia and the peripheral nerves that lie outside the brain and the spinal cord. One of skill in the art realizes that the nervous system may be linguistically separated and categorized, but functionally the system is interconnected and interactive. Yet further, the peripheral nervous system is divided into the autonomic system (parasympathetic and sympathetic), the somatic system and the enteric system. Thus, any condition, disorder and/or disease that effect any component or aspect of the nervous system (either central or peripheral) are referred to as a neurological condition, disorder and/or disease. As used herein, the term "neurological" or "neurology" encompasses the terms "neuropsychiatric" or "neuropsychiatry" and "neuropsychological" or "neuropsychology". Thus,

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a neurological disease, condition, or disorder includes, but is not limited to tinnitus, epilepsy, depression, anxiety, Parkinson's Disease, autonomic dysfunctions, etc.

[0042] As used herein, the term "neuropsychiatry" or "neuropsychiatric" refers to conditions, disorders and/or diseases that relate to both organic and psychic disorders of the nervous system.

[0043] As used herein, the term "neuropsychological" or "neuropsychologic" or neuropsychology refers to conditions, disorders and/or disease that relate to the functioning of the brain and the cognitive processors or behavior.

[0044] As used herein, "spinal cord," "spinal nervous tissue associated with a vertebral segment," "nervous tissue associated with a vertebral segment" or "spinal cord associated with a vertebral segment or level" includes any spinal nervous tissue associated with a vertebral level or segment. Those of skill in the art are aware that the spinal cord and tissue associated therewith are associated with cervical, thoracic and lumbar vertebrae. As used herein, C1 refers to cervical vertebral segment 1, C2 refers to cervical vertebral segment 2, and so on. T1 refers to thoracic vertebral segment 1, T2 refers to thoracic vertebral segment 2, and so on. L1 refers to lumbar vertebral segment 1, L2 refers to lumbar vertebral segment 2, and so on, unless otherwise specifically noted. In certain cases, spinal cord nerve roots leave the bony spine at a vertebral level different from the vertebral segment with which the root is associated. For example, the T11 nerve root leaves the spinal cord myelum at an area located behind vertebral body T8-T9 but leaves the bony spine between T11 and T12.

[0045] As used herein, the term "stimulate" or "stimulation" refers to electrical, chemical, magnetic, thermal and/or other such stimulation that modulates the predetermined neuronal sites.

[0046] As used herein, the term "treating" and "treatment" refers to modulating predetermined neuronal sites (central neuronal tissue and/or peripheral neuronal tissue) so that the subject has an improvement in the disease or condition, for example, beneficial or desired clinical results. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (*e.g.*, not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or

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undetectable. One of skill in the art realizes that a treatment may improve the disease condition, but may not be a complete cure for the disease.

II. Nervous System

[0047] The nervous system comprises two general components, the central nervous system, which is composed of the brain and the spinal cord, and the peripheral nervous system, which is composed of ganglia or dorsal root ganglia and the peripheral nerves that lie outside the brain and the spinal cord. One of skill in the art realizes that the nervous system may be linguistically separated and categorized, but functionally they are interconnected and interactive.

[0048] The central nervous system comprises the brain and spinal cord, which together function as the principal integrator of sensory input and motor output. In general terms, the brain consists of the cerebrum (cerebral hemispheres and the diencephalons), the brainstem (midbrain, pons, and medulla); and the cerebellum. It is well known that the cerebrum represents the highest center for sensory and motor and emotional and cognitive processing. In general, the frontal lobe processes motor, visual, speech, and personality modalities; the parietal lobe processes sensory information; the temporal lobe, auditory and memory modalities; and the occipital lobe vision. The cerebellum, in general, coordinates smooth motor activities and processes muscle position, while the brainstem conveys motor and sensory information and mediates important autonomic functions. These structures are of course integrated with the spinal cord which receives sensory input from the body and conveys somatic and autonomic motor information to peripheral targets. Thus, one of skill in the art realizes that the central nervous system is capable of evaluating incoming information and formulating response to changes that threaten the homeostasis of the individual.

[0049] The peripheral nervous system is divided into the autonomic system (parasympathetic and sympathetic), the somatic system and the enteric system. The term peripheral nerve is intended to include both motor and sensory neurons and neuronal bundles of the autonomic system, the somatic system, and the enteric system that reside outside of the spinal cord and the brain. Peripheral nerve ganglia and nerves located outside of the brain and spinal cord are also described by the term peripheral nerve.

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A. Action Potentials and Their Propagation

[0050] Information is conveyed through the nervous system via neuronal cells along their membranes and across synaptic junctions. Thus, the neuronal cells process information by both passive processes (*e.g.,* electrical properties of the membrane which enable spatial and temporal summation) and active processes (*e.g.,* propagation of the action potential, signal amplification or attenuation, and synaptic transmission). Generation of an action potential at the axon initial segment requires passive summation of multiple inputs, as well as signal amplification before membrane depolarization reaches threshold, thus the passive and active processes are interdependent.

[0051] The generation of the action potential initially depends upon the electrical properties of the cell. It is known that cells have an electrical voltage difference across their membranes, the membrane potential. Several types of protein pores or ion channels are responsible for maintaining and altering the membrane potential of the cell. Voltage-gated sodium channels, which have a low threshold, are responsible for the explosive depolarization of the membrane potential that forms the action potential or spike, whereas, the voltage-gated potassium channels are responsible for the repolarization of the membrane potential. For excitation, stimulatory input results in a net increase in the inward flow of sodium ions compared to an outward flow of potassium ions results in a depolarizing cell membrane potential change. For inhibitory inputs, potassium and chloride ion channels are opened which drives the membrane potential away from threshold (hyperpolarization). As one of skill in the art realizes neurons receive multiple excitatory and inhibitory inputs, thus summation of these inputs occurs, for example temporal and spatial summation. Temporal summation occurs when a series of subthreshold impulses in one excitatory fiber produces an action potential in postsynaptic cell. Spatial summation occurs when subthreshold impulses from two or more different fibers trigger an action potential.

[0052] Once the initial action potential is generated, the information is conveyed via axonal conduction or synaptic transmission (*e.g.,* chemical or electrical). Electrical synapses are found not only in the brain, but in heart and smooth muscle and epithelial liver cells. However, in the brain, electrical synapses (also known as gap junctions) are less common than chemical synapses, and are characterized by rapid speed of transmission and do not readily allow inhibitory actions or long-lasting changes in effectiveness. Gap junctions allow the passage of not only ions, but other small molecules. In humans, astrocytes contain gap junctions to mediate

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potassium buffering, and they are also present in the retina, inferior olive, vestibular nuclei, nucleus of the trigeminal nerve, and the reticular nucleus of the thalamus.

[0053] Chemical synapses, on the contrary, do mediate either excitatory or inhibitory actions, and are generally considered more flexible. Another difference between chemical and electrical transmission is that electrical can be bidirectional since the ion channels connect the cytoplasm of the pre and postsynaptic cells, whereas chemical transmission is typically unidirectional since there is no continuity between the cells. Chemical synapses comprise a presynaptic element that contain vesicles comprising neurotransmitters and a postsynaptic element which contains receptors for the neurotransmitters. Transmitter release is initiated when the nerve terminal is depolarized by an action potential resulting in a rapid influx of calcium ions into the nerve terminal. This rapid influx of calcium ions cause fusion of the vesicles to the presynaptic membrane and ultimately release of the neurotransmitters which then bind to their receptor located on the postsynaptic membrane.

[0054] The ability of the neuronal cell to fire or produce action potentials may vary depending upon its biophysical properties (*e.g.,* types of ionic channels, etc.) and/or its position in the circuit or nervous system. Thus, cells can respond to an input (stimulatory or inhibitory) with a decelerating train of action potentials, an accelerating train of action potentials or a constant firing frequency. For example, an increase in firing of a neuronal cell may be a result from increased amounts of calcium ions or a function of residual increase in calcium ions left over from the first stimulation (also known as facilitation) in the presynaptic element which results in increase release of neurotransmitter. Thus, a second stimulation can occur within milliseconds of the first. Conversely, a second stimulation may result in inhibition and not facilitation of the response if an inhibitory interneuron is activated which feedback to the first neuronal cell to inhibit firing.

B. Firing Modes

[0055] Different firing modes or frequencies occur in the brain and/or other neuronal tissue, for example tonic firing and burst firing (irregular or regular burst firing), as shown in FIGURES 3 and 4. The thalamus utilizes both types of firing modes. The two thalami (bilateral paired structures) are the gateways to the cerebral cortex and, thus, to consciousness. The thalamic nuclei specialize in several different signaling functions: transmitting signals from sensory input to the cortex; transmitting signals from cortical motor centers to effectors;

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transmitting control signals that select which input and output will be permitted to pass to and from the cortex and how the signals will be sequenced (thalamic reticular nuclei (TRN)); and modulating (controlling intensity) and synchronizing (grouping) the signals (Intralaminar Nuclei (ILN)).

[0056] All thalamic relay neurons pass through the TRN, which opens and closes their "gates" going to the cortex, (McAlonan and Brown, 2002). One mode that TRN neurons use to transmit these relays is burst firing mode. This mode is useful for activating a small population of neurons in the cortex for a short period. In contrast, the continuous (tonic) firing mode permits a thalamic neuron to transmit a steady stream of signals to the cortex. The tonic firing pattern triggers looping activation in the cortical circuits that receive the signals. Evoking looping, or "recurrent" activation in the cortex requires a steady neural input.

[0057] The ILN are a tiny cluster of cells in the central body of the thalamus, hidden inside of the "laminae," the white layers that separate the bigger nuclei of the thalamus. In contrast to the bigger relay nuclei, most of the ILN send signals that change the activity of the cortical receiving area (Sherman and Guillery, 2002). For example, an ILN might receive signals from one cortical area and send them on to several other cortical areas to increase excitation in the receiving areas (a cortico-thalamo-cortical pattern, C-T-C).

[0058] Tonic or burst firing mode may be related to the molecules which are associated with the neurons. Such molecules include either parvalbumin (an egg-derived protein also a calcium-binding protein) or calbindin (a calcium-binding protein). Tonic firing is found especially in cells that contain parvalbumin. It behaves in a linear fashion, for example, the auditory thalamus (MGBV) fires at a specific frequency and the auditory cortex will follow at the same pace with a minor phase difference (Miller *et al.,* 2001) of 2 ms. Tonic firing, however, can be overruled by burst firing (Lisman 1997; Sherman 2001; Swadlow and Gusev 2001).

[0059] Burst firing is typically found in calbindin positive cells (Kawaguchi and Kubota 1993; Hu *et al.,* 1994; Hu 1995; He and Hu 2002). Thus, burst mode firing may utilize a calbindin system to generate the burst. Generally, burst firing is accomplished through the activation of either a subthreshold membrane conductance that initiates action potentials or a suprathreshold membrane conductance that once activated evokes two or more action potentials. Sodium (Na^{+}) and calcium (Ca^{2+}) activated conductances have all been implicated in burst generation. Hippocampal (Wong and Stewart, 1992; Traub *et al.*, 1994) and layer V neocortical

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(Schwindt and Crill, 1999) pyramidal cells may initiate somatic Na^+ action potentials from a slow Ca^{2+} potential generated within the dendrites. Alternatively, bursts in subicular (Mattia *et al.,* 1997) and sensorimotor cortical neurons (Franceschetti *et al.*, 1995; Guatteo *et al.,* 1996) may be generated through a voltage-dependent Na^+ conductance, independent of Ca^{2+} (Brumberg, 2000).

[0060] Burst firing acts in a non-linear fashion (Lisman 1997; Sherman 2001; Swadlow and Gusev 2001) with a summation effect of each spike, thus more readily activating a target cell (Lisman 1997) than tonic firing. Burst firing has been described in drowsiness, slow wave sleep, and anesthesia (Steriade *et al.,* 1989; McCormick and Feeser 1990), as well as epilepsy (Futatsugi and Riviello 1998; Huguenard 1999) in the thalamus, and it functionally shuts off external auditory sensory stimuli to gain access to the cortex (Edeline *et al.,* 2000; Massaux and Edeline 2003; Massaux *et al.,* 2004), though not completely (Edeline *et al.,* 2000). Neural network modeling has further demonstrated that bursts are generated by positive feedback through excitatory connections (Tabak and Latham 2003). In networks of two populations, one excitatory and one inhibitory, decreasing the inhibitory feedback can cause the network to switch from a tonically active, asynchronous state to the synchronized bursting state (van Vreeswijk and Hansel 2001).

[0061] The generation of repetitive burst discharges in neurons is correlated with the generation of gamma frequency (30–70 Hz) oscillations in the local field potential (Gray and Singer, 1989). It is believed that conscious perception depends on gamma band frequency activity (Gray and Singer, 1989; Joliot, 1994; Steriade, 2000).

[0062] Increasing depolarization to hyperpolarization induces a prolonged refractory period of tonic firing resulting in single spike bursts (Ramcharan, Cox *et al.,* 2000) (in the visual system), further depolarization results in progressively more spikes per burst (Ramcharan, Cox *et al.,* 2000). Further depolarization will silence the cell (Beurrier, Congar *et al.,* 1999).

[0063] The transient membrane hyperpolarization leads to activation of voltage dependent T type calcium channels generating low threshold calcium spikes. Riding on top of the low thresholds calcium spikes are bursts of sodium spikes mediated by fast voltage-gated sodium channels (Steriade and Llinas 1988). Calcium entry during the burst leads to calcium activated potassium channels then in combination with voltage gated potassium channels the

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membrane is repolarized (McCormick and Feeser 1990). The low threshold calcium spikes act as a pacemaker (Perez-Reyes 2003).

[0064] It is hypothesized according to the present invention that burst stimulation may be used by neuronal tissue to process information in a manner that is similar to amplitude modulation. Specifically, the spacing between individual bursts in a burst stimulus may be used to signal information to various regions in the brain. That is, the spacing between the bursts can vary (hence are "amplitude modulated") to convey information. The signaled information can be related to relevance information. The signaled information could also be related to signaling the beginning and ending of certain packets of information. By providing electrical burst stimulation from an implantable pulse generator, it is possible that the stimulated brain tissue will change its processing of other stimulus information. For example, by appropriately selecting an interburst interval, auditory information that would otherwise be problematic to a patient could become ignored by a respective segment of the brain due to a lack of "relevance" and/or a lack of synchronization with the arrival of the burst stimulus.

III. Electrical Stimulation Devices

[0065] FIGURES 1A-1B illustrate example neurological stimulation systems 10 for electrically stimulating a predetermined site area to treat one or more neurological disorders or conditions. In general terms, stimulation system 10 includes an implantable pulse generating source or electrical stimulation source 12 and one or more implantable electrodes or electrical stimulation leads 14 for applying electrical stimulation pulses to the a predetermined site. In operation, both of these primary components are implanted in the person's body, as discussed below. In certain embodiments, stimulation source 12 is coupled directly to a connecting portion 16 of stimulation lead 14. In certain other embodiments, stimulation source 12 is incorporated into the stimulation lead 14 and stimulation source 12 instead is embedded within stimulation lead 14. For example, such a stimulation system 10 may be a Bion® stimulation system manufactured by Advanced Bionics Corporation. Whether stimulation source 12 is coupled directly to or embedded within the stimulation lead 14, stimulation source 12 controls the stimulation pulses transmitted to one or more stimulation electrodes 18 located on a stimulating portion 20 of stimulation lead 14, positioned in communication with a predetermined site, according to suitable stimulation parameters (*e.g.,* duration, amplitude or intensity, frequency, pulse width, *etc.*).

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[0066] As contemplated in the present invention, a predetermined site can include either peripheral neuronal tissue and/or central neuronal tissue. Neuronal tissue includes any tissue associated with the peripheral nervous system or the central nervous system. Peripheral neuronal tissue can include a nerve root or root ganglion or any neuronal tissue that lies outside the brain, brainstem or spinal cord. Peripheral nerves can include, but are not limited to olfactory nerve, optic, nerve, oculomotor nerve, trochlear nerve, trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear (auditory) nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, hypoglossal nerve, suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, brachial plexus, radial axillary nerves, musculocutaneous nerves, radial nerves, ulnar nerves, median nerves, intercostal nerves, lumbosacral plexus, sciatic nerves, common peroneal nerve, tibial nerves, sural nerves, femoral nerves, gluteal nerves, thoracic spinal nerves, obturator nerves, digital nerves, pudendal nerves, plantar nerves, saphenous nerves, ilioinguinal nerves, gentofemoral nerves, and iliohypogastric nerves.

[0067] Central neuronal tissue includes brain tissue, spinal tissue or brainstem tissue. Brain tissue can include thalamus/sub-thalamus, basal ganglia, hippocampus, amygdala, hypothalamus, mammilary bodies, substantia nigra or cortex or white matter tracts afferent to or efferent from the abovementioned brain tissue, inclusive of the corpus callosum. Spinal tissue can include the ascending and descending tracts of the spinal cord, more specifically, the ascending tracts of that comprise intralaminar neurons or the dorsal column. The brainstem tissue can include the medulla oblongata, pons or mesencephalon, more particular the posterior pons or posterior mesencephalon, Lushka's foramen, and ventrolateral part of the medulla oblongata.

[0068] A doctor, the patient, or another user of stimulation source 12 may directly or indirectly input stimulation parameters to specify or modify the nature of the stimulation provided.

[0069] In one embodiment, as shown in FIG. 1A, stimulation source 12 includes an implantable pulse generator (IPG). One of skill in the art is aware that any commercially available implantable pulse generator can be used in the present invention, as well as a modified version of any commercially available pulse generator. Thus, one of skill in the art would be able to modify an IPG to achieve the desired results. An exemplary IPG is one that is

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manufactured by Advanced Neuromodulation Systems, Inc., such as the Genesis® System, part numbers 3604, 3608, 3609, and 3644. Another example of an IPG is shown in FIGURE 1B, which shows stimulation source 12 including an implantable wireless receiver. An example of a wireless receiver may be one manufactured by Advanced Neuromodulation Systems, Inc., such as the Renew® System, part numbers 3408 and 3416. In another embodiment, the IPG can be optimized for high frequency operation as described in U.S. Provisional Application Serial No. 60/685,036, filed May 26, 2005, entitled "SYSTEMS AND METHODS FOR USE IN PULSE GENERATION," which is incorporated herein by reference. The wireless receiver is capable of receiving wireless signals from a wireless transmitter 22 located external to the person's body. The wireless signals are represented in FIG. 1B by wireless link symbol 24. A doctor, the patient, or another user of stimulation source 12 may use a controller 26 located external to the person's body to provide control signals for operation of stimulation source 12. Controller 26 provides the control signals to wireless transmitter 22, wireless transmitter 22 transmits the control signals and power to the wireless receiver of stimulation source 12, and stimulation source 12 uses the control signals to vary the signal parameters of electrical signals transmitted through electrical stimulation lead 14 to the stimulation site. Thus, the external controller 26 can be for example, a handheld programmer, to provide a means for programming the IPG. An example wireless transmitter 122 may be one manufactured by Advanced Neuromodulation Systems, Inc., such as the Renew® System, part numbers 3508 and 3516.

[0070] Conventional neuromodulation devices can be modified to apply burst stimulation to nerve tissue of a patient by modifying the software instructions stored in the devices. Specifically, conventional neuromodulation devices typically include a microprocessor and a pulse generation module. The pulse generation module generates the electrical pulses according to a defined pulse width and pulse amplitude and applies the electrical pulses to defined electrodes. The microprocessor controls the operations of the pulse generation module according to software instructions stored in the device.

[0071] These conventional neuromodulation devices can be adapted by programming the microprocessor to deliver a number of spikes (relatively short pulse width pulses) that are separated by an appropriate interspike interval. Thereafter, the programming of the microprocessor causes the pulse generation module to cease pulse generation operations for an interburst interval. The programming of the microprocessor also causes a repetition of the spike generation and cessation of operations for a predetermined number of times. After the

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predetermined number of repetitions have been completed, the microprocessor can cause burst stimulation to cease for an amount of time (and resume thereafter). Also, in some embodiments, the microprocessor could be programmed to cause the pulse generation module to deliver a hyperpolarizing pulse before the first spike of each group of multiple spikes.

[0072] The microprocessor can be programmed to allow the various characteristics of the burst stimulus to be set by a physician to allow the burst stimulus to be optimized for a particular pathology of a patient. For example, the spike amplitude, the interspike interval, the interburst interval, the number of bursts to be repeated in succession, the amplitude of the hyperpolarizing pulse, and other such characteristics could be controlled using respective parameters accessed by the microprocessor during burst stimulus operations. These parameters could be set to desired values by an external programming device via wireless communication with the implantable neuromodulation device.

[0073] In another embodiment, a neuromodulation device can be implemented to apply burst stimulation using a digital signal processor and one or several digital-to-analog converters. The burst stimulus waveform could be defined in memory and applied to the digital-to-analog converter(s) for application through electrodes of the medical lead. The digital signal processor could scale the various portions of the waveform in amplitude and within the time domain (e.g., for the various intervals) according to the various burst parameters.

[0074] FIGURES 2A-2I illustrate example stimulation leads 14 that may be used for electrically stimulating the predetermined site to treat one or more neurological disorders or conditions. As described above, each of the one or more stimulation leads 14 incorporated in stimulation system 10 includes one or more stimulation electrodes 18 adapted to be positioned in communication with the predetermined site and used to deliver to the stimulation pulses received from stimulation source 12. A percutaneous stimulation lead 14, such as example stimulation leads 14a-d, includes one or more circumferential electrodes 18 spaced apart from one another along the length of stimulating portion 20 of stimulation lead 14. Circumferential electrodes 18 emit electrical stimulation energy generally radially (*e.g.,* generally perpendicular to the axis of stimulation lead 14) in all directions. A laminotomy, paddle, or surgical stimulation lead 14, such as example stimulation leads 14e-i, includes one or more directional stimulation electrodes 18 spaced apart from one another along one surface of stimulation lead 14. Directional stimulation electrodes 18 emit electrical stimulation energy in a direction generally perpendicular

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to the surface of stimulation lead 14 on which they are located. Although various types of stimulation leads 14 are shown as examples, the present invention contemplates stimulation system 10 including any suitable type of stimulation lead 14 in any suitable number. In addition, stimulation leads 14 may be used alone or in combination. For example, medial or unilateral stimulation of the predetermined site may be accomplished using a single electrical stimulation lead 14 implanted in communication with the predetermined site in one side of the head, while bilateral electrical stimulation of the predetermined site may be accomplished using two stimulation leads 14 implanted in communication with the predetermined site in opposite sides of the head.

[0075] In one embodiment, the stimulation source is transcutaneously in communication with the electrical stimulation lead. In "transcutaneous" electrical nerve stimulation (TENS), the stimulation source is external to the patient's body, and may be worn in an appropriate fanny pack or belt, and the electrical stimulation lead is in communication with the stimulation source, either remotely or directly. In another embodiment, the stimulation is percutaneous. In "percutaneous" electrical nerve stimulation (PENS), needles are inserted to an appropriate depth around or immediately adjacent to a predetermined stimulation site, and then stimulated.

[0076] In addition to electrical stimulation, other forms of stimulation can be used, for example magnetic. Magnetic stimulation can be provided by internally implanted probes or by externally applied directed magnetic fields, for example, U.S. Patent Nos. 6,592,509; 6,132,361; 5,752,911; and 6,425,852, each of which is incorporated herein in its entirety. Quick pulses of magnetic stimulation can be applied externally or transcranially, for example repetitive transcranially magnetic stimulation (rTMS).

[0077] Whether using percutaneous leads, laminotomy leads, or some combination of both, the leads are coupled to one or more conventional neurostimulation devices, or signal generators. The devices can be totally implanted systems and/or radio frequency (RF) systems. An example of an RF system is a MNT/MNR-916CC system manufactured by Advanced Neuromodulation Systems, Inc.

[0078] The preferred neurostimulation devices should allow each electrode of each lead to be defined as a positive, a negative, or a neutral polarity. For each electrode combination (*e.g.*, the defined polarity of at least two electrodes having at least one cathode and at least one

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anode), an electrical signal can have at least a definable amplitude (*e.g.,* voltage), pulse width, and frequency, where these variables may be independently adjusted to finely select the sensory transmitting nerve tissue required to inhibit transmission of neuronal signals. Generally, amplitudes, pulse widths, and frequencies are determinable by the capabilities of the neurostimulation systems, which are known by those of skill in the art. Voltages that may be used can include, for example about 0.5 to about 10 volts, more preferably about 1 to about 10 volts.

[0079] In the present invention, the stimulation parameter of signal frequencies are varied to achieve a burst type rhythm, or burst mode stimulation, as shown in FIGURE 3B. Generally, the burst stimulus frequency may be in the range of about 1 Hz to about 100 Hz, more particular, in the range of about 1 Hz to about 12Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4Hz to about 7Hz or about 8Hz to about 12Hz for each burst. One skilled in the art will further realize that each burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 2 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 50Hz to about 1000Hz, more particularly, in the range of about 200Hz to about 500Hz. One of skill in the art is aware that the frequency for each spike within a burst can be variable, thus it is not necessary for each spike to contain similar frequencies, e.g., the frequencies can vary in each spike. The inter-spike interval can be also vary, for example, the inter-spike interval, can be about 0.5 milliseconds to about 100 milliseconds or any range therebetween.

[0080] The burst stimulus can be followed by an inter-burst interval, as shown in FIGURES 4A-4B. The inter-burst interval has duration in the range of about 5 milliseconds to about 5 seconds, more preferably, 10 milliseconds to about 300 milliseconds. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particular, in the range of about 250 msec to 1000 msec (1-4 Hz burst firing), 145 msec to about 250 msec (4-7 Hz,), 145 msec to about 80 msec (8-12 Hz) or 1 to 5 seconds in plateau potential firing. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (*e.g.,* random or irregular harmonics), as shown in FIGURES 4A-4B. More specifically, the burst stimulus can have a physiological pattern or a pathological pattern.

[0081] It is envisaged that the patient will require intermittent assessment with regard to patterns of stimulation. Different electrodes on the lead can be selected by suitable

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computer programming, such as that described in U.S. Pat. No. 5,938,690, which is incorporated by reference here in full. Utilizing such a program allows an optimal stimulation pattern to be obtained at minimal voltages. This ensures a longer battery life for the implanted systems.

IV. Implantation of Electrical Devices

[0082] The stimulation system 10, described above, can be implanted into a person's body with stimulation lead 14 located in communication with a predetermined site. It is envisioned that the predetermined site can be a central or peripheral neuronal tissue.

A. Deep Brain Stimulation

[0083] In certain embodiments, for example, patients who are to have an electrical stimulation lead or electrode implanted into the brain, generally, first have a stereotactic head frame, such as the Leksell, CRW, or Compass, mounted to the patient's skull by fixed screws. However, frameless techniques may also be used. Subsequent to the mounting of the frame, the patient typically undergoes a series of magnetic resonance imaging sessions, during which a series of two dimensional slice images of the patient's brain are built up into a quasi- three dimensional map in virtual space. This map is then correlated to the three dimensional stereotactic frame of reference in the real surgical field. In order to align these two coordinate frames, both the instruments and the patient must be situated in correspondence to the virtual map. The current way to do this is to rigidly mount the head frame to the surgical table. Subsequently, a series of reference points are established to relative aspects of the frame and patient's skull, so that either a person or a computer software system can adjust and calculate the correlation between the real world of the patient's head and the virtual space model of the patient MRI scans. The surgeon is able to target any region within the stereotactic space of the brain with precision (*e.g.,* within 1 mm). Initial anatomical target localization is achieved either directly using the MRI images or functional imaging (PET or SPECTscan, fMRI, MSI), or indirectly using interactive anatomical atlas programs that map the atlas image onto the stereotactic image of the brain. As is described in greater detail elsewhere in this application, the anatomical targets or predetermined site may be stimulated directly or affected through stimulation in another region of the brain.

[0084] In preferred embodiments, the predetermined site or implant sites include, but are not limited to thalamus/sub-thalamus, basal ganglia, hippocampus, amygdala, hypothalamus, mammilary bodies, substantia nigra or cortex or white matter tracts afferent to or

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efferent from the abovementioned brain tissue, inclusive of the corpus callosum. Still further, the predetermined site may comprise the auditory cortex and/or somatosensory cortex in which the stimulation devices is implanted cortically.

[0085] Based upon the coordinates, the electrical stimulation lead 14 can be positioned in the brain. Typically, an insertion cannula for electrical stimulation lead 14 is inserted through the burr hole into the brain, but a cannula is not required. For example, a hollow needle may provide the cannula. The cannula and electrical stimulation lead 14 may be inserted together or lead 14 may be inserted through the cannula after the cannula has been inserted.

[0086] Once electrical stimulation lead 14 has been positioned in the brain, lead 14 is uncoupled from any stereotactic equipment present, and the cannula and stereotactic equipment are removed. Where stereotactic equipment is used, the cannula may be removed before, during, or after removal of the stereotactic equipment. Connecting portion 16 of electrical stimulation lead 14 is laid substantially flat along the skull. Where appropriate, any burr hole cover seated in the burr hole may be used to secure electrical stimulation lead 14 in position and possibly to help prevent leakage from the burr hole and entry of contaminants into the burr hole. Example burr hole covers that may be appropriate in certain embodiments are illustrated and described in co-pending U.S. Application Nos. 11/010,108 and 11/010,136, both filed December 10, 2004 and entitled "Electrical Stimulation System and Associated Apparatus for Securing an Electrical Stimulation Lead in Position in a Person's Brain", both of which are incorporated herein in their entirety.

[0087] Once electrical stimulation lead 14 has been inserted and secured, connecting portion 16 of lead 14 extends from the lead insertion site to the implant site at which stimulation source 12 is implanted. The implant site is typically a subcutaneous pocket formed to receive and house stimulation source 12. The implant site is usually positioned a distance away from the insertion site, such as near the chest, below the clavicle or alternatively near the buttocks or another place in the torso area. Once all appropriate components of stimulation system 10 are implanted, these components may be subject to mechanical forces and movement in response to movement of the person's body. A doctor, the patient, or another user of stimulation source 12 may directly or indirectly input signal parameters for controlling the nature of the electrical stimulation provided.

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[0088] Although example steps are illustrated and described, the present invention contemplates two or more steps taking place substantially simultaneously or in a different order. In addition, the present invention contemplates using methods with additional steps, fewer steps, or different steps, so long as the steps remain appropriate for implanting an example stimulation system 10 into a person for electrical stimulation of the person's brain.

B. Spinal and Peripheral Neuronal Tissue

[0089] Electrical energy can be delivered through electrodes positioned external to the dura layer surrounding the spinal cord. Stimulation on the surface of the cord (subdurally) is also contemplated, for example, stimulation may be applied to the dorsal columns as well as to the dorsal root entry zone or the dorsal root ganglia and/or nerve root. Any area of the spinal cord may be stimulated in the present invention for example the any neuronal tissue associated with any of the cervical vertebral segments (C1, C2, C3, C4, C5, C6, C7 and C8) and/or any tissue associated with any of the thoracic vertebral segments (T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, 12) and/or any tissue associated with any of the lumbar vertebral segments (L1, L2, L3, L4. L5, L6) and/or any tissue associated with the sacral vertebral segments (S1, S2, S3, S4, S5). Peripheral nerves can include, but are not limited to olfactory nerve, optic, nerve, oculomotor nerve, trochlear nerve, trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear (auditory) nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, hypoglossal nerve, suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, brachial plexus, radial axillary nerves, musculocutaneous nerves, radial nerves, ulnar nerves, median nerves, intercostal nerves, lumbosacral plexus, sciatic nerves, common peroneal nerve, tibial nerves, sural nerves, femoral nerves, gluteal nerves, thoracic spinal nerves, obturator nerves, digital nerves, pudendal nerves, plantar nerves, saphenous nerves, ilioinguinal nerves, gentofemoral nerves, and iliohypogastric nerves. In addition peripheral nerves also includes the nerves of the autonomic nervous system, including both sympathetic and parasympathetic system

[0090] Stimulation electrodes 18 may be positioned in various body tissues and in contact with various tissue layers; for example, subdural, subarachnoid, epidural, cutaneous, transcutaneous and subcutaneous implantation is employed in some embodiments. The electrodes are carried by two primary vehicles: a percutaneous leads and a laminotomy lead.

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[0091] In certain embodiments, one or more stimulation electrodes 18 are positioned in communication with a peripheral nerve. Stimulation electrodes 18 are commonly positioned in communication with the peripheral nerve by electrodes applied cutaneously to the dermatome area of a peripheral nerve. Stimulation electrodes 18 can be positioned subcutaneously in communication with the peripheral nerve or on the nerve root ganglion.

[0092] For spinal cord stimulation, percutaneous leads commonly have two or more, equally-spaced electrodes, which are placed above the dura layer through the use of a Touhy-like needle. For insertion, the Touhy-like needle is passed through the skin, between desired vertebrae, to open above the dura layer. For unilateral stimulation, percutaneous leads are positioned on a side of a spinal column corresponding to the "afflicted" side of the body, as discussed above, and for bilateral stimulation, a single percutaneous lead is positioned along the patient midline (or two or more leads are positioned on each side of the midline).

[0093] An example of an eight-electrode percutaneous lead is an OCTRODE® lead manufactured by Advanced Neuromodulation Systems, Inc. A stimulation system such as is described in US Patent numbers 6,748,276 is also contemplated.

[0094] Laminotomy leads have a paddle configuration and typically possess a plurality of electrodes (for example, two, four, eight, or sixteen) arranged in one or more columns. An example of a sixteen-electrode laminotomy lead is shown in FIG. 2.

[0095] Implanted laminotomy leads are commonly transversely centered over the physiological midline of a patient. In such position, multiple columns of electrodes are well suited to address both unilateral and bilateral stimulation requirements, where electrical energy may be administered using either column independently (on either side of the midline) or administered using both columns to create an electric field which traverses the midline. A multi-column laminotomy lead enables reliable positioning of a plurality of electrodes, and in particular, a plurality of electrode columns that do not readily deviate from an initial implantation position.

[0096] Laminotomy leads require a surgical procedure for implantation. The surgical procedure, or partial laminectomy, requires the resection and removal of certain vertebral tissue to allow both access to the dura and proper positioning of a laminotomy lead. The laminotomy lead offers a more stable platform, which is further capable of being sutured in

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place, that tends to migrate less in the operating environment of the human body. Unlike the needle-delivered percutaneous leads, laminotomy leads have a paddle configuration. The paddle typically possess a plurality of electrodes (for example, two, four, eight, or sixteen) arranged in some pattern, for example, columns. An example of an eight-electrode, two column laminotomy lead is a LAMITRODE® 44 lead manufactured by Advanced Neuromodulation Systems, Inc.

[0097] In the context of conventional spinal cord stimulation, the surgical procedure, or partial laminectomy, requires the resection and removal of certain vertebral tissue to allow both access to the dura and proper positioning of a laminotomy lead. Depending on the position of insertion, however, access to the dura may only require a partial removal of the ligamentum flavum at the insertion site.

[0098] If necessary, stimulation source 12 may be coupled directly to connecting portion 16 of stimulation lead 14. Alternatively, as described above and if necessary, stimulation source 12 may not be coupled directly to stimulation lead 14 and may instead be coupled to stimulation lead 14 via an appropriate wireless link. Of course, as those skilled in the art know, an embedded stimulation system will not need to be so coupled.

C. Brainstem Stimulation

[0099] The stimulation system 10, described above, can be implanted into a person's body with stimulation lead 14 located in communication with a predetermined brainstem tissue and/or area. Such systems that can be used are described in WO2004062470, which is incorporated herein by reference in its entirety.

[0100] The predetermined brainstem tissue can be selected from medulla oblongata, pons or mesencephalon, more particular the posterior pons or posterior mesencephalon, Lushka's foramen, and ventrolateral part of the medulla oblongata.

[0101] Implantation of a stimulation lead 14 in communication with the predetermined brainstem area can be accomplished via a variety of surgical techniques that are well known to those of skill in the art. For example, an electrical stimulation lead can be implanted on, in, or near the brainstem by accessing the brain tissue through a percutaneous route, an open craniotomy, or a burr hole. Where a burr hole is the means of accessing the brainstem, for example, stereotactic equipment suitable to aid in placement of an electrical

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stimulation lead 14 on, in, or near the brainstem may be positioned around the head. Another alternative technique can include, a modified midline or retrosigmoid posterior fossa technique.

[0102] In certain embodiments, electrical stimulation lead 14 is located at least partially within or below the aura mater adjacent the brainstem. Alternatively, a stimulation lead 14 can be placed in communication with the predetermined brainstem area by threading the stimulation lead up the spinal cord column, as described above, which is incorporated herein.

[0103] As described above, each of the one or more leads 14 incorporated in stimulation system 10 includes one or more electrodes 18 adapted to be positioned near the target brain tissue and used to deliver electrical stimulation energy to the target brain tissue in response to electrical signals received from stimulation source 12. A percutaneous lead 14 may include one or more circumferential electrodes 18 spaced apart from one another along the length of lead 14. Circumferential electrodes 18 emit electrical stimulation energy generally radially in all directions and may be inserted percutaneously or through a needle. The electrodes 18 of a percutaneous lead 14 may be arranged in configurations other than circumferentially, for example as in a "coated" lead 14. A laminotomy or paddle style lead 14, such as example leads 14e-i, includes one or more directional electrodes 18 spaced apart from one another along one surface of lead 14. Directional electrodes 18 emit electrical stimulation energy in a direction generally perpendicular to the surface of lead 14 on which they are located. Although various types of leads 14 are shown as examples, the present invention contemplates stimulation system 10 including any suitable type of lead 14 in any suitable number, including three-dimensional leads and matrix leads as described below. In addition, the leads may be used alone or in combination.

[0104] Yet further, a stimulation lead 14 can be implanted in communication with the predetermined brainstem area by a using stereotactic procedures similar to those described above, which are incorporated herein, for implantation via the cerebrum.

[0105] Still further, a predetermined brainstem area can be indirectly stimulated by implanting a stimulation lead 14 in communication with a cranial nerve (*e.g.,* olfactory nerve, optic, nerve, oculomoter nerve, trochlear nerve, trigeminal nerve, abducent nerve, facial nerve, vestibulocochlear nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, and the hypoglossal nerve) as well as high cervical nerves (cervical nerves have anastomoses with lower cranial nerves) such that stimulation of a cranial nerve indirectly stimulates the predetermined

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brainstem tissue. Such techniques are further described in US Patent Nos. 6,721,603; 6,622,047; and 5,335,657, and U.S. Provisional Application 60/591,195 entitled "Stimulation System and Method for Treating a Neurological Disorder" each of which are incorporated herein by reference.

[0106] Although example steps are illustrated and described, the present invention contemplates two or more steps taking place substantially simultaneously or in a different order. In addition, the present invention contemplates using methods with additional steps, fewer steps, or different steps, so long as the steps remain appropriate for implanting stimulation system 10 into a person for electrical stimulation of the predetermined site.

V. Infusion pumps

[0107] In further embodiments, it may be desirable to use a drug delivery system independently or in combination with electrical stimulation to result in the stimulation parameters of the present invention. Drug delivery may be used independent of or in combination with a lead/electrode to provide electrical stimulation and chemical stimulation. When used, the drug delivery catheter is implanted such that the proximal end of the catheter is coupled to a pump and a discharge portion for infusing a dosage of a pharmaceutical or drug. Implantation of the catheter can be achieved by combining data from a number of sources including CT, MRI or conventional and/or magnetic resonance angiography into the stereotactic targeting model. Thus, implantation of the catheter can be achieved using similar techniques as discussed above for implantation of electrical leads, which is incorporated herein. The distal portion of the catheter can have multiple orifices to maximize delivery of the pharmaceutical while minimizing mechanical occlusion. The proximal portion of the catheter can be connected directly to a pump or via a metal, plastic, or other hollow connector, to an extending catheter.

[0108] Any type of infusion pump can be used in the present invention. For example, "active pumping" devices or so-called peristaltic pumps are described in U.S. Pat. Nos. 4,692,147, 5,840,069, and 6,036,459, which are incorporated herein by reference in their entirety. Peristaltic pumps are used to provide a metered amount of a drug in response to an electronic pulse generated by control circuitry associated within the device. An example of a commercially available peristaltic pump is SynchroMed® implantable pump from Medtronic, Inc., Minneapolis, Minn.

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[0109] Other pumps that may be used in the present invention include accumulator-type pumps, for example certain external infusion pumps from Minimed, Inc., Northridge, Calif. and Infusaid® implantable pump from Strato/Infusaid, Inc., Norwood, Mass. Passive pumping mechanisms can be used to release an agent in a constant flow or intermittently or in a bolus release. Passive type pumps include, for example, but are not limited to gas-driven pumps described in U.S. Pat. Nos. 3,731,681 and 3,951,147; and drive-spring diaphragm pumps described in U.S. Pat. Nos. 4,772,263, 6,666,845, 6,620,151 all of which are incorporated by reference in their entirety. Pumps of this type are commercially available, for example, Model 3000® from Arrow International, Reading, Penn. and IsoMed® from Medtronic, Inc., Minneapolis, Minn.; AccuRx® pump from Advanced Neuromodulation Systems, Inc., Plano, TX.

[0110] In certain embodiments, the catheter can be in the form of a lead catheter combination, similar to the ones described in U.S. Patent 6,176,242 and U.S. Pat. No. 5,423,877, which are incorporated herein by reference in their entirety.

[0111] Still further, the present invention can comprise a chemical stimulation system that comprises a system to control release of neurotransmitters (*e.g.,* glutamate, acetylcholine, norepinephrine, epinephrine), chemicals (*e.g.,* zinc, magnesium, lithium) and/or pharmaceuticals that are known to alter the activity of neuronal tissue. For example, infusion formulation delivery system can utilize a control system having an input-response relationship. A sensor generates a sensor signal representative of a system parameter input (such as levels of neurotransmitters), and provides the sensor signal to a controller. The controller receives the sensor signal and generates commands that are communicated to the infusion formulation delivery device. The infusion formulation delivery device then delivers the infusion formulation output to the predetermined site at a determined rate and amount in order to control the system parameter.

[0112] Sensor may comprise a sensor, sensor electrical components for providing power to the sensor and generating the sensor signal, a sensor communication system for carrying the sensor signal to controller, and a sensor housing for enclosing the electrical components and the communication system. Controller may include one or more programmable processors, logic circuits, or other hardware, firmware or software components configured for implementing the control functions described herein, a controller communication system for

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receiving the sensor signal from the sensor, and a controller housing for enclosing the controller communication system and the one or more programmable processors, logic circuits, or other hardware, firmware or software components. The infusion formulation delivery device may include a suitable infusion pump, infusion pump electrical components for powering and activating the infusion pump, an infusion pump communication system for receiving commands from the controller, and an infusion pump housing for enclosing the infusion pump, infusion pump electrical components, and infusion pump communication system. Such systems are described in US Patent No. 6,740,072, which is incorporated herein by reference in its entirety.

[0113] In certain embodiments, the sensor can be an electrode that senses a hyperactive burst pattern of activity or tonic firing, which in turns stimulates the infusion pump to release a chemical or stimulating drug or agent to modify the neuronal activity. The chemical or stimulating agent can be either an inhibiting agent or stimulating agent

[0114] Herein, stimulating drugs comprise medications, anesthetic agents, synthetic or natural peptides or hormones, neurotransmitters, cytokines and other intracellular and intercellular chemical signals and messengers, other agents such as zinc and the like. In addition, certain neurotransmitters, hormones, and other drugs are excitatory for some tissues, yet are inhibitory to other tissues. Therefore, where, herein, a drug is referred to as an "excitatory" drug, this means that the drug is acting in an excitatory manner, although it may act in an inhibitory manner in other circumstances and/or locations. Similarly, where an "inhibitory" drug is mentioned, this drug is acting in an inhibitory manner, although in other circumstances and/or locations, it may be an "excitatory" drug. In addition, stimulation of an area herein includes stimulation of cell bodies and axons in the area.

[0115] Similarly, excitatory neurotransmitter agonists (*e.g.,* norepinephrine, epinephrine, glutamate, acetylcholine, serotonin, dopamine), agonists thereof, and agents that act to increase levels of an excitatory neurotransmitter(s) (*e.g.,* edrophonium; Mestinon; trazodone; SSRIs (*e.g.,* flouxetine, paroxetine, sertraline, citalopram and fluvoxamine); tricyclic antidepressants (*e.g.,* imipramine, amitriptyline, doxepin, desipramine, trimipramine and nortriptyline), monoamine oxidase inhibitors (*e.g.,* phenelzine, tranylcypromine, isocarboxasid)), generally have an excitatory effect on neural tissue, while inhibitory neurotransmitters (*e.g.,* dopamine, glycine, and gamma-aminobutyric acid (GABA)), agonists thereof, and agents that act to increase levels of an inhibitory neurotransmitter(s) generally have an inhibitory effect (*e.g.,*

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benzodiasepine (*e.g.,* chlordiazepoxide, clonazepam, diazepam, lorazepam, oxazepam, prazepam alprazolam); flurazepam, temazepam, or triazolam). (Dopamine acts as an excitatory neurotransmitter in some locations and circumstances, and as an inhibitory neurotransmitter in other locations and circumstances.) However, antagonists of inhibitory neurotransmitters (*e.g.,* bicuculline) and agents that act to decrease levels of an inhibitory neurotransmitter(s) have been demonstrated to excite neural tissue, leading to increased neural activity. Similarly, excitatory neurotransmitter antagonists (*e.g.,* prazosin, and metoprolol) and agents that decrease levels of excitatory neurotransmitters may inhibit neural activity. Yet further, lithium salts, anesthetics (*e.g.,* lidocane), and magnesium may also be used in combination with electrical stimulation.

VI. Treating Neurological Conditions

[0116] The present stimulation system and/or method acts to stimulate neuronal tissue which in turn stimulate the brain and cause/allow the brain to act in the best interest of the host through use of the brain's natural mechanisms. The prior art fails to recognize that stimulation of at least one the predetermined areas using the stimulation parameters of the present invention can provide the therapeutic treatments according to the instant invention.

[0117] Accordingly, the present invention relates to modulation of neuronal activity to affect neurological, neuropsychological or neuropsychiatric activity. The present invention finds particular application in the modulation of neuronal function or processing to affect a functional outcome. The modulation of neuronal function is particularly useful with regard to the prevention, treatment, or amelioration of neurological, psychiatric, psychological, conscious state, behavioral, mood, and thought activity (unless otherwise indicated these will be collectively referred to herein as "neurological activity" which includes "psychological activity" or "psychiatric activity"). When referring to a pathological or undesirable condition associated with the activity, reference may be made to a neurological disorder which includes "psychiatric disorder" or "psychological disorder" instead of neurological activity or psychiatric or psychological activity. Although the activity to be modulated usually manifests itself in the form of a disorder such as a attention or cognitive disorders (*e.g.,* Autistic Spectrum Disorders); mood disorder (*e.g.,* major depressive disorder, bipolar disorder, and dysthymic disorder) or an anxiety disorder (*e.g.,* panic disorder, posttraumatic stress disorder, obsessive-compulsive disorder and phobic disorder); neurodegenerative diseases (*e.g.,* multiple sclerosis, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), Parkinson's disease, Huntington's Disease, Guillain-Barre syndrome, myasthenia gravis, and chronic idiopathic demyelinating disease (CID)), movement

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disorders (e.g, dyskinesia, tremor, dystonia, chorea and ballism, tic syndromes, Tourette's Syndrome, myoclonus, drug-induced movement disorders, Wilson's Disease, Paroxysmal Dyskinesias, Stiff Man Syndrome and Akinetic-Ridgid Syndromes and Parkinsonism), epilepsy, tinnitus, pain, phantom pain, diabetes neuropathy, one skilled in the art appreciates that the invention may also find application in conjunction with enhancing or diminishing any neurological or psychiatric function, not just an abnormality or disorder. Neurological activity that may be modulated can include, but not be limited to, normal functions such as alertness, conscious state, drive, fear, anger, anxiety, repetitive behavior, impulses, urges, obsessions, euphoria, sadness, and the fight or flight response, as well as instability, vertigo, dizziness, fatigue, photofobia, concentration dysfunction, memory disorders, headache, dizziness, irritability, fatigue, visual disturbances, sensitivity to noise (misophonia, hyperacusis,, phonofobia), judgment problems, depression, symptoms of traumatic brain injury (whether physical, emotional, social or chemical), autonomic functions, which includes sympathetic and/or parasympathetic functions (*e.g.,* control of heart rate), somatic functions, and/or enteric functions. Thus, the present invention encompasses modulation of central and/or peripheral nervous systems.

[0118] Other neurological disorders can include, but are not limited to headaches, for example, migraine, trigeminal autonomic cephalgia (cluster headache (episodic and chronic)), paroxysmal hemicrania (epidsodic and chronic), hemicrania continua, SUNCT (shortlasting unilateral neuralgiform headache with conjunctival injection and tearing), cluster tic syndrome, trigenminal neuroalgia, tension type headache, idiopathic stabbing headache, etc. The neurostimulation device can be implanted intracranially or peripherally, for example, but not limited to implanting a neurostimulation device occipitally for the treatment of headaches.

[0119] Autonomic and/or enteric nervous system disorders that can be treated using the stimulation system and/or method of the present invention include, but are not limited to hypertension, neurosis cordis or heart rhythm disorders, obesity, gastrointestinal motion disorders, respiratory disorders, diabetes, sleep disorders, snoring, incontinence both urologic and gastrointestinal, sexual dysfunction, chronic fatigue syndrome, fibromyalgia, whiplash associated symptoms, post-concussion syndrome, posttraumatic stress disorder etc.

[0120] Yet further immunological disorders may also be treated using the stimulation system and/or method of the present invention. This is based on the fact that the

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immune system senses antigens coordinates metabolic, endocrine and behavioral changes that support the immune system and modulates the immune system via neuroendocrine regulation and direct immune cell regulation. Such immunological disorders include, such as allergy, rhinitis, asthma, rheumatoid arthritis, psoriasis arthritis, lupus erythematosus disseminatus, multiple sclerosis and other demyelinating disorders, autoimmune thyroiditis, Crohn's disease, diabetis melitus etc.

[0121] Yet further tumoral disorders, both malignant and benign may also be treated using the stimulation system and/or method of the present invention. This is based on the fact that tumoral behavior is linked to immunological function. This is seen in immunodeficiency syndromes such as AIDS and hematological disorders, where multiple and different tumors develop. In this setting neuromodulation could indirectly influence tumoral behavior.

[0122] Yet further neuroendocrine disorders may also be treated using the stimulation system and/or method of the present invention. Such disorders are stress reactions, hypothalamic-pituitary axis dysfunction, etc

[0123] Yet further functional disorders may also be treated using the stimulation system and/or method of the present invention. Such disorders can be anorexia, boulemia, phobias, addictions, paraphilia, psychosis, depression, bipolar disorder, kleptomania, aggression, or antisocial sexual behavior. One skilled in the art appreciates that the invention may also find application in conjunction with enhancing or diminishing any neurological or psychiatric function, not just an abnormality or disorder.

[0124] The present invention finds particular utility in its application to human neurological disorders, for example psychological or psychiatric activity/disorder and/or physiological disorders. One skilled in the art appreciates that the present invention is applicable to other animals which exhibit behavior that is modulated by the neuronal tissue. This may include, for example, primates, canines, felines, horses, elephants, dolphins, etc. Utilizing the various embodiments of the present invention, one skilled in the art may be able to modulate neuronal functional outcome to achieve a desirable result.

[0125] One technique that offers the ability to affect neuronal function is the delivery of electrical and/or chemical and/or magnetic stimulation for neuromodulation directly to target tissues or predetermined neuronal sites via an implanted device having a probe. The

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probe can be stimulation lead or electrode assembly. The electrode assembly may be one electrode, multiple electrodes, or an array of electrodes in or around the target area. The proximal end of the probe is coupled to a system to operate the device to stimulate the target site. Thus, the probe is coupled to an electrical signal source, which, in turn, is operated to stimulate the target tissue or predetermined site.

[0126] A predetermined site is a neuronal tissue, which can include either peripheral neuronal tissue and/or central neuronal tissue. Neuronal tissue includes any tissue associated with the peripheral nervous system or the central nervous system. Peripheral neuronal tissue can include a nerve root or root ganglion or any neuronal tissue that lies outside the brain, brainstem or spinal cord. Central neuronal tissue includes brain tissue, spinal tissue or brainstem tissue.

[0127] Peripheral nerves can include, but are not limited to olfactory nerve, optic, nerve, oculomotor nerve, trochlear nerve, trigeminal nerve, abducens nerve, facial nerve, vestibulocochlear (auditory) nerve, glossopharyngeal nerve, vagal nerve, accessory nerve, hypoglossal nerve, suboccipital nerve, the greater occipital nerve, the lesser occipital nerve, the greater auricular nerve, the lesser auricular nerve, the phrenic nerve, brachial plexus, radial axillary nerves, musculocutaneous nerves, radial nerves, ulnar nerves, median nerves, intercostal nerves, lumbosacral plexus, sciatic nerves, common peroneal nerve, tibial nerves, sural nerves, femoral nerves, gluteal nerves, thoracic spinal nerves, obturator nerves, digital nerves, pudendal nerves, plantar nerves, saphenous nerves, ilioinguinal nerves, gentofemoral nerves, and iliohypogastric nerves. Also all sympathetic and parasympathetic nerves and all sympathetic and parasympathetic parts of peripheral nerves.

[0128] Brain tissue can include thalamus/sub-thalamus (all thalamic nuclei, inclusive of medial and lateral geniculate body, intralaminar nuclei, nucleus reticularis, pulvinar, etc) basal ganglia (inclusive of putamen, caudate nucleus, globus pallidus), hippocampus, amygdala, hypothalamus, epithalamus, mammilary bodies, substantia nigra or cortex or white matter tracts afferent to or efferent from the abovementioned brain tissue, inclusive of the corpus callosum, fornix, internal capsula, anterior and posterior commissural, cerebral peduncles etc. Brain tissue also includes cerebellum, inclusive of cerebellar peduncles, and cerebeller nuclei such as fastigial nucleus, globose nucleus, dentate nucleus, emboliform nucleus. Brain tissue also includes auditory cortex and the somatosensory cortex.

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[0129] Spinal tissue can include the ascending and descending tracts of the spinal cord, more specifically, the ascending tracts of that comprise intralaminar neurons or the dorsal column, fsciculus gracilis and cuneatus, dorsolateral fasciculus of Lissauer, spinocerebellar and cerebellospinal tracti, spinothalamic, spinoolivary, spinotectal and spinoreticular tracti. Also inclusive are the rubrospinal, reticulospinal, vestibulospinal, tectospinal and corticospinal tracti and the medial longitudinal fasciculus etc. Any area of the spinal cord may be stimulated in the present invention for example the any neuronal tissue associated with any of the cervical vertebral segments (C1, C2, C3, C4, C5, C6, C7) and/or any tissue associated with any of the thoracic vertebral segments (T1, T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, 12) and/or any tissue associated with any of the lumbar vertebral segments (L1, L2, L3, L4. L5, L6) and/or any tissue associated with the sacral vertebral segments (S1, S2, S3, S4, S5).

[0130] The brainstem tissue can include the medulla oblongata, pons or mesencephalon, more particular the posterior pons or posterior mesencephalon, Lushka's foramen, and ventrolateral part of the medulla oblongata inclusive of the cranial nerve nuclei, the reticular formatio, substantia nigra, red nucleus, the periaquaductal grey. This is also inclusive of white matter tracts such as the medial longitudinal fasciculus, lemniscus medialis, trigeminalis, spinalis and lateralis and sinothalamic, spinocerebellar, corticospinal and corticonuclear tracti, etc.

[0131] Using the stimulation system of the present invention, the predetermined site or target area is stimulated in an effective amount or effective treatment regimen to decrease, reduce, modulate or abrogate the neurological disorder. Thus, a subject is administered a therapeutically effective stimulation so that the subject has an improvement in the parameters relating to the neurological disorder or condition including subjective measures such as, for example, neurological examinations and neuropsychological tests (e.g., Minnesota Multiphasic Personality Inventory, Beck Depression Inventory, Mini-Mental Status Examination (MMSE), Hamilton Rating Scale for Depression, Wisconsin Card Sorting Test (WCST), Tower of London, Stroop task, MADRAS, CGI, N-BAC, or Yale-Brown Obsessive Compulsive score (Y-BOCS)), motor examination, and cranial nerve examination, and objective measures including use of additional psychiatric medications, such as anti-depressants, or other alterations in cerebral blood flow or metabolism and/or neurochemistry.

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[0132] Patient outcomes may also be tested by health-related quality of life (HRQL) measures: Patient outcome measures that extend beyond traditional measures of mortality and morbidity, to include such dimensions as physiology, function, social activity, cognition, emotion, sleep and rest, energy and vitality, health perception, and general life satisfaction. (Some of these are also known as health status, functional status, or quality of life measures.)

[0133] Treatment regimens may vary as well, and often depend on the health and age of the patient. Obviously, certain types of disease will require more aggressive treatment, while at the same time, certain patients cannot tolerate more taxing regimens. The clinician will be best suited to make such decisions based on the known subject's history.

[0134] For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, improvement of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether objective or subjective. The improvement is any observable or measurable improvement. Thus, one of skill in the art realizes that a treatment may improve the patient condition, but may not be a complete cure of the disease.

[0135] In certain embodiments, in connection with improvement in one or more of the above or other neurological disorders, the electrical stimulation may have a "brightening" effect on the person such that the person looks better, feels better, moves better, thinks better, and otherwise experiences an overall improvement in quality of life.

[0136] In certain embodiments, it is envisioned that the present invention provides at least one burst stimulus (*e.g.,* electrical, chemical, magnetic and/or thermal) to a predetermined neuronal tissue site whereby the stimulus alters neuronal activity thereby treating the disorder or condition. The burst stimulus comprises a frequency in the range of about 1 Hz to about 300 Hz, more particular, in the range of about 1 Hz to about 12 Hz, and more particularly, in the range of about 1 Hz to about 4 Hz, 4 Hz to about 7 Hz or about 8 Hz to about 12 Hz, 18 Hz to 20 Hz, and 40 Hz. The burst stimulus comprises at least two spikes, for example, each burst stimulus can comprise about 2 to about 100 spikes, more particularly, about 2 to about 10 spikes. Each spike can comprise a frequency in the range of about 1Hz to about 1000 Hz, more particularly, in the range of about 50 to about 200 Hz or in the range of about

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200 Hz to about 500 Hz. Those of skill in the art understand that the frequency for each spike within a burst can vary. Yet further, the spike interval can also vary from about 0.5 milliseconds to about 100 milliseconds.

[0137] In further embodiments, the burst stimulus is followed by an inter-burst interval. The inter-burst interval has duration in the range of about 5 milliseconds to about 5 seconds, more preferably, about 10 milliseconds to about 300 milliseconds. It is envisioned that the burst stimulus has a duration in the range of about 10 milliseconds to about 5 seconds, more particular, in the range of about 250 msec to 1000 msec (1-4 Hz burst firing), 145 msec to about 250 msec (4-7 Hz,), 145 msec to about 80 msec (8-12 Hz) or 1 to 5 seconds in plateau potential firing. The burst stimulus and the inter-burst interval can have a regular pattern or an irregular pattern (*e.g.,* random or irregular harmonics).

[0138] In further embodiments, the stimulation system of the present invention can incorporate an infusion or drug delivery device. The device can contain a sensor, for example an electrode, that senses a hyperactive burst pattern of activity, which in turns stimulates the infusion pump to release a chemical or stimulating drug or agent to modify the neuronal activity. The chemical or stimulating agent can be either an inhibiting agent or stimulating agent, as described above.

[0139] In addition to electrical stimulation and/or chemical stimulation, other forms of stimulation can be used, for example magnetic, or thermal or combinations thereof. Magnetic stimulation can be provided by internally implanted probes or by externally applied directed magnetic fields, for example, U.S. Patent Nos. 6,592,509; 6,132,361; 5,752,911; and 6,425,852, each of which is incorporated herein in its entirety. Thermal stimulation can be provided by using implanted probes that are regulated for heat and/or cold temperatures which can stimulate or inhibit neuronal activity, for example, U.S. Patent No. 6,567,696, which is incorporated herein by reference in its entirety.

[0140] The neuromodulation method of the present invention can be used to alter a physiological and/or pathological signaling pattern. Thus, it is envisioned that the stimulation method as used herein can alter such patterns to alleviate the neurological condition or disease, or to improve or enhance a desired physiological function (e.g., self confidence, alleviating shyness, distrust etc).

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[0141] In certain embodiments, the neuromodulation method can be used to treat neurological disorders or diseases that result from incorrect central nervous system control in which the disorder comprises a regular bursting rhythm. Such disorders having a regular bursting rhythm include, but are not limited to Parkinson's, epilepsy, tinnitus and phantom pain or other forms of deafferentation or central pain. Thus, it is envisioned that the neuromodulation of the present invention will alter or disrupt the regular bursting rhythm associated with the disorder.

[0142] In further embodiments, it is envisioned that other central neuronal tissue may be stimulated, for example, tissue associated with the spinal cord, more specially the dorsal horn or column to treat any neurological condition or disorder associated with innervations from such, for example, pain. It is known that deafferented dorsal horn cells fire in a burst mode firing (Guenot 2003), which namely adding a valence to the high frequency tonic information (Jeanmonod 1989; Swadlow 2001, Sherman 2001). Thus, the present invention can modulate or disrupt the burst mode firing of the dorsal horn in such conditions thereby treating the condition.

[0143] Still further, it is contemplated that the neuromodulation system of the present invention can be used to alter the firing mode for predetermined peripheral neuronal tissue. For example, it is known that brief bursts that come from the periphery can more reliably transmit neural information between primary afferent fibers and spinal dorsal horn neurons (Wan 2004). One of the reasons might be that in contrast to tonic firing (both low frequency - 1 Hz - or high frequency - 100 Hz), burst firing releases BDNF (brain derived neurotrophic factor) from dorsal horn cells (Lever 2001), which is known to be part of a general mechanism for activity-dependent modification of synapses in the developing and adult nervous system. Thus, diseases of abnormal trophic support (such as neurodegenerative diseases) and diseases of abnormal excitability (such as epilepsy and central pain sensitization) can be related in some cases to abnormal BDNF signaling (Binder 2004). As such, it is envisioned that stimulation of peripheral neuronal tissue using the stimulation parameters or neuromodulation system of the present invention will alter, override, or disrupt the burst firing, thus altering release of BDNF, thereby treating the neurological condition or disorder.

[0144] Still further, it is known that the sympathetic system fires in bursts, and the parasympathetic system as well. Any neurological or non-neurological disorder associated with a

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hypoactive, hyperactive or maladaptive sympathetic or parasympathetic firing can be modified using this method.

[0145] Still further, the neuromodulation method of the present invention can be used to treat neurological disorders or diseases that result from incorrect central nervous system control in which the disorder comprises an irregular bursting rhythm. Such disorders can include, but are not limited to dystonia or chorea or hallucinations. Thus, it is envisioned that such conditions are caused or linked to arrhythmic burst firing or desynchronized tonic firing can be treated utilizing the neuromodulation system or stimulation parameters of the present invention.

[0146] In different motor, sensory and autonomic neurological disorders two mechanisms might be involved: the firing rate is altered in tonic and burst firing cells and the amount of burst firing is increased. A second mechanism involved is an alteration in the synchrony of neuronal firing, which is often increased.

[0147] Thus, burst firing neuromodulation is indicated for modifying both physiological or abnormal tonic and burst firing in the brain, brainstem, spinal cord and peripheral nervous system, inclusive of the autonomic system. This type of neuromodulation can be modify burst firing patterns, but also for tonic firing patterns

A. Sensory disorders

1. Tinnitus

[0148] In the auditory system, tonic firing transmits the contents of auditory information, while burst firing transmit the valence or importance attached to that sound (Lisman 1997; Sherman 2001; Swadlow and Gusev 2001). Repetitive stimulus presentation results in decreased neuronal response to that stimulus, known as auditory habituation at the single cell level (Ulanovsky *et al.,* 2003), auditory mismatch negativity at multiple cell level (Naatanen *et al.,* 1993; Ulanovsky *et al.,* 2003).

[0149] Tinnitus is a noise in the ears, often described as ringing, buzzing, roaring, or clicking. Subjective and objective forms of tinnitus exist, with objective tinnitus often caused by muscle contractions or other internal noise sources in the area proximal to auditory structures. In certain cases, external observers can hear the sound generated by the internal source of

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objective tinnitus. In subjective forms, tinnitus is audible only to the subject. Tinnitus varies in perceived amplitude, with some subjects reporting barely audible forms and others essentially deaf to external sounds and/or incapacitated by the intensity of the perceived noise.

[0150] Tinnitus is usually constantly present, *e.g.,* a non-rational valence is attached to the internally generated sound, and there is no auditory habituation to this specific sound, at this specific frequency. Thus, tinnitus is the result of hyperactivity of lesion-edge frequencies, and auditory mismatch negativity in tinnitus patients is specific for frequencies located at the audiometrically normal lesion edge (Weisz 2004).

[0151] As pathological valence of the tinnitus sound is mediated by burst firing, burst firing is increased in tinnitus in the extralemniscal system (Chen and Jastreboff 1995; Eggermont and Kenmochi 1998; Eggermont 2003), in the inner hair cells (Puel 1995; Puel *et al.,* 2002), the auditory nerve (Moller 1984), the dorsal and external inferior colliculus (Chen and Jastreboff 1995), the thalamus (Jeanmonod, Magnin *et al.,* 1996) and the secondary auditory cortex (Eggermont and Kenmochi 1998; Eggermont 2003). Furthermore, quinine, known to generate tinnitus, induces an increased regularity in burst firing, at the level of the auditory cortex, inferior colliculus and frontal cortex (Gopal and Gross 2004). It is contemplated that tinnitus can only become conscious if an increased tonic firing rate is present in the lemniscal system, generating the sound. This increased firing activity has been demonstrated in the lemniscal dorsal cochlear nucleus (Kaltenbach, Godfrey *et al.,* 1998; Zhang and Kaltenbach 1998; Kaltenbach and Afman 2000; Brozoski, Bauer *et al.,* 2002; Zacharek *et al.,* 2002; Kaltenbach *et al.,* 2004), inferior colliculus (Jastreboff and Sasaki 1986; Jastreboff, Brennan *et al.,* 1988; Jastreboff 1990) (Gerken 1996) and primary auditory cortex (Komiya, 2000). Interestingly, not only tonic firing is increased generating the tinnitus sound, but also the burst firing (Ochi and Eggermont 1997) (keeping it conscious) at a regular basis. Repetitive burst firing is known to generate tonic gamma band activity (Gray and Singer 1989; Brumberg, 2000). Thus, it is envisioned that the present invention can be used to modify burst firing, thus modifying tonic gamma activity.

[0152] Burst mode firing boosts the gain of neural signaling of important or novel events by enhancing transmitter release and enhancing dendritic depolarization, thereby increasing synaptic potentiation. Conversely, single spiking mode may be used to dampen neuronal signaling and may be associated with habituation to unimportant events (Cooper 2002).

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It is believed that the main problem in tinnitus is that the internally generated stimulus does not decay due to the presence of regular bursting activity telling the cortex this signal is important and has to remain conscious.

[0153] Thus, in the present invention, it is envisioned that the neuromodulation system can attack either of these two pathways: slowing down tonic firing in the lemniscal system (below 40 Hz) or removing the valence attached to it by the extralemniscal system by suppressing the regular bursting rhythm, thereby treating tinnitus. Yet further, the neuromodulation system of the present invention can also make the tinnitus disappear via auditory habituation. Suppressing the rhythmic burst firing in the frontal cortex may alter the emotional affect given to the tinnitus, with the tinnitus persisting, a situation known by many people perceiving tinnitus, but without much influence on their daily life. Such methods of treating tinnitus are further described in U.S. Provisional Applications entitled "Deep Brain Stimulation to Treat Tinnitus" filed October 21, 2004; "Peripheral Nerve Stimulation to Treat Tinnitus" filed October 21, 2004; and "Dorsal Column Stimulation to Treat Tinnitus" filed October 21, 2004, each of which is incorporated by reference in its entirety.

2. Phantom pain

[0154] In phantom pain the same is noted as in Parkinson's Disease (PD) and tinnitus. In humans, the tonic firing rate increases (Yamashiro *et al.,* 2003), as well as the amount of burst firing in the deafferented receptive fields (Rinaldi *et al.,* 1991; Jeanmonod *et al.,* 1996; Radhakrishnan *et al.,* 1999) in the somatosensory thalamic nuclei (Rinaldi *et al.,* 1991; Lenz *et al.,* 1998), as well as activity in the in the intralaminar nuclei (Weigel and Krauss 2004). Synchrony in firing is also increased. This is similar to what is seen in animal neuropathic pain models (Lombard and Besson 1989; Nakamura and Atsuta 2004) (Yamashiro *et al.,* 1991). These results suggest that in pain decreased spike frequency adaptation and increased excitability develops after injury to sensory neurons. Through decreased Ca^{2+} influx, the cell becomes less stable and more likely to initiate or transmit bursts of action potentials (McCallum *et al.,* 2003).

[0155] Thus, it is envisioned that that the neuromodulation system or method of the present invention will alter or disrupt the regular bursting rhythm associated with the phantom pain.

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3. Motor disorders

[0156] In Parkinson's disease (PD), the striatum is viewed as the principal input structure of the basal ganglia, while the internal pallidal segment (GPi) and the substantia nigra pars reticulata (SNr) are output structures. Input and output structures are linked via a monosynaptic "direct" pathway and a polysynaptic "indirect" pathway involving the external pallidal segment (GPe) and the subthalamic nucleus (STN). According to current schemes, striatal dopamine (DA) enhances transmission along the direct pathway (via D1 receptors), and reduces transmission over the indirect pathway (via D2 receptors) (Wichmann and DeLong 2003) .

[0157] Increased firing rates are noted in PD, both in the globus pallidus (Magnin *et al.,* 2000) and the subthalamic nucleus (Levy *et al.,* 2002) and is reversed in successful STN stimulation in PD (Welter *et al.,* 2004; Boraud *et al.,* 1996). Synchronization between firing rates is important: lower frequency oscillations facilitate slow idling rhythms in the motor areas of the cortex, whereas synchronization at high frequency restores dynamic task-related cortical ensemble activity in the gamma band (Brown 2003). In PD, a (hyper)synchronization is related to tremor (Levy *et al.,* 2002), similarly to what is seen in the animal Parkinson model (Raz *et al.,* 2000; Nini *et al.,* 1995).

[0158] Two or more firing modes exist in the subthalamic nucleus: tonic firing (68%), phasic or burst firing (25%) and phasic-tonic (7%) (Magarinos-Ascone *et al.,* 2002).

[0159] In the monkey MPTP Parkinson model, burst firing, which occurs at 4 to 8 Hz, increases in the STN and Gpi in comparison to normal firing (from 69% and 78% in STN and GPi to 79% and 89%, respectively) (Bergman *et al.,* 1994), as well as burst duration, without increase in the amount of spikes per burst (Bergman *et al.,* 1994). Abnormally increased tonic and phasic activity in STN leads to abnormal GPi activity and is a major factor in the development of parkinsonian motor signs (Wichmann *et al.,* 1994). The percentage of cells with 4- to 8-Hz periodic activity correlates with tremor and is significantly increased from 2% to 16% in STN and from 0.6% to 25% in GPi with the MPTP treatment (Bergman *et al.,* 1994). These cells are also recorded in humans with PD (Hutchison *et al.,* 1997). Furthermore, synchronization increases, *e.g.,* a decrease in independent activity (Raz *et al.,* 2000; Nini *et al.,* 1995), both in tonically firing cells (Raz *et al.,* 2001) and burst firing cells. Thus, it is envisioned

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that that the neuromodulation or stimulation system or method of the present invention will alter or disrupt or override the regular bursting rhythm associated with PD.

[0160] Other movement disorders, for example, chorea, Huntington's chorea, hemiballism and parkinsonian tremor all differ in the amount of regularity in their muscle contractions. (Hashimoto and Yanagisawa 1994). The regularities of interval, amplitude, rise time, and EMG activity differs within order of regularity, such PD, vascular chorea, Huntington chorea and hemiballism being least regular (Hashimoto and Yanagisawa 1994). However, in chorea (Hashimoto *et al.,* 2001), hemiballism (Postuma and Lang 2003) and Huntington's disease (Cubo *et al.,* 2000), the firing rate might be decreased in contrast to PD. Burst discharges are, however, correlated to the choreatic movements (Kanazawa *et al.,* 1990), similarly to what is noted in PD(Bergman, Wichmann *et al.,* 1994). Thus, the neuromodulation system and/or method of the present invention is used to alter or disrupt the dysfunctional firing rate of the disease or condition.

B. Autonomic disorders

[0161] The autonomic nervous system (ANS) is predominantly an efferent system transmitting impulses from the central nervous system (CNS) to peripheral organ systems. Its effects include control of heart rate and force of contraction, constriction and dilatation of blood vessels, contraction and relaxation of smooth muscle in various organs, visual accommodation, pupillary size and secretions from exocrine and endocrine glands. In addition to it being predominantly an efferent system, there are some afferent autonomic fibers (*e.g.,* transmit information from the periphery to the CNS), which are concerned with the mediation of visceral sensation and the regulation of vasomotor and respiratory reflexes, for example the baroreceptors and chemoreceptors in the carotid sinus and aortic arch which are important in the control of heart rate, blood pressure and respiratory activity. These afferent fibers are usually carried to the CNS by major autonomic nerves such as the vagus, splanchnic or pelvic nerves, although afferent pain fibers from blood vessels may be carried by somatic nerves.

[0162] The ANS is divided into two separate divisions, the parasympathetic and sympathetic systems. This division is based on anatomical and functional differences. Both of these systems consist of myelinated preganglionic fibres that make synaptic connections with unmyelinated postganglionic fibres, and it is these which then innervate the effector organ. These synapses usually occur in clusters called ganglia. Most organs are innervated by fibers from both

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divisions of the ANS, and the influence is usually opposing (*e.g.,* the vagus slows the heart, whilst the sympathetic nerves increase its rate and contractility), although it may be parallel (*e.g.,* the salivary glands).

[0163] The activity recorded from mammalian sympathetic nerves comes in bursts, which result from large numbers of fibers firing synchronously. Human sympathetic nerve activity behaves similarly. Vasomotor, cardiac and sudomotor nerve fibers all fire in bursts. Bursts in post-ganglionic nerves are driven by synchronously firing preganglionic neurons. Burst amplitude, which reflects the number of fibers firing together, and burst probability are controlled independently (McAllen and Malpas 1997). The sympathetic nerve also fires in a 10 Hz tonic mode (Barman, Kitchens *et al.,* 1997). This 10-Hz rhythm is also involved in cardiovascular regulation, as blood pressure falls significantly when the 10-Hz rhythm is eliminated. Cardiac-related burst activity and 10-Hz rhythms are generated by different pools of brainstem neurons (Barman, Kitchens *et al.,* 1997).

[0164] When electrical stimulation is applied to the sympathetic nerve, burst stimulation is more powerful (vasoconstrictor) than tonic mode. The amount of spikes per burst also determines the efficacy of stimulation (Ando, Imaizumi *et al.,* 1993). The same is seen with electrical stimulation of the cervical sympathetic nerve trunk delivered at 50 Hz in bursts of 1 s every 10 s. Burst stimulation evoked a more copious, uniform and reproducible flow of saliva than when delivered at 10 Hz continuously (Anderson, Garrett *et al.,* 1988). Similar superior results with burst stimulation have been obtained studying nasal mucosa reactivity: both types of stimulation reduced nasal blood flow and volume, but the responses were significantly larger with burst stimulation at 0.59 Hz compared to tonic 0.59 Hz stimulation (Lacroix, Stjarne *et al.,* 1988).

[0165] In the parasympathetic system, burst firing and tonic firing co-exist. For example, one population of neurons responds with a brief burst of action potentials at the onset of the depolarization, accommodating to the stimulus, and the other population responds with repetitive action potentials persisting throughout the duration of the stimulus, not accommodating to the stimulus (Myers 1998; Bertrand 2004).

[0166] Burst stimulation at 0.1 Hz with 20 Hz spiking of the parasympathetic nerve results in a 200-fold more powerful enzyme induction than 2 Hz tonic stimulation, when delivering the same amount of pulses (in the sublingual gland) (Nilsson, Rosengren *et al.,* 1991).

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1. Hypertension and Heart Rhythm Disorders

[0167] The nucleus of the solitary tract (NTS), a termination site for primary afferent fibers from baroreceptors and other peripheral cardiovascular receptors, and the paratrigeminal nucleus (Pa5) contain blood pressure-sensitive neurons, some of which have rhythmic activity locked to the cardiac cycle, making them key components of the central pathway for cardiovascular regulation. NTS and Pa5 baroreceptor-activated neurons possess phasic discharge patterns locked to the cardiac cycle (Junior, Caous *et al.,* 2004). The human insular cortex is involved in cardiac regulation. The left insula is predominantly responsible for parasympathetic cardiovascular effects. On stimulation of the left insular cortex, parasympathetic tone increases resulting in bradycardia and depressor responses more frequently than tachycardia and pressor effects ($p < 0.005$) (Oppenheimer, Gelb *et al.,* 1992). The converse applies for the right insular cortex: stimulation of the human right insula increases sympathetic cardiovascular tone (Oppenheimer 1993). Acute left insular stroke increases basal cardiac sympathetic tone and is associated with a decrease in randomness of heart rate variability (Oppenheimer, Kedem *et al.,* 1996). Increased sympathoadrenal tone, resulting from damage to cortical areas involved in cardiac and autonomic control can induce cardiac damage by nonischemic mechanisms (Oppenheimer and Hachinski 1992).

[0168] Brain noradrenaline (NA) neurons in the locus coeruleus (LC) and major parts of the SNS respond by burst activation in concert to stressful stimuli implying novelty or fear. (Svensson 1987). In hypertension, burst firing is increased (Schlaich, Lambert *et al.,* 2004) (Esler, Rumantir *et al.,* 2001).

[0169] The autonomic nervous system plays an important role in the genesis of various cardiac rhythm disorders. In patients with paroxysmal atrial fibrillation, it is important to distinguish vagally mediated from adrenergically mediated atrial fibrillation. The former is considered to represent a form of lone atrial fibrillation affecting particularly males aged 40 to 50 years. The arrhythmic episodes manifest themselves most often during the night lasting from minutes to hours, whereas in adrenergic mediated atrial fibrillation, atrial fibrillation is often provoked by emotional or physical stress. (Hohnloser, van de Loo *et al.,* 1994)

[0170] Thus, hypertension (*e.g.,* neurogenic hypertension) can be treated with burst stimulation of the left insula using the stimulation system of the present invention. In a similar fashion, bradycardia can be treated by burst stimulation of the right insula as subjects with

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bradycardia have significantly higher metabolic activity in the right ($p < 0.0001$) and in the left temporal insula ($p < 0.015$) than those with normal heart rates (Volkow, Wang *et al.,* 2000). Lone atrial fibrillation can be treated by either by left or rightsided burst stimulation depending on whether it is vagally or adrenergicly induced.

2. Sleep apnea

[0171] Activity in the sympathetic nervous system is enhanced not only in obstructive apnea, but also in central and mixed apnea (Shimizu, Takahashi *et al.,* 1997). Burst rate during apnea is higher in central apneas than in obstructive apneas. Burst rate is the central component of mixed apnea and the obstructive component of mixed apneas (Shimizu, Takahashi *et al.,* 1997).

[0172] This intense sympathoexcitation is due to chronic or intermittent hypoxia (Cutler, Swift *et al.,* 2004; Cutler, Swift *et al.,* 2004). Pathological sympathoexcitation appears to depend on both recruitment and increased burst firing frequency. In OSAS, also the amount of spikes per burst is increased, (Elam, McKenzie *et al.,* 2002) and at night, arousal-induced reduction in sympathetic burst latency is noted (Xie, Skatrud *et al.,* 1999).

[0173] Functional MRI or FMRI studies demonstrate reduced neural signals within the frontal cortex, anterior cingulate, cerebellar dentate nucleus, dorsal pons, anterior insula and lentiform nuclei. Signal increases in OSA over control subjects are seen in the dorsal midbrain, hippocampus, quadrangular cerebellar lobule, ventral midbrain and ventral pons (Macey, Macey *et al.,* 2003). In the rat, the respiratory area in the anterior insular cortex consist of two distinct zones which overlap a region modulating the gastrointestinal activity (Aleksandrov, Aleksandrova *et al.,* 2000). In the more rostral area, there is a decrease in respiratory airflow and tidal volume with no alteration of the respiratory rate (the inhibition response), and in the other there is an increase in respiratory rate and inspiratory airflow (the excitation response).

[0174] Thus, the present invention can be used to activate respiration during apneas by burst stimulation of the anterior insula.

C. Obesity

[0175] Food presentation in normal healthy, non-obese individuals significantly increases metabolism in the whole brain (24%, $P < 0.01$), and these changes are largest in

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superior temporal, anterior insula, and orbitofrontal cortices (Wang, Volkow *et al.,* 2004). Food-related visual stimuli elicit greater responses in the amygdala, parahippocampal gyrus and anterior fusiform gyrus when participants are in a hungry state relative to a satiated state (LaBar, Gitelman *et al.,* 2001). Hunger is associated with significantly increased rCBF in the vicinity of the hypothalamus and insular cortex and in additional paralimbic and limbic areas (orbitofrontal cortex, anterior cingulate cortex, and parahippocampal and hippocampal formation), thalamus, caudate, precuneus, putamen, and cerebellum (Tataranni, Gautier *et al.,* 1999). Satiation is associated with increased rCBF in the vicinity of the ventromedial prefrontal cortex, dorsolateral prefrontal cortex, and inferior parietal lobule (Tataranni, Gautier *et al.,* 1999). High-calorie foods yield significant activation within the medial and dorsolateral prefrontal cortex, thalamus, hypothalamus, corpus callosum, and cerebellum. Low-calorie foods yield smaller regions of focal activation within medial orbitofrontal cortex, primary gustatory/somatosensory cortex, and superior, middle, and medial temporal regions (Killgore, Young *et al.,* 2003). Activity within the temporo-insular cortex in normal appetitive function is associated with the desirability or valence of food stimuli, prior to ingestion (Gordon, Dougherty *et al.,* 2000). When a food is eaten to satiety, its reward value decreases. Responses of gustatory neurons in the secondary taste area within the orbitofrontal cortex are modulated by hunger and satiety, in that they stop responding to the taste of a food on which an animal has been fed to behavioral satiation, yet may continue to respond to the taste of other foods (Critchley and Rolls 1996; O'Doherty, Rolls *et al.,* 2000). In the OFC, the rCBF decreases in the medial OFC and increases in the lateral OFC as the reward value of food changes from pleasant to aversive for non-liquid (Small, Zatorre *et al.,* 2001) and liquid foods (Kringelbach, O'Doherty *et al.,* 2003). In the insular gustatory cortex, neuronal responses to gustatory stimuli are not influenced by the normal transition from hunger to satiety. This is in contrast to the responses of a population of neurons recorded in the hypothalamus, which only respond to the taste of food when the monkey is hungry (Yaxley, Rolls *et al.,* 1988). Brain responses to hunger/satiation in the hypothalamus, limbic/paralimbic areas (commonly associated with the regulation of emotion), and prefrontal cortex (thought to be involved in the inhibition of inappropriate response tendencies) might be different in obese and lean individuals (Del Parigi, Gautier *et al.,* 2002). Compared with lean women, obese women have significantly greater increases in rCBF in the ventral prefrontal cortex and have significantly greater decreases in the paralimbic areas and in areas of the frontal and temporal cortex (Gautier, Del Parigi *et al.,* 2001). In obese women, the rCBF is higher in the right parietal and temporal cortices during the food exposure than in the control condition. In addition, in obese women the activation of the

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right parietal cortex is associated with an enhanced feeling of hunger when looking at food (Karhunen, Lappalainen *et al.,* 1997). This significantly higher metabolic activity in the bilateral parietal somatosensory cortex is noted in the regions where sensation to the mouth, lips and tongue are located. The enhanced activity in somatosensory regions involved with sensory processing of food in the obese subjects can make them more sensitive to the rewarding properties of food related to palatability and can be one of the variables contributing to their excess food consumption (Wang, Volkow *et al.,* 2002).

[0176] Based on the abovementioned model, the stimulation system and/or method of the present invention can be used to produce burst stimulation of the - orbitofrontal cortex or - insula to treat obesity especially in those people who are constant eaters rather than binge or high volume eaters. Other targets that can be stimulated are the dorsolateral prefrontal cortex, thalamus, hypothalamus, corpus callosum, and cerebellum, as well as the medial orbitofrontal cortex, primary gustatory/somatosensory cortex, and superior, middle, and medial temporal regions and the amygdalohippocampal area and anterior cingulated area.

D. Cognitive and psychological disorders

1. Depression

[0177] In patients suffering from a depression, a hypometabolism and hypoperfusion localized to the left middorsolateral frontal cortex (MDLFC) is noted (Baxter, Schwartz *et al.,* 1989; Brody, Saxena *et al.,* 2001). Furthermore decreased neural activity in the MDLFC, aka the dorsolateral prefrontal cortex, is correlated with severity of depression (Bench, Friston *et al.,* 1992; Bench, Friston *et al.,* 1993; Dolan, Bench *et al.,* 1994) and is reversed upon recovery from depression (Bench, Frackowiak *et al.,* 1995). Electroencephalography demonstrates increased alpha power. Alpha power is thought to be inversely related to neural activity in left frontal regions of the brains of depressed patients (Bruder, Fong *et al.,* 1997).

[0178] Metabolic activity in the ventral perigenual ACC is increased in depressed patients relative to control subjects (Videbech, Ravnkilde *et al.,* 2001) and is positively correlated with severity of depression (Drevets 1999). Furthermore, neural activity in this region decreases in response to antidepressant treatment (Brody, Saxena *et al.,* 2001).

[0179] The MDLFC occupies the middle frontal and superior frontal gyri and comprises cytoarchitectonic areas 46 and 9/46 (middle frontal gyrus) and area 9 (superior frontal

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gyrus) (Paus and Barrett 2004). The MDLFC has connections with sensory areas processing visual (prestriate and inferior temporal cortices), auditory (superior temporal cortex) and somatosensory (parietal cortex) information (Petrides and Pandya 1999). The MDLFC also reciprocally connects with the anterior and, to a lesser extent, posterior cingulate cortices (Bates and Goldman-Rakic 1993).

[0180] Transcranial magnetic stimulation has been performed in the treatment of depression. The left MDLFC is the most common target for rTMS treatment of depression (Paus and Barrett 2004), and rTMS of the left MDLFC modulates the blood-flow response in the ACC (Barrett, Della-Maggiore *et al.,* 2004; Paus and Barrett 2004). High-frequency (20 Hz) and low-frequency (1 Hz) stimulation seem to have an opposite effect. High-frequency stimulation (HFS) increases and low-frequency stimulation (LFS) decreases cerebral blood flow (CBF) and/or glucose metabolism in the frontal cortex and other linked brain regions (Speer, Kimbrell *et al.,* 2000; Kimbrell, Little *et al.,* 1999; and Post, Kimbrell *et al.,* 1999).

[0181] Successful treatment of depression with TMS results in normalization of hypoperfusion (with HFS) and normalization hyperperfusion (with LFS) (Kimbrell, Little *et al.,* 1999). Thus, TMS treatment for depression can be proposed using 20 Hz left frontal cortex (Kimbrell, Little *et al.,* 1999; Paus and Barrett 2004) or 1 Hz right frontal cortex (Klein, Kreinin *et al.,* 1999).

[0182] In the ACC of the rat, three kinds of burst firing is recorded. Rhythmic burst firing with inter-burst intervals of 80 and 200 ms and non rhythmic burst firing (Gemmell, Anderson *et al.,* 2002). ACC stimulations evoke both tonic and burst reactions in the dorsolateral prefrontal cortex (Desiraju 1976). Similarly to other cortical areas, the dorsolateral prefrontal cortex has burst firing cells, tonic firing cells and mixed firing cells. Similarly to other areas, the burst firing notices new incoming sensory (auditory, visual) information, and tonic firing continues as long as the stimulus lasts (Ito 1982). TMS in burst mode is more powerful than TMS in tonic mode. For example, 20 seconds of 5 Hz burst firing with 3 pulses at 50 Hz per burst have the same effect as 10 minutes 1 Hz tonic TMS.

[0183] Thus, the present stimulation system and/or method can be used to treat depression. For example, a cortical electrode is implanted on the right MDLFC and a 5 Hz burst mode is used to treat recurring depressions that react to a test stimulation with TMS.

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2. Obsessive convulsive disorder

[0184] Obsessive-compulsive disorder is a worldwide psychiatric disorder with a lifetime prevalence of 2% and mainly characterized by obsessional ideas and compulsive behaviors and rituals. Bilateral stimulation in the anterior limbs of the internal capsules (Nuttin, Cosyns *et al.,* 1999; Nuttin, Gabriels *et al.,* 2003) or nucleus accumbens stimulation (Sturm, Lenartz *et al.,* 2003) can improve symptoms but at high frequency and high intensity stimulation. Thus, the present invention can be used to produce burst mode stimulation to treat an obsessive-compulsive disorder.

3. Tourette's syndrome

[0185] Tourette syndrome (TS) is a neuropsychiatric disorder with onset in early childhood. It is characterized by tics and often accompanied by disturbances in behavior, such as obsessive-compulsive disorder (OCD). Bilateral thalamic stimulation, with promising results on tics and obsessive-compulsive symptoms has been performed as a treatment. (Visser-Vandewalle, Temel *et al.,* 2003; Temel and Visser-Vandewalle 2004). Thus, it is envisioned that the stimulation system and/or method of the present invention can be used to treat TS.

VII. Examples

[0186] The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventors to function well in the practice of the invention, and thus can be considered to constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

Example
Burst Mode Neuromodulation using TMS

[0187] It has been demonstrated that white noise does not react to electrical stimulation of the auditory cortex (De Ridder, De Mulder et al. 2005). Transcranial magnetic stimulation (TMS) is capable of verifying tinnitus suppression in a non-invasive way (Plewnia, Bartels et al. 2003; De Ridder, Verstraeten et al. 2005). However, effects of tonic transcranial magnetic simulation on synaptic plasticity are often weak, highly variable between individuals, and rarely last longer than 30 min. Theta burst TMS on the other hand produces a controllable,

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consistent, long-lasting, and powerful effect on motor cortex physiology and behavior after an application period of only 20-190 s (Huang, Edwards et al. 2005). In other words it is a more powerful way of modifying brain functioning.

[0188] To demonstrate that the above, 22 patients with unilateral white noise or narrow band tinnitus were evaluated using both tonic and burst mode transcranial magnetic stimulation (TMS). Tinnitus attenuation was measured using a Visual Analog Scale, and the amount of tinnitus suppression was compared using both stimulation settings.

[0189] Three patients were excluded because of a placebo positive result, 10 patients did not demonstrate a tinnitus suppression, neither with tonic, nor with burst TMS, so 9 patients were finally included for comparison.

[0190] Average tinnitus suppression in these patients was 8,3% for tonic mode, and 54,5 % for burst mode, a statistically significant difference (Wilcoxon matched pairs test, Z= 2,520504, p = 0.012 (0,011719)), demonstrating the clinical superiority of burst mode stimulation for treating tinnitus.

REFERENCES CITED

[0191] All patents and publications mentioned in the specifications are indicative of the levels of those skilled in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

U.S. Application No. 60/528,604
U.S. Application No. 60/528,689
U.S. Patent No. 5,335,657
U.S. Patent No. 5,938,690
U.S. Patent No. 6,567,696
U.S. Patent No. 6,622,047
U.S. Patent No. 6,671,555
U.S. Patent No. 6,690,974
U.S. Patent No. 6,721,603
U.S. Patent No. 6,740,072
U.S. Patent No. 6,748,276

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00551

Alain, C., D. L. Woods, *et al.,* (1998). Brain Res 812(1-2): 23-37.

Alho, K. (1995). Ear Hear 16(1): 38-51.

Bandrowski, A. E., S. L. Moore, *et al.,* (2002). Synapse 44(3): 146-57.

Beurrier, C., P. Congar, *et al.,* (1999). J Neurosci 19(2): 599-609.

Binder, Adv Exp Med Biol. 2004;548:34-56.

Brozoski, T. J., C. A. Bauer, *et al.,* (2002). J Neurosci 22(6): 2383-90.

Brumberg, The Journal of Neuroscience, 20 (13):4829–4843), 2000

Brumberg, The Journal of Neuroscience, July 1, 2000, 20(13):4829–4843.

Cazals, Y., K. C. Horner, *et al.,* (1998). J Neurophysiol 80(4): 2113-20.

Chen, G. D. and P. J. Jastreboff (1995). Hear Res 82(2): 158-78.

Chernigovskii, V. N., S. S. Musyashchikova, *et al.,* (1979). Biol Bull Acad Sci USSR 6(1): 1-7.

Condon, C. D. and N. M. Weinberger (1991). Behav Neurosci 105(3): 416-30.

Cooper, D. C. (2002). Neurochem Int 41(5): 333-40.

Coro, F., P. E. M, *et al.,* (1998). J Exp Biol 201(Pt 20): 2879-2890.

Coutinho, V. and T. Knopfel (2002). Neuroscientist 8(6): 551-61.

De Ridder, D., G. De Mulder, et al. (2005). ORL in press.

De Ridder, D., E. Verstraeten, et al. (2005). Otol Neurotol 26(4): 616-619.

Huang, Y. Z., M. J. Edwards, et al. (2005). Neuron 45(2): 201-6.

Plewnia, C., M. Bartels, et al. (2003). Ann Neurol 53(2): 263-6.

Csepe, V., G. Karmos, *et al.,* (1987). Electroencephalogr Clin Neurophysiol 66(6): 571-8.

Deouell, L. Y., S. Bentin, *et al.,* (1998). Psychophysiology 35(4): 355-65.

Diamond, D. M. and N. M. Weinberger (1984). Behav Neurosci 98(2): 189-210.

Disney, A. and M. B. Calford (2001). J Neurophysiol 86(2): 1052-6.

Edeline, J. M., N. Neuenschwander-el Massioui, *et al.,* (1990). Behav Brain Res 39(2): 145-55.

Edeline, J. M., Y. Manunta, *et al.,* (2000). J Neurophysiol 84(2): 934-52.

Eggermont, J. J. (1990). Hear Res 48(1-2): 111-23.

Eggermont, J. J. (2003). Auris Nasus Larynx 30 Suppl: S7-12.

Eggermont, J. J. and M. Kenmochi (1998). Hear Res 117(1-2): 149-60.

Fairhall, A. L., G. D. Lewen, *et al.,* (2001). Nature 412(6849): 787-92.

Feig, S. L. (2004). J Comp Neurol 468(1): 96-111.

Fischer, C., D. Morlet, *et al.,* (2000). Audiol Neurootol 5(3-4): 192-7.

Franceschetti et al., Brain Res. 1995 Oct 23;696(1-2):127-39.

Futatsugi, Y. and J. J. Riviello, Jr. (1998). Brain Dev 20(2): 75-9.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00552

Gerken, G. M. (1996). Hear Res 97(1-2): 75-83.

Givois, V. and G. S. Pollack (2000). J Exp Biol 203 Pt 17: 2529-37.

Gopal, K. V. and G. W. Gross (2004). Hear Res 192(1-2): 10-22.

Gray and Singer, Proc Natl Acad Sci U S A. 1989 Mar;86(5):1698-702.

Guatteo et al., Brain Res. 1996 Nov 25;741(1-2):1-12.

He, J. (1997). J Neurophysiol 77(2): 896-908.

He, J. (2003). Exp Brain Res 153(4): 579-90.

He, J. and B. Hu (2002). J Neurophysiol 88(4): 2152-6.

He, J., Y. Q. Yu, *et al.,* (2002). J Neurophysiol 88(2): 1040-50.

Hsieh, C. Y., S. J. Cruikshank, *et al.,* (2000). Brain Res 880(1-2): 51-64.

Hu, B. (1995). J Physiol 483 (Pt 1): 167-82.

Hu, B., V. Senatorov, *et al.,* (1994). J Physiol 479 (Pt 2): 217-31.

Huguenard, J. R. (1999). Adv Neurol 79: 991-9.

Jastreboff, P. J. (1990). Neurosci Res 8(4): 221-54.

Jastreboff, P. J. and C. T. Sasaki (1986). J Acoust Soc Am 80(5): 1384-91.

Jastreboff, P. J., J. F. Brennan, *et al.,* (1988). Laryngoscope 98(3): 280-6.

Javitt, D. C., M. Steinschneider, *et al.,* (1994). Brain Res 667(2): 192-200.

Javitt, D. C., M. Steinschneider, *et al.,* (1996). Proc Natl Acad Sci U S A 93(21): 11962-7.

Jeanmonod, D., M. Magnin, *et al.,* (1996). Brain 119 (Pt 2): 363-75.

Joliot et al., Proc Natl Acad Sci U S A. 1994 Nov 22;91(24):11748-51.

Jongsma, M. L., C. M. Van Rijn, *et al.,* (1998). Eur J Pharmacol 341(2-3): 153-60.

Kaltenbach, J. A. and C. E. Afman (2000). Hear Res 140(1-2): 165-72.

Kaltenbach, J. A., D. A. Godfrey, *et al.,* (1998). Hear Res 124(1-2): 78-84.

Kaltenbach, J. A., M. A. Zacharek, *et al.,* (2004). Neurosci Lett 355(1-2): 121-5.

Kawaguchi, Y. and Y. Kubota (1993). J Neurophysiol 70(1): 387-96.

Kelly, J. B. and H. Zhang (2002). Hear Res 168(1-2): 35-42.

Kepecs, A. and J. Lisman (2003). Network 14(1): 103-18.

Kepecs, A., X. J. Wang, *et al.,* (2002). J Neurosci 22(20): 9053-62.

Kraus, N., T. McGee, *et al.,* (1992). Ear Hear 13(3): 158-64.

Kraus, N., T. McGee, *et al.,* (1994). J Neurophysiol 72(3): 1270-7.

LeDoux, J. E., A. Sakaguchi, *et al.,* (1984). J Neurosci 4(3): 683-98.

Lee et al., J Neurosci. 2001 Mar 1;21(5):1757-66.

Lever et al., J Neurosci. 2001 Jun 15;21(12):4469-77.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00553

Lisman, J. E. (1997). Trends Neurosci 20(1): 38-43.

Ma, C. L., J. B. Kelly, *et al.,* (2002). Hear Res 168(1-2): 25-34.

Martin, W. H., J. W. Schwegler, *et al.,* (1993). Laryngoscope 103(6): 600-4.

Massaux, A. and J. M. Edeline (2003). Exp Brain Res 153(4): 573-8.

Massaux, A., G. Dutrieux, *et al.,* (2004). J Neurophysiol 91(5): 2117-34.

Mattia et al., Hippocampus. 1997;7(1):48-57.

Matveev, Cerebral Cortex, Vol. 10, No. 11, 1143-1153, November 2000.

McAlonan and Brown, Neuroscientist. 2002 Aug;8(4):302-5.

McCormick, D. A. and H. R. Feeser (1990). Neuroscience 39(1): 103-13.

McCormick, D. A. and M. von Krosigk (1992). Proc Natl Acad Sci U S A 89(7): 2774-8.

Miller, L. M., M. A. Escabi, *et al.,* (2001). J Neurosci 21(20): 8136-44.

Miller, L. M., M. A. Escabi, *et al.,* (2001). Neuron 32(1): 151-60.

Moller, A. R. (1984). Ann Otol Rhinol Laryngol 93(1 Pt 1): 39-44.

Mooney, D. M., L. Zhang, *et al.,* (2004). Proc Natl Acad Sci U S A 101(1): 320-4.

Muller, J. R., A. B. Metha, *et al.,* (1999). Science 285(5432): 1405-8.

N. Urbain, et al., J. Neurosci., October 1, 2002; 22(19): 8665 – 8675

Naätanen, R. (1992). Attention and brain function. Hillsdale, New Jersey, Lawrence Erlbaum.

Naatanen, R. (2001). Psychophysiology 38(1): 1-21.

Naatanen, R., P. Paavilainen, *et al.,* (1993). Psychophysiology 30(5): 436-50.

Nousak, J. M., D. Deacon, *et al.,* (1996). Brain Res Cogn Brain Res 4(4): 305-17.

Ochi, K. and J. J. Eggermont (1996). Hear Res 95(1-2): 63-76.

Ochi, K. and J. J. Eggermont (1997). Hear Res 105(1-2): 105-18.

Ohzawa, I., G. Sclar, *et al.,* (1985). J Neurophysiol 54(3): 651-67.

Oleskevich, S. and B. Walmsley (2002). J Physiol 540(Pt 2): 447-55.

Pantev, C., H. Okamoto, *et al.,* (2004). Eur J Neurosci 19(8): 2337-44.

Perez-Reyes, E. (2003). Physiol Rev 83(1): 117-61.

Poremba, A., D. Jones, *et al.,* (1998). Eur J Neurosci 10(10): 3035-43.

Puel, J. L. (1995). Prog Neurobiol 47(6): 449-76.

Puel, J. L., J. Ruel, *et al.,* (2002). Audiol Neurootol 7(1): 49-54.

Ramcharan, E. J., C. L. Cox, *et al.,* (2000). J Neurophysiol 84(4): 1982-7.

Ritter, W., D. Deacon, *et al.,* (1995). Ear Hear 16(1): 52-67.

Romanski, L. M. and J. E. LeDoux (1992). J Neurosci 12(11): 4501-9.

Sakurai, Y. (1990). Behav Neurosci 104(2): 253-63.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00554

Sakurai, Y. (2002). Neuroscience 115(4): 1153-63.

Sanes, D. H., J. McGee, *et al.,* (1998). J Neurophysiol 80(1): 209-17.

Schwarz, D. W., F. Tennigkeit, *et al.,* (2000). Acta Otolaryngol 120(2): 251-4.

Schwindt and Crill, J Neurophysiol. 1999 Mar;81(3):1341-54.

Sherman , S. M. (2001). Nat Neurosci 4(4): 344-6.

Sherman and Guillery, Neuron. 2002 Jan 17;33(2):163-75.

Sherman and Guillery, Philos Trans R Soc Lond B Biol Sci. 2002 Dec 29;357(1428):1695-708.

Sherman and Guillery, Philos Trans R Soc Lond B Biol Sci. 2002 Dec 29;357(1428):1809-21.

Sherman, S. M. (2001). Trends Neurosci 24(2): 122-6.

Steriade, M. and R. R. Llinas (1988). Physiol Rev 68(3): 649-742.

Steriade, M., D. Pare, *et al.,* (1989). J Neurosci 9(7): 2215-29.

Steriade, Neuroscience. 2000;101(2):243-76.

Suga, N., Y. Zhang, *et al.,* (1997). J Neurophysiol 77(4): 2098-114.

Swadlow, H. A. and A. G. Gusev (2001). Nat Neurosci 4(4): 402-8.

Tabak, J. and P. E. Latham (2003). Neuroreport 14(11): 1445-9.

Tennigkeit, F., D. W. Schwarz, *et al.,* (1996). J Neurophysiol 76(6): 3597-608.

Tennigkeit, F., E. Puil, *et al.,* (1997). Acta Otolaryngol 117(2): 254-7.

Tiitinen, H., K. Alho, *et al.,* (1993). Psychophysiology 30(5): 537-40.

Traub et al., J Physiol. 1994 Nov 15;481 (Pt 1):79-95.

Ulanovsky, N., L. Las, *et al.,* (2003). Nat Neurosci 6(4): 391-8.

van Vreeswijk, C. and D. Hansel (2001). Neural Comput 13(5): 959-92.

Wan et al., Neuroscience. 2004;125(4):1051-60.

Webster, W. R. (1971). Electroencephalogr Clin Neurophysiol 30(4): 318-30.

Weinberger, N. M. (1998 Neurobiol Learn Mem 70(1-2): 226-51.

Weinberger, N. M. (2004). Nat Rev Neurosci 5(4): 279-90.

Weinberger, N. M. and J. S. Bakin (1998). Audiol Neurootol 3(2-3): 145-67.

Wong and Stewart, J Physiol. 1992 Nov;457:675-87.

Wu, S. H., C. L. Ma, *et al.,* (2004). J Neurosci 24(19): 4625-34.

Zacharek, M. A., J. A. Kaltenbach, *et al.,* (2002). Hear Res 172(1-2): 137-43.

Zhang, J. S. and J. A. Kaltenbach (1998). Neurosci Lett 250(3): 197-200.

Zhang, Y., N. Suga, *et al.,* (1997). Nature 387(6636): 900-3.

[0192] Although the present invention and its advantages have been described in detail, it should be understood that various changes, substitutions and alterations can be made

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herein without departing from the invention as defined by the appended claims. Moreover, the scope of the present application is not intended to be limited to the particular embodiments of the process, machine, manufacture, composition of matter, means, methods and steps described in the specification. As one will readily appreciate from the disclosure, processes, machines, manufacture, compositions of matter, means, methods, or steps, presently existing or later to be developed that perform substantially the same function or achieve substantially the same result as the corresponding embodiments described herein may be utilized. Accordingly, the appended claims are intended to include within their scope such processes, machines, manufacture, compositions of matter, means, methods, or steps.

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CLAIMS

What is claimed is:

1. A method of stimulating nerve tissue of a patient using an implantable pulse generator, the method comprising:

generating, by the implantable pulse generator, a burst stimulus that comprises a plurality of groups of spike pulses, wherein the burst stimulus is substantially quiescent between the plurality of groups, wherein each spike within each group is separated by a maximum inter-spike interval and each group of spikes is separated by a minimum inter-group interval, wherein the maximum inter-spike interval is 5 milliseconds and the minimum inter-group interval is 20 milliseconds;

providing the burst stimulus from the implantable pulse generator to a medical lead; and

applying the burst stimulus to nerve tissue of the patient via one or several electrodes of the medical lead.

2. The method of claim 1 further comprising: controlling a number of spikes within a group of spikes of the burst stimulus according a parameter stored in the implantable pulse generator.

3. The method of claim 1 further comprising: controlling a spike amplitude according to a parameter stored in the implantable pulse generator.

4. The method of claim 1 further comprising: controlling an inter-spike interval according to a parameter stored in the implantable pulse generator.

5. The method of claim 1 further comprising: controlling an inter-group interval according to a parameter stored in the implantable pulse generator.

6. The method of claim 1 further comprising: controlling a number of groups within the burst stimulus according to a parameter stored in the implantable pulse generator.

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7. The method of claim 1 further comprising: generating a hyperpolarizing pulse immediately before each group of spikes within the burst stimulus.

8. The method of claim 7 wherein an amplitude of the hyperpolarizing pulse is controllable by a parameter stored in the implantable pulse generator.

9. The method of claim 1 further comprising: detecting, by the implantable pulse generator, hyperactivity within neural tissue using a sensor in the implantable pulse generator, wherein the generating the burst stimulus occurs in response to the detecting.

10. The method of claim 9 wherein the sensor is coupled to one or several electrodes of the medical lead.

11. The method of claim 1 wherein each spike in each group occurs from a plateau potential.

12. The method of claim 11 wherein the plateau potential is controllable by a parameter stored in the implantable pulse generator.

13. The method of claim 1, wherein the neurological disorder is an autonomic nervous system disorder or an immunological disorder.

14. The method of claim 13, wherein the autonomic nervous system disorder is hypertension, heart rhythm disorders or sleep apnea.

15. The method of claim 1, wherein the neurological disorder is depression or obsessive-compulsive disorder.

16. The method of claim 1, wherein the neurological disorder is obesity.

17. The method of claim 1, wherein the neurological disorder comprises a regular bursting rhythm.

18. The method of claim 17, wherein the disorder is Parkinson's, epilepsy, tinnitus and phantom pain.

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19. The method of claim 1, wherein the neurological disorder comprises an irregular bursting rhythm.

20. The method of claim 19, wherein the disorder is dystonia or chorea.

21. The method of claim 1, wherein the nerve tissue is associated with peripheral neuronal tissue or central neuronal tissue.

22. The method of claim 21, wherein the peripheral neuronal tissue is a nerve root or root ganglion.

23. The method of claim 21 wherein the central neuronal tissue is associated with brain tissue, spinal tissue or brainstem tissue.

24. The method of claim 23, wherein the brain tissue is thalamus/sub-thalamus, basal ganglia, medulla, hippocampus, hypothalamus or cortex.

25. The method of claim 23, wherein the brainstem tissue is the posterior pons.

26. A stimulation system for treating a neurological disorder comprising:

an implantable pulse generator that is programmable to generate a burst stimulus that comprises a plurality of groups of spike pulses, wherein the burst stimulus is substantially quiescent between the plurality of groups, wherein each spike within each group is separated by a maximum inter-spike interval and each group of spikes is separated by a minimum inter-group interval, wherein the maximum inter-spike interval is 5 milliseconds and the minimum inter-group interval is 20 milliseconds; and

a medical lead for delivering the burst stimulus from the implantable pulse generator to a patient via one or several electrodes.

27. The system of claim 26, wherein the medical lead is implanted in a patient such that one or several electrodes provide the burst stimulus to central nervous tissue or peripheral nervous tissue.

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28. The system of claim 26 wherein the implantable pulse generator is adapted to detect hyperactivity within neural tissue using a sensor associated with the implantable pulse generator.

29. The system of claim 28 wherein the sensor is coupled to one or several electrodes of the medical lead.

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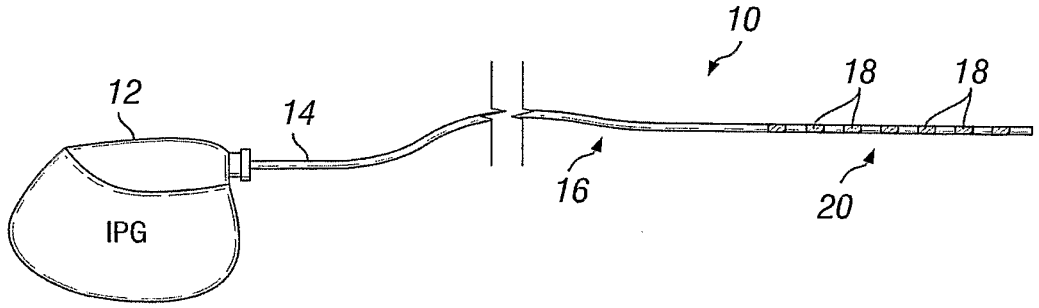


FIG. 1A

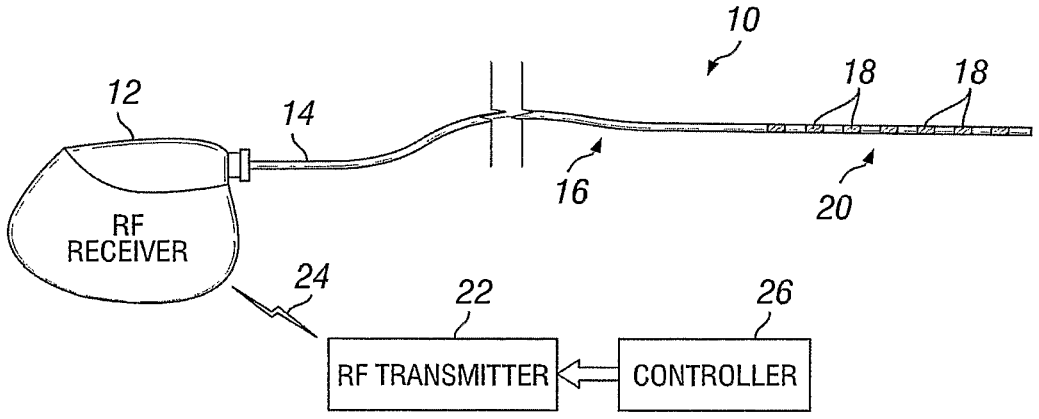


FIG. 1B

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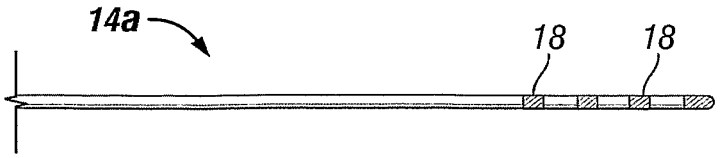


FIG. 2A

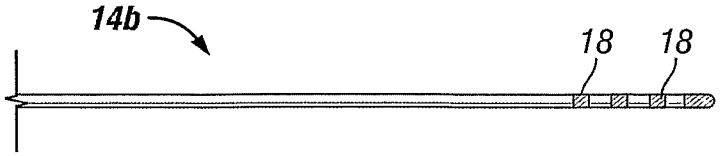


FIG. 2B

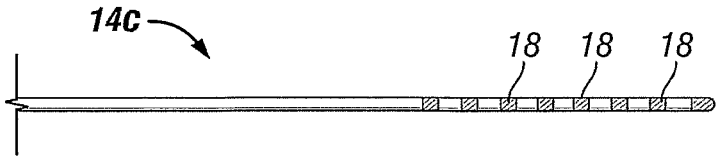


FIG. 2C

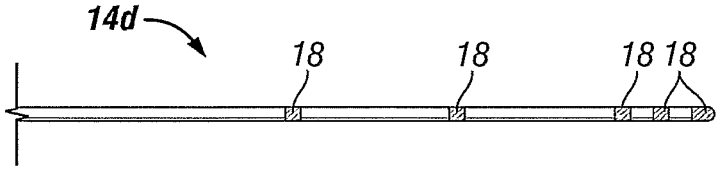


FIG. 2D

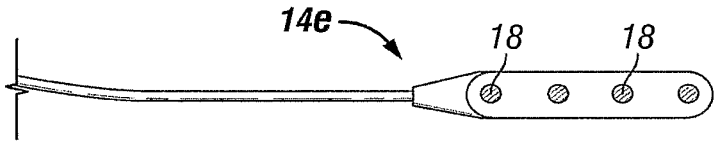


FIG. 2E

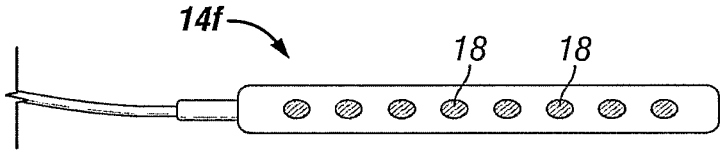


FIG. 2F

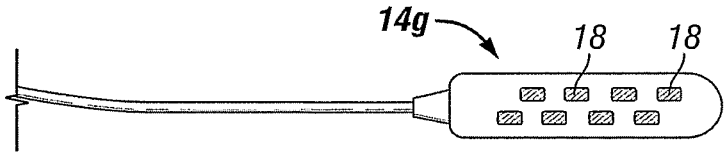


FIG. 2G

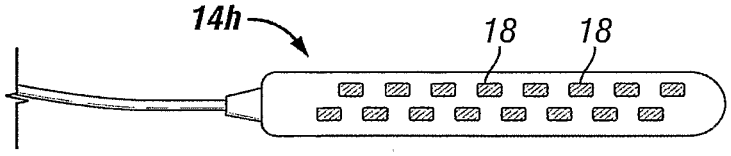


FIG. 2H

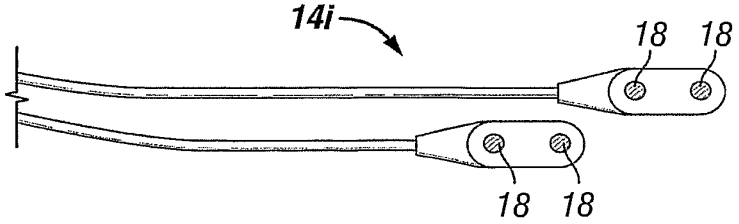
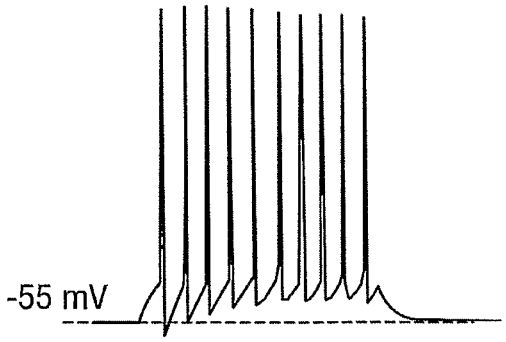


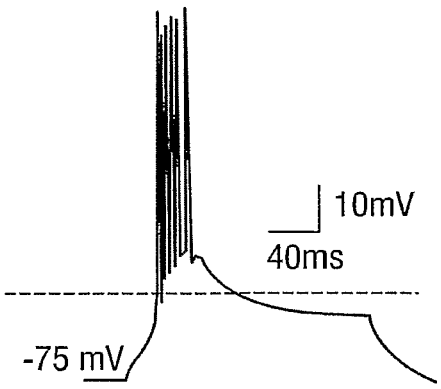
FIG. 2I

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Regular Firing

FIG. 3A



Burst Firing

FIG. 3B

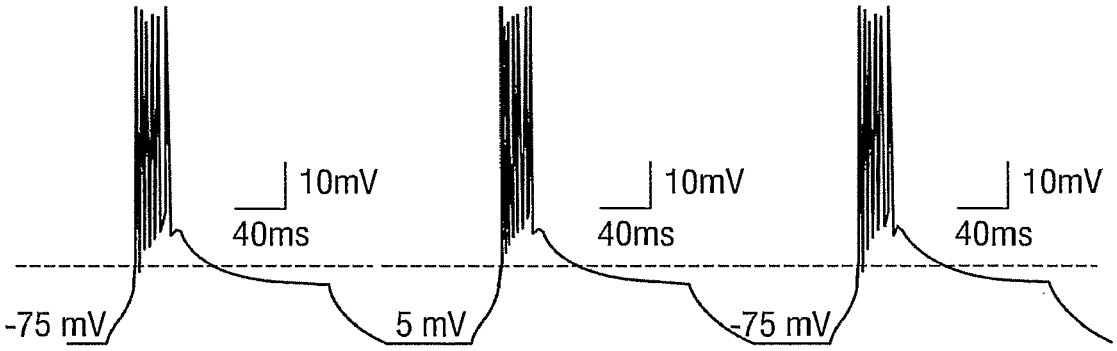


FIG. 4A

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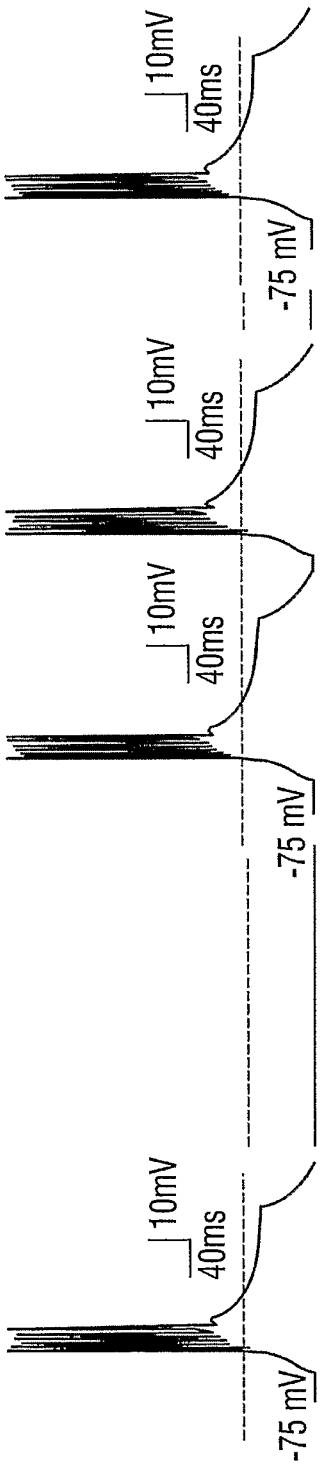


FIG. 4B

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INTERNATIONAL SEARCH REPORT

ınal application No
PCT/US2005/037736

A. CLASSIFICATION OF SUBJECT MATTER
A61N1/05 A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/133248 A1 (FREI MARK G ET AL) 8 July 2004 (2004-07-08) paragraphs [0002], [0054] - [0070], [0152] - [0185]; figures 11,12	26-29
X	US 2004/193231 A1 (DAVID TAMIR B ET AL) 30 September 2004 (2004-09-30) paragraphs [0382], [0383]	26
A	EP 1 145 735 A (NEUROPACE, INC) 17 October 2001 (2001-10-17) the whole document	26-29
A	WO 03/010540 A (NYXIS NEUROTHERAPIES, INC; MOSKAL, JOSEPH, R) 6 February 2003 (2003-02-06) the whole document	26-29

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 March 2006	18/04/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Aronsson, F

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INTERNATIONAL SEARCH REPORT

inal application No
PCT/US2005/037736

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 581 046 B1 (AHISSAR EHUD) 17 June 2003 (2003-06-17) the whole document	26-29

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

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ıational application No.
PCT/US2005/037736

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-25
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapyClaims 1-25 refer to therapeutic methods of treatment practised on the human or animal body, due to the application of stimulus to nerve tissue.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT

information on patent family members

nal application No
PCT/US2005/037736

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2004133248 A1	08-07-2004	NONE	
US 2004193231 A1	30-09-2004	NONE	
EP 1145735 A	17-10-2001	US 2005222641 A1 US 6944501 B1	06-10-2005 13-09-2005
WO 03010540 A	06-02-2003	NONE	
US 6581046 B1	17-06-2003	NONE	

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
28 September 2006 (28.09.2006)

PCT

(10) International Publication Number
WO 2006/102591 A2

(51) International Patent Classification:
A61N 1/08 (2006.01)

(21) International Application Number:
PCT/US2006/010784

(22) International Filing Date: 24 March 2006 (24.03.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/664,729 24 March 2005 (24.03.2005) US

(71) Applicant *(for all designated States except US)*: **VANDERBILT UNIVERSITY** [US/US]; 1207 17TH AVENUE SOUTH, Suite 105, Nashville, Tennessee 37212 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **ZEALEAR, David, L.** [US/US]; 6837 Pennywell Drive, Nashville, Tennessee 37205 (US).

(74) Agent: **WILSON, Jeffrey, L.**; JENKINS, WILSON, TAYLOR & HUNT, P.A., UNIVERSITY TOWER SUITE 1200, 3100 Tower Boulevard, Durham, North Carolina 27707 (US).

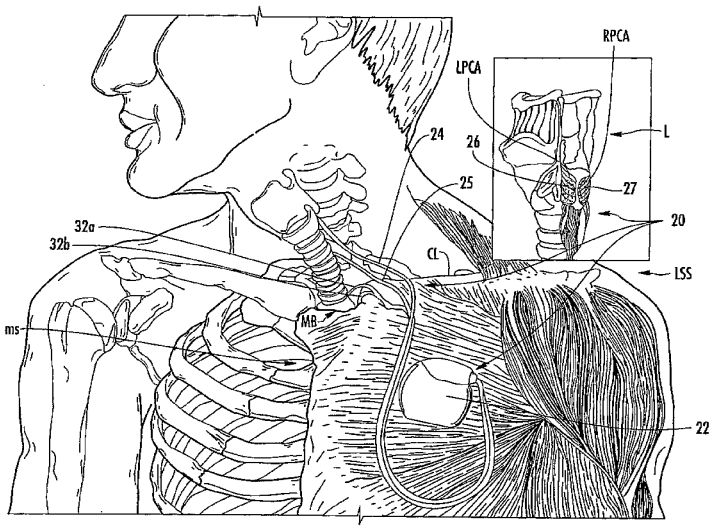
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) **Title:** RESPIRATORY TRIGGERED, BILATERAL LARYNGEAL STIMULATOR TO RESTORE NORMAL VENTILATION IN VOCAL FOLD PARALYSIS



(57) **Abstract:** A laryngeal stimulation system including a sensor for detecting an occurrence of a respiratory signal in a subject and a laryngeal stimulator adapted for coupling to a laryngeal muscle and operable to stimulate the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal is provided. A method for laryngeal stimulation including detecting an occurrence of a respiratory signal in a subject and then stimulating a laryngeal muscle in response to detecting the occurrence of the respiratory signal is also provided.

WO 2006/102591 A2

DESCRIPTION

RESPIRATORY TRIGGERED, BILATERAL LARYNGEAL STIMULATOR TO RESTORE NORMAL VENTILATION IN VOCAL FOLD PARALYSIS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Patent Application Serial No. 60/664,729, filed March 24, 2005; the disclosure of which is incorporated herein by reference in its entirety.

GOVERNMENT INTEREST

The presently disclosed subject matter was made with U.S. Government support under Grant No. RO1 DC001149 awarded by National Institutes of Health. Thus, the U.S. Government has certain rights in the subject matter.

TECHNICAL FIELD

The presently disclosed subject matter relates to laryngeal stimulation systems and methods of using the same. In particular embodiments, the presently disclosed subject matter relates to a laryngeal stimulation system that can provide independent bilateral stimulation of multiple laryngeal muscles in response to detection of a respiratory signal in a subject and methods of using the system for stimulating laryngeal muscles, particularly as applied to inducing abduction of vocal folds to facilitate normal breathing.

ABBREVIATIONS

°C	=	degrees Celsius
BVFP	=	bilateral vocal fold paralysis
EMG	=	electromyographic
ENG	=	electroneurographic
FES	=	functional electrical stimulation
g	=	grams
h	=	hours
kg	=	kilograms
M	=	molar

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mL	=	milliliters
mm	=	millimeters
mM	=	millimolar
PCA	=	posterior cricoarytenoid
RLN	=	recurrent laryngeal nerve

BACKGROUND

Bilateral laryngeal paralysis is a serious and often life-threatening clinical condition. The recurrent laryngeal nerve (RLN) carries motor fibers that innervate both the abductor (posterior cricoarytenoid, PCA) muscle and adductor muscles of the vocal folds. Damage to the nerve compromises both of these functions and arrests the vocal folds in a near-closed position. In cases of bilateral vocal fold paralysis (BVFP), voice tends to be functional but airway embarrassment is often severe enough to warrant emergency tracheotomy to relieve inspiratory stridor and dyspnea.[1,2] If spontaneous recovery from nerve injury does not occur within one year, it is likely the patient will be chronically paralyzed. In such instances, long-term tracheostomy could be considered. Unfortunately, permanent tracheostomy is known to have the complications of tracheal stenosis, chronic infection, and psycho-social impairment.[3-5]

For this reason, laryngeal surgery is usually recommended to enlarge the airway and restore breathing through the mouth. Procedures such as arytenoidectomy and cordotomy, regarded as the standard of care for enlarging the airway, also have inherent complications [6-9]. Specifically, they destroy voice and compromise airway protection during swallowing.

As such, there is presently an unmet need for improved therapies for the treatment of laryngeal paralysis to facilitate return of normal ventilation.

SUMMARY

This Summary lists several embodiments of the presently disclosed subject matter, and in many cases lists variations and permutations of these embodiments. This Summary is merely exemplary of the numerous and varied embodiments. Mention of one or more representative features of a given

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embodiment is likewise exemplary. Such an embodiment can typically exist with or without the feature(s) mentioned; likewise, those features can be applied to other embodiments of the presently disclosed subject matter, whether listed in this Summary or not. To avoid excessive repetition, this Summary does not list or suggest all possible combinations of such features.

In accordance with the presently disclosed subject matter, a laryngeal stimulation system is provided. In some embodiments, all or part of the system is implantable within the subject. In some embodiments, the laryngeal stimulation system comprises a sensor for detecting an occurrence of a respiratory signal in a subject and a laryngeal stimulator adapted for coupling to a laryngeal muscle and operable to stimulate the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal. In some embodiments the respiratory signal comprises an inspiratory phase. In some embodiments, the laryngeal muscle is one or more PCA muscles. In some embodiments, the stimulator is operable to reanimate the laryngeal muscle. In some embodiments, the laryngeal muscle is one of paralyzed, denervated, synkinetically reinnervated, and combinations thereof. In some embodiments, the stimulation of the laryngeal muscle abducts vocal folds of the subject. In some embodiments, the subject suffers from bilateral vocal fold paralysis.

In some embodiments of the system, the sensor is adapted for positioning adjacent to an intrapleural space of the subject. In some embodiments, the sensor is adapted for positioning within a mediastinum of the subject. In some embodiments, the sensor is adapted for positioning within a manubrium of the subject.

In some embodiments of the system, the sensor comprises a nerve cuff adapted for attachment to a nerve of the subject, such as for example a phrenic nerve, and operable to detect action potentials of the nerve and transmit a signal to the laryngeal simulator for indicating the occurrence of an action potential. In some embodiments, the nerve cuff comprises a plurality of electrodes for detecting the action potentials of the nerve. In some embodiments, the laryngeal stimulation system comprises electrical circuitry coupled to the sensor for amplifying and conditioning the signal indicating the action potential. Further, in some embodiments, the sensor is adapted to

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indicate the occurrence of an action potential in response to the action potential having a predetermined relationship with respect to a threshold.

In some embodiments of the system, the sensor comprises a differential pressure transducer adapted to detect a pressure difference between intrapleural pressure of the subject and atmospheric pressure, wherein the difference indicates the occurrence of the respiratory signal.

In some embodiments of the system, the laryngeal muscle is a first laryngeal muscle, the stimulator is adapted for attachment to a second laryngeal muscle, and the stimulator is operable to stimulate the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

In some embodiments of the system, the stimulator is operable to provide electrical stimulation to the laryngeal muscle.

In some embodiments of the system, the stimulator comprises first and second electrically-conductive rods adapted for insertion into the first and second laryngeal muscles, respectively, and wherein the first and second electrically-conductive rods are operable to emit an electrical signal for stimulating the first and second laryngeal muscles, respectively.

In some embodiments of the system, the stimulator is operable to provide independent bilateral stimulation of the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal with respect to each muscle.

In some embodiments of the system, the stimulator comprises a plurality of electrodes operable to emit an electrical signal for stimulating the laryngeal muscle. In some embodiments, the stimulator comprises an electrode array operable to emit an electrical signal for stimulating the laryngeal muscle. Further, in some embodiments, the stimulator comprises a paddle-shaped body including a first side, and wherein the electrode array is arranged on the first side of the paddle-shaped body. Still further, in some embodiments, the electrode array is arranged in a plurality of columns.

In some embodiments of the system, the stimulator comprises a pulse generator for emitting electrical pulses to stimulate the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal. In

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some embodiments, the emitted electrical pulses are square-wave pulses. Further, in some embodiments, the square-wave pulses include pulse durations from about 1 to about 2 milliseconds. Still further, in some embodiments, the emitted electrical pulses are emitted at a frequency of from about 30 to about 40 pulses per second and in some embodiments the pulses have an amplitude ranging from about 2 milliamps to about 20 milliamps.

In some embodiments, the system further comprises a timer for determining whether the respiratory signal is detected within a predetermined time interval, and the laryngeal stimulator is adapted to stimulate the laryngeal muscle in response to the timer not detecting the occurrence of the respiratory signal within the predetermined time interval.

In another embodiment of the presently disclosed subject matter, a method for laryngeal stimulation is provided. In some embodiments, the method comprises detecting an occurrence of a respiratory signal in a subject and then stimulating a laryngeal muscle in response to detecting the occurrence of the respiratory signal. In some embodiments, the respiratory signal comprises an inspiratory phase. In some embodiments, stimulation of the laryngeal muscle abducts vocal folds of the subject. In some embodiments, the laryngeal muscle is a PCA muscle. Further, in some embodiments, the laryngeal muscle is paralyzed, denervated, synkinetically reinnervated, or combinations thereof. In some embodiments, the subject suffers from BVFP.

In some embodiments, detecting the occurrence of a respiratory signal comprises detecting action potentials of a nerve, such as for example a phrenic nerve, for indicating the occurrence of the respiratory signal. In some embodiments of the method, detecting the respiratory signal comprises positioning a sensor adjacent the nerve for detecting the action potentials of the nerve. In some embodiments, detecting the respiratory signal further comprises indicating the occurrence of an action potential when the action potential has a predetermined relationship with respect to a threshold.

In some embodiments, detecting the occurrence of a respiratory signal comprises detecting a pressure difference between intrapleural pressure of the subject and atmospheric pressure, wherein the difference indicates the occurrence of the respiratory signal.

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In some embodiments of the method, stimulating the laryngeal muscle comprises reanimating the laryngeal muscle in response to detecting the occurrence of the respiratory signal. In some embodiments, stimulating the laryngeal muscle comprises electrically stimulating the laryngeal muscle. In some embodiments, the laryngeal muscle is a first laryngeal muscle and a second laryngeal muscle, and comprising stimulating both first and second laryngeal muscles in response to detecting the occurrence of the respiratory signal. In some embodiments, an electrical signal (*e.g.*, electrical pulses) is emitted for stimulating the first and second laryngeal muscles. Further, in some embodiments, the first and second laryngeal muscles are stimulated independently. In particular, in some embodiments, independent bilateral stimulation of the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal is provided.

In some embodiments of the method, the electrical signals emitted are electrical pulses, which are square-wave pulses. In some embodiments, the square-wave pulses include pulse durations from about 1 millisecond to about 2 milliseconds. In some embodiments, the electrical pulses are emitted at a frequency ranging from about 30 pulses per second to about 40 pulses per second and in some embodiments, the pulses have an amplitude ranging from about 2 milliamps to about 20 milliamps.

In some embodiments, the method further comprises determining whether the respiratory signal is detected by a timer within a predetermined time interval, and comprising stimulating the laryngeal muscle in response to the timer not detecting the occurrence of the respiratory signal within the predetermined time interval.

Accordingly, it is an object of the presently disclosed subject matter to provide a respiratory triggered, bilateral laryngeal stimulation system to restore normal ventilation in vocal fold paralysis. This object is achieved in whole or in part by the presently disclosed subject matter.

An object of the presently disclosed subject matter having been stated above, other objects and advantages will become apparent to those of ordinary

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skill in the art after a study of the following Description of the presently disclosed subject matter and non-limiting Examples.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a front perspective view illustrating the laryngeal stimulation device of the presently disclosed subject matter comprising a multiprogrammable pulse generator and sensor circuits positioned in a pocket below the clavicle. The inset is a perspective view illustrating an electrode array positioned behind the PCA muscles and connected to the pulse generator for independent bilateral stimulation of the PCA muscles.

Figure 2 is a section detailed view of a larynx illustrating one embodiment of an end of a laryngeal stimulator with paddle-shaped body comprising an electrode array of button contacts (electrodes) forming two columns on the sides of each paddle and positioned to contact either the left or right PCA muscle.

Figure 3 is a side perspective view illustrating an implanted tripolar cuff sensor for recording ENG potentials from a phrenic nerve.

Figures 4A-4C illustrate several embodiments of sensors for detecting respiratory signals. Figure 4A is a perspective view of an exemplary nerve cuff. Figure 4B is a schematic diagram of an exemplary logic circuit for determining a true respiratory signal detected by a nerve cuff. Letters A, B, and C correspond to signals generated from ring electrodes **35**, **36**, and **37**shown in Figure 4A, respectively. Figure 4C is a perspective view of an exemplary pressure transducer chamber.

Figures 5A-5D are a series of oscillographic recordings from the external intercostal muscle (Figure 5A), PCA muscle (Figure 5B), and phrenic nerve (Figure 5C) in a canine subject. The trace in Figure 5D shows the rectified and integrated recording of the phrenic nerve activity, which can be inputted into the threshold detector.

Figures 6A and 6B show endoscopic video still-frames of the glottis in a patient with BVFP. Oscillographic recordings from the chest wall transducer (top trace), threshold detector (middle trace) and pulse generator (bottom trace) are superimposed on each frame of Figures 6A and 6B. A black arrow

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indicates when a still-frame was obtained relative to the phase of respiration shown in the belt transducer recording: Figure 6A shows peak expiration; and Figure 6B shows peak inspiration. White arrows identify the glottal edge.

DETAILED DESCRIPTION

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which the presently disclosed subject matter belongs. Although any methods, devices, and materials similar or equivalent to those described herein can be used in the practice or testing of the presently disclosed subject matter, representative methods, devices, and materials are now described.

Following long-standing patent law convention, the terms "a", "an", and "the" refer to "one or more" when used in this application, including the claims. Thus, for example, reference to "a muscle" (*e.g.*, "a PCA muscle") includes a plurality of such muscles (*e.g.*, a plurality of PCA muscles), and so forth.

Unless otherwise indicated, all numbers expressing quantities of ingredients, reaction conditions, electrical measurements and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about". Accordingly, unless indicated to the contrary, the numerical parameters set forth in this specification and attached claims are approximations that can vary depending upon the desired properties sought to be obtained by the presently disclosed subject matter.

As used herein, the term "about," when referring to a value or to an amount of mass, weight, time, quantity, volume, current, concentration or percentage is meant to encompass variations of in some embodiments ±20%, in some embodiments ±10%, in some embodiments ±5%, in some embodiments ±1%, in some embodiments ±0.5%, and in some embodiments ±0.1% from the specified value, as such variations are appropriate.

I. Laryngeal Stimulation System

The presently disclosed subject matter provides a system or device to restore "normal ventilation" (*i.e.*, meet respiratory needs) by relieving airway obstruction in a subject due to, for example, impairment of mobility of the vocal

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folds, including bilateral impairment, using an implantable (optionally, totally implantable) laryngeal stimulation system.

The terms "subject" and "patient" are used interchangeably herein and each term refers preferably to a vertebrate subject or patient. A representative vertebrate is warm-blooded; a representative warm-blooded vertebrate is a mammal. A representative mammal is a human. As used herein, the terms "subject" and "patient" include both human and animal subjects. Thus, veterinary therapeutic uses are provided in accordance with the presently disclosed subject matter.

As such, the presently disclosed subject matter provides for the treatment of mammals such as humans, as well as those mammals of importance due to being endangered, such as Siberian tigers; of economic importance, such as animals raised on farms for consumption by humans; and/or animals of social importance to humans, such as animals kept as pets or in zoos. Examples of such animals include but are not limited to: carnivores such as cats and dogs; swine, including pigs, hogs, and wild boars; ruminants and/or ungulates such as cattle, oxen, sheep, giraffes, deer, goats, bison, and camels; and horses. Also provided is the treatment of birds, including the treatment of those kinds of birds that are endangered and/or kept in zoos, as well as fowl, and more particularly domesticated fowl, *i.e.*, poultry, such as turkeys, chickens, ducks, geese, guinea fowl, and the like, as they are also of economic importance to humans. Thus, also provided is the treatment of livestock, including, but not limited to, domesticated swine, ruminants, ungulates, horses (including race horses and show horses), poultry, and the like.

The phrase "impairment of mobility of the vocal folds" refers to a decreased ability of the vocal cords to abduct, such decrease being sufficient to result in respiratory compromise of the patient, which is manifested by the subjective symptom of shortness of breath and/or the objective clinical signs of stridor and restricted peak inspiratory flow. Bilateral vocal fold paralysis (BVFP) is one non-limiting example of an impairment of mobility of the vocal folds, as the term is used herein. The impairment of mobility can result from a deficit in nerve or muscle or both. For example, but not by way of limitation, the

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impairment can result from laryngeal muscle paralysis, denervation, synkinetic reinnervation, and combinations thereof.

The phrases "meet respiratory needs" and "normal ventilation" refer to the amount of ventilation necessary and/or desirable to satisfy the patient's oxygen requirements and/or render the patient subjectively comfortable during periods of resting or aerobic stress, such as periods of exertion, emotional excitement, exposure to high altitude, etc.

Normal ventilation can be restored in both timing and magnitude using a laryngeal stimulation system of the presently disclosed subject matter. In some embodiments the laryngeal stimulation system comprises a respiratory sensor, which can detect the occurrence of a respiratory signal in a subject, such as for example the initiation of the inspiratory phase of respiration, and a laryngeal muscle stimulator adapted for coupling to a laryngeal muscle, including one or more nerves or nerve terminals that innervate the laryngeal muscle. The laryngeal stimulator can stimulate the laryngeal muscle to which it is coupled in response to the sensor detecting the occurrence of the respiratory signal. Thus, "stimulating a laryngeal muscle" as the phrase is used herein refers to stimulating the laryngeal muscle directly and/or stimulating the laryngeal muscle by stimulation of one or more nerves, nerve branches, or nerve terminals that innervate the laryngeal muscle (e.g., with regard to PCA muscles, the superior laryngeal nerve, the recurrent laryngeal nerve, and branches therefrom). In some embodiments, the laryngeal stimulator comprises an electrode array which directly contacts the laryngeal muscle and/or one or more nerves that innervate the muscle and transmits a stimulating electrical impulse to the muscle, and a multiprogrammable pulse generator which emits electrical pulses transmitted to the muscle and/or an innervating nerve by the electrode array. In a particular embodiment, the stimulator terminates in a body to which the electrode array is positioned, wherein the body is either rod-shaped or paddle-shaped and tailored to the anatomy of the one or more laryngeal muscles to be stimulated (*e.g.*, left and right PCA muscles) for generation of a maximum response with conservation of electrical charge.

Referring now to the Figures, where like referenced characters refer to like parts throughout, Figures 1 and 2 illustrate one embodiment of the

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laryngeal stimulation system of the presently disclosed subject matter. Device **LSS** comprises a laryngeal stimulator **20** including a multiprogrammable pulse generator **22**, to which are attached sensor circuits. Pulse generator **22** can be surgically implanted in a pocket below a clavicle **CL** of the patient. Device **LSS** further comprises a sensor (not visible in Figures 1 and 2; two embodiments shown in Figures 3 and 4) for sensing respiratory signals and relaying those signals to laryngeal stimulator **20**. Three leads **24**, **25**, and **32** interfaced with laryngeal stimulator **20** can be tunneled to an incision in the anterior neck. A first and a second stimulus lead **24** and **25** each terminate in a rod- or paddle-shaped first and second body **26** and **27**, respectively. First and second laryngeal stimulator bodies **26** and **27** comprise a first side **28** (best seen in Figure 2) having an array of electrodes **29** arranged thereon that contacts or closely approximates the laryngeal muscle and/or innervating nerves or nerve branches. As shown in the inset of Figure 1, first and second bodies **26** and **27** are positioned on each side of the larynx **L** in a subperichondrial or submuscular pocket beneath left and right PCA muscles **LPCA** and **RPCA**. The insert of Figure 1 shows paddle-shaped bodies **26** and **27** in position following implantation. Lead **32** of device **LSS** further comprises first and second sensor leads **32a** and **32b**, each terminating in a pressure sensitive chamber **31** (not visible in Figure 1), positioned in some embodiments in the mediastinum **MS**, with the active chamber (that is, the chamber that senses intrapleural pressure) near the intrapleural space and the reference chamber (that is, the chamber that senses atmospheric pressure) positioned a few centimeters away from the intrapleural space, so as not to detect any respiratory signal.

I.A. Laryngeal Muscle Stimulator

A multiprogrammable pulse generator, for example pulse generator **22** in Figure 1, can provide independent stimulation of laryngeal muscles bilaterally. For example, pulse generator **22** can provide for independent bilateral stimulation of a first and a second laryngeal muscle, such as for example left and right PCA muscles **LPCA** and **RPCA**, to reanimate the muscles, in turn resulting in abduction of the vocal folds by both muscles and restoring ventilation to normal. The term "abduction of vocal folds" refers to that amount

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of abduction sufficient to permit inspiration, to relieve stridor, and/or to increase the peak inspiratory flow.

The presently disclosed laryngeal stimulation system can comprise a demand-type pacemaker functioning as a laryngeal stimulator (referred to as **20** in Figure 1) which, when coupled with an inspiratory sensor, can sense changes in ventilatory need and adjust timing of vocal fold opening in synchrony with inspiration. Thus, one aspect of the presently disclosed laryngeal stimulation system includes the independent bilateral stimulation of first and second laryngeal muscles (*e.g.*, left and right PCA muscles **LPCA** and **RPCA**) by a laryngeal stimulator in response to a respiratory signal (*e.g.*, an inspiratory phase signal) detected by a respiratory sensor.

In some embodiments of the presently disclosed subject matter, a laryngeal stimulator comprising a terminal body with an electrode array having electrode contacts that are smaller and more closely spaced is provided, such as for example first and second bodies **26** and **27** comprising an array of electrodes **29** arranged on first side **28**, as shown in Figure 2. Continuing with Figure 2, shown is a portion of larynx **L** with paddle-like electrode first and second bodies **26** and **27** inserted therein. Electrodes **29** can be arrayed on paddle-shaped bodies **26** and **27** forming two parallel columns on each body **26** and **27**. Electrodes **29** can be "button contacts" in some embodiments. This type of paddle-shape is symmetrical and could be used for either left or right PCA muscle **LPCA** and **RPCA**. Once inserted into a PCA pocket, a column of electrode contacts can be situated optimally for activation of a synkinetically reinnervated muscle, and avoid stray activation of antagonistic adductor nerve fibers. Eyelets **21** at the base of each of first and second bodies **26** and **27** can be used as an anchor by suturing each of first and second bodies **26** and **27** to the cricoid cartilage (not shown in Figure 2). A wire stylet **23** can be inserted through stimulus leads **24** and **25** and extended to the tip of paddle-shaped bodies **26** and **27** to give rigidity to the stimulus leads **24** and **25** and bodies **26** and **27** during insertion into the pocket. First and second bodies **26** and **27** can comprise any suitable material, including but not limited to an elastic material such as a silastic DACRON®-mesh patch (Invista North America, Wilmington, Delaware, U.S.A.). However, a stiffer material can also be used if greater

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stability and longevity is desired. Once each of first and second bodies **26** and **27** is implanted, stylet **23** can be removed.

This embodiment effectively increases the number of electrode channels available for laryngeal muscle stimulation by at least twofold over systems currently under study in the art. The additional channels provide redundancy in face of a potential shift in electrode **29** position or loss of channel, both of which have been encountered in the art. For example, in some embodiments, each electrode **29** in the electrode array can be one-and-a-half millimeters wide with one-and-a-half millimeters between channels.

Another potential disadvantage of a rod-shaped electrode used in prior art systems is that once placed in a pocket between the PCA muscle and underlying cricoid cartilage, the charge emanating from the cartilage side would be wasted. Thus, particular embodiments of the presently disclosed subject matter provide, such as those shown in Figures 1 and 2, an array of electrodes **29** is positioned on first side **28** of paddle-shaped body **26** or **27** of laryngeal stimulator **20**, where button electrodes **29** contact against the PCA muscle **LPCA** or **RPCA** and/or innervating nerves, while the opposite surface of paddle-shaped body **26** or **27** can contain no electrodes **29**. The paddle shape can prevent body **26** or **27** from rotating 180 degrees and disrupting proper alignment. In some embodiments, electrodes **29** can be arranged in two to three columns, running down a long axis of body **26** or **27** (Figure 2). The flexibility of having more than one column of contact electrodes **29** can increase the redundancy two to three times over that of a rod-shaped electrode array. Increased number of contacts can require a decrease in button contact surface area to hold the total surface area and electrode impedance relatively constant. In some embodiments of the presently disclosed subject matter, rectangular rather than circular contact electrodes **29** are incorporated into the electrode array to minimize shunting between adjacent contact electrodes **29**.

In some embodiments, multiprogrammable pulse generator, shown at **22** in Figure 1, can include a power supply, a stimulus generation circuit, a sensor conditioning and trigger circuit, and a radio frequency receiver. Stimulation and sensor parameters can be programmed through the skin after implantation using an external programmer and radio frequency transmitter. In one

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embodiment, the circuits in the implantable system are powered by a non-rechargeable lithium battery (*e.g.*, Genesis XP model, Advanced Neuromodulation Systems, Plano, Texas, U.S.A.). A calculation of charge utilization by this circuit during bilateral laryngeal muscle stimulation presently estimates battery life to be six to eight years. In another embodiment, the battery utilized can be one that is recharged through the skin, extending the lifetime to as long as twenty years. This represents a significant improvement over the power supply used in earlier clinical trials in which the battery lifespan was only approximately three and a half years.

Continuing with Figures 1 and 2, multiprogrammable laryngeal stimulator **20** facilitates bilateral laryngeal muscle stimulation with each muscle (*e.g.*, each PCA muscle **LPCA** and **RPCA**) controlled independently. The prior art unifunctional stimulator devices can deliver only a single paradigm and therefore cannot activate both left and right PCA muscles **LPCA** and **RPCA** optimally where the electrode positions differ relative to their respective PCA muscle. Thus, the presently disclosed subject matter differs advantageously from the prior art in which a single stimulus paradigm is used to produce abduction on only one side of the larynx. Even though it is possible to close the tracheostomy and return breathing through the mouth with unilateral stimulation, the patient is still relegated to a relatively sedentary lifestyle. In contrast, the presently disclosed subject matter provides in some embodiments a stimulator capable of independent bilateral stimulation, which can restore a normal level of ventilation and allow the patient to lead an active lifestyle.

The presently disclosed subject matter further provides a stimulus paradigm incorporated within the laryngeal stimulator effective for activation of denervated or synkinetically reinnervated laryngeal muscles. A stimulus train of biphasic, charge-balanced square-wave pulses can be delivered to produce laryngeal muscle stimulation (*e.g.*, PCA muscle **LPCA** and/or **RPCA** stimulation) bilaterally, resulting in contraction of the laryngeal muscle and abduction of the vocal folds during inspiration.

The pulse duration can differ from that generally used to activate innervated muscles paralyzed from a central nervous system injury. In this case, muscles are activated indirectly through their nerve terminals, and require

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only a short pulse duration. Based on this requirement, most commercial stimulators designed for activation of nervous tissue are programmed for pulse durations of less than 0.1-0.2 milliseconds. In the case of denervated muscle, muscle fibers must be activated directly and can require longer pulse durations of 1-2 milliseconds. In most instances, synkinetic reinnervation of laryngeal muscle also occurs. Muscle activation is mediated indirectly through nerve terminal stimulation, yet longer pulse durations are required than for that activation of normally innervated muscle. In some embodiments of the presently disclosed subject matter, longer pulse durations (*e.g.*, about 1-2 milliseconds or longer) are beneficial for activation of denervated or synkinetically human laryngeal muscles.

In some embodiments, the pulse train can be delivered at a frequency of approximately 30-40 pulses per second to produce a fused, tetanizing contraction of the PCA muscle and a smooth abduction of the vocal fold. Further, in some embodiments, the laryngeal stimulator disclosed herein provides for a train rate that can be varied depending on the respiratory rate, with a stimulus train triggered by an inspiratory sensor. Train duration can be set by the decline of the inspiratory signal below a predetermined threshold level. In some embodiments, the stimulation duty cycle can be around 50%. However, during rapid breathing with exercise, the stimulus "on" time can be programmed to not be allowed to fall below a minimum level (*e.g.*, about 1.0 seconds). In some embodiments, the amplitude of the stimulus required can be varied from about 2 milliamps to about 20 milliamps, in some embodiments from about 5 milliamps to about 15 milliamps, and in some embodiments from about 8 milliamps to about 12 milliamps, depending upon a number of factors, including for example the total contact surface area in apposition to a laryngeal muscle (*e.g.*, PCA muscle **LPCA** and/or **RPCA**), the muscle-contact distance, the resistance of intervening tissue (*i.e.*, fibrosis), and the degree of current shunting between cathode and anode poles. The parameter requirements can be varied from muscle to muscle (*e.g.*, left and right PCA muscles **LPCA** and **RPCA**) within a patient, or between patients because of these variables. The stimulus requirements can also vary depending upon the degree of muscle denervation, reinnervation and atrophy and the laryngeal stimulation device

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disclosed herein can accommodate the varying requirements.

I.B. Respiratory Signal Sensor

The presently disclosed subject matter provides in some embodiments a laryngeal stimulation system comprising a respiratory signal sensor (*e.g.*, an inspiratory sensor) for triggering and controlling one or more laryngeal muscles, including for example PCA muscles **LPCA** and **RPCA**, seen in Figures 1 and 2. Previous laryngeal pacing devices disclosed in the art have not been coupled to a sensor of respiration, including for example a sensor of the inspiratory drive. With prior art devices, stimulation of the PCA muscle occurs in a "free-run" configuration and is not synchronized to respiration with respect to the rate and timing of inspiration. With the prior art devices, the patient must entrain his or her breathing rate to that of the device. However, failure of entrainment poses the risk of stimulated glottal opening during voice production or swallowing, leading to interruption of speech or inhalation of food.

In contrast, the laryngeal stimulation system disclosed herein comprises a sensor for detecting respiration signals, such as inspiration, to permit stimulated glottal opening which is synchronized with inspiration. Speech interruption and aspiration can thus be avoided utilizing the presently disclosed laryngeal stimulation system. Further, the "demand-type" stimulation system disclosed herein can increase the frequency of stimulated glottal opening when respiratory rate increases during exercise or stress.

There are several sources of respiratory signal (*e.g.*, inspiratory drive) from a subject available for monitoring that can be considered for use in time-controlled laryngeal muscle stimulation. For example, sensors have been used in acute animal experiments to actually trigger PCA muscle stimulation, however none of the trigger sites were demonstrated as practical for chronic laryngeal pacing, and all have inherent shortcomings. More specifically, diaphragm electromyographic (EMG) activity has been tested as a signal source since the diaphragm becomes active during each inspiration. However, chronic recording from the thin muscular layer of the diaphragm with implantable electrodes is likely to be unstable.

Tracheal elongation has also been suggested as a signal source, but this action also occurs during swallowing. Stimulated glottal opening during

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swallowing could result in aspiration, which makes use of this source potentially dangerous. A decrease in intratracheal temperature during inspiration has been studied as a signal source in acute animal experiments. Unfortunately, an indwelling tracheal thermistor would not likely be tolerated over the long term. Measurement of chest wall expansion is another choice as a trigger for laryngeal pacing. This technology utilized an external belt transducer to trigger the external pacing circuit. Yet, an external sensor would not be a suitable candidate for a totally implantable laryngeal stimulation device. In addition, false triggering would occur with extraneous chest wall movements unrelated to inspiration.

With chest wall impedance, the resistance or impedance between two fixed points in the chest wall will increase with inflation of the chest. However, it is possible the small change in impedance might be immeasurable in a patient population with airway obstruction, such as for example as occurs in BVFP. In fact, the issue of airway obstruction can impact the feasibility of every approach mentioned hereinabove.

In subjects with airway obstruction, the rate and volume of inspired air can be nonexistent or marginal because the airway is obstructed by, for example, a paralyzed glottis. With the inability to inflate the lungs through the obstruction, there can be a compensatory increase in phrenic nerve electroneurographic (ENG) activity, an increase in diaphragm EMG activity, and an increase in intrapleural pressure negativity. As such, the presently disclosed subject matter provides sensors that can measure these respiratory signals and transmit one or more of these respiratory signals to the laryngeal stimulator, such as for example laryngeal stimulator **20** seen in Figures 1 and 2, for stimulation of one or more laryngeal muscles (*e.g.*, left and right PCA muscles **LPCA** and **RPCA** in Figures 1 and 2), wherein the muscle stimulation results in opening of the obstructed airway (*e.g.*, laryngeal fold abduction) and restoration of normal ventilation. As noted hereinabove, measurement of diaphragm EMG as an accurate indicator of inspiration can be difficult in certain subjects, and therefore in these subjects it may prove advantageous to utilize sensors that measure phrenic nerve ENG activity and/or intrapleural pressure negativity preferentially.

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During inspiration, negative intrapleural pressure can be monitored directly from the intrapleural space, such as for example in subjects having an obstructed glottis. In some embodiments where negative intrapleural pressure is measured as a signal of respiration (*e.g.*, the inspiration phase of respiration), the sensor (*e.g.*, a differential pressure transducer) can be implanted in a portal made in a region of the sternum, such as for example the top portion of the sternum (*i.e.*, the manubrium **MB**), affixed to the bone and sealed in place with an adhesive. Although penetrating the intrapleural space could yield a measurement with a high signal to noise ratio, it could also potentially lead to pneumothorax and lung collapse. Therefore, in some embodiments, the pressure sensor is located near, rather than within, the intrapleural space, within the mediastinum **MS**. Mediastinum **MS**, also referred to as the "interpleural space", lies between the right and left pleura in and near the median sagittal plane of the chest. It extends from the sternum in front to the vertebral column behind, and contains all the thoracic viscera excepting the lungs. Alternatively, the pressure sensor can be placed in some embodiments directly within manubrium **MB**. In some embodiments, the pressure sensor can be positioned within the body through a primary neck incision also used to position the laryngeal muscle stimulus arrays (see Figure 1).

The pressure sensor can be a dual-chambered differential pressure transducer system. Each of the two chambers of the system can utilize the same type of sensor chamber to detect pressure changes at either an "active site" where inspiration signals are detected (the active chamber) and a "remote site" (reference chamber) where atmospheric pressure is measured and compared against pressure changes detected by the active chamber. The active chamber can be positioned to detect intrapleural pressure changes relative to atmospheric, while the reference chamber can be positioned more remotely, and would only detect the atmospheric pressure.

Referring now to Figure 4C, an exemplary pressure transducer chamber **31** for use as either the active or reference chamber of the dual-chambered differential pressure transducer system is illustrated. Chamber **31** comprises a shell case enclosing an internal space in flow communication with an open end, which is covered with an elastic membrane **39b** (*e.g.*, a biocompatible elasic

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membrane) coupled to a film **39a**. Membrane **39b** is sensitive to pressure changes, which are transferred to piezoelectric film **39a** and converted from mechanical into electrical signals. The signals are amplified and filtered by circuitry within chamber **31**. The circuitry is powered by a battery in laryngeal stimulator through lead **32**. The amplified and conditioned electrical signals are then transferred via lead **32a** or **32b** to laryngeal stimulator **20**.

A differential type of pressure transducer can be particularly beneficial, as inspiratory effort can be detected in comparison to a relative atmospheric pressure rather than according to a predetermined set value. Thus, the differential pressure transducer detects a pressure difference between the interpleural pressure of the patient and the atmospheric pressure, and if a difference is detected above a chosen threshold, it is indicative of an inspiratory phase. The respiratory signal is then transmitted to the laryngeal stimulator for stimulation of the laryngeal muscles and subsequent opening of the airway to facilitate breathing. In the face of a change in atmospheric pressure, such as might occur with a change in altitude (*e.g.,* ascendance in elevator, mountain climbing, air travel, etc.), the pressure sensor will adjust to measure a change in intrapleural pressure relevant to the new atmospheric pressure.

In some embodiments of the presently disclosed laryngeal stimulation system, a sensor comprising a nerve cuff, such as for example a phrenic nerve cuff, can be utilized for sensing inspiratory signals and for synchronous triggering of an implantable laryngeal stimulator. The phrenic nerve arises from the third, fourth, and fifth cervical spinal nerves (C3-C5). It provides motor innervation to the diaphragm and is thus responsible for the act of breathing, including stimulation of the diaphragm to initiate the inspiration phase. A nerve cuff sensor coupled to the phrenic nerve can detect action potentials of the nerve as the nerve pulse travels through the phrenic nerve to the diaphragm to initiate inspiration. The detected action potentials are registered as respiration signals by the sensor and transmitted to the laryngeal stimulator, such as for example laryngeal stimulator **20** in Figure 1. The laryngeal stimulator then stimulates the laryngeal muscle, facilitating normal ventilation as disclosed herein.

Referring now to Figures 3 and 4A, illustrated in Figure 3 is a partially

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dissected head and neck of a human subject showing a phrenic nerve **PN** with a nerve cuff **34** attached to phrenic nerve **PN**. Figure 4A shows a close-up perspective view of nerve cuff **34.** In some embodiments, a silastic nerve cuff **34** can be utilized, which can have three equally-spaced ring electrodes **35**, **36**, and **37** embedded in the inside wall, as shown in Figures 3 and 4A, which can be connected by cuff leads **38** (Figure 3) to pulse generator **22**, as shown in Figure 1. Cuff **34** has a single slit made along the length of the silastic tube for positioning cuff **34** around a nerve, such as for example phrenic nerve **PN**. In another embodiment, a self-sizing spiral cuff can be used. The self-sizing spiral cuff has a slit made in the form of a spiral, which allows it to fit around a broad range of nerves of various diameters and avoids nerve compression.

As such, a "tripolar cuff", as shown in Figures 3 and 4A, allows relatively large EMG potentials originating outside the cuff to be nullified, while relatively smaller ENG potentials from the nerve inside cuff **34** can be reproduced faithfully. More specifically, the EMG potential differences between central electrode **36** and first and second outer electrodes **35** and **37** are equal and opposite, and can be cancelled by differential amplifier recording. In contrast, action potentials propagating down phrenic nerve **PN** during inspiration would reach first outer electrode **35** and second outer electrode **37** at different times, and therefore would not cancel with differential recording, providing for an accurate measurement of nerve activity. Figure 4B diagrams an exemplary logic circuit **50** for determining the detection of true ENG potentials.

For embodiments utilizing nerve cuff sensor **34**, the conditioning and trigger circuit can include a quasi-tripole or a true-tripole type of amplifier (Figure 4B) incorporated in electrical circuitry, which is connected to cuff leads **38.** If interference from EMG activity does not cancel because of cuff imbalances due to asymmetrical tissue ingrowth into cuff **34**, then an adaptive type EMG amplifier can be substituted. The amplified output signal can be rectified and integrated following the amplifier and filter (see Figure 5). In this manner, the summated activity from axons during an inspiratory burst can be integrated and fed into the next component in sequence, a threshold detector. The threshold level can be set low enough to provide a gated PCA muscle stimulation and glottal opening sufficient for ventilation, but high enough to

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prevent any mistriggering of stimulation. For example, the threshold can be set high enough to avoid false triggering of stimulation by EMG noise or chest wall movements, resulting in aspiration or voice interruption. Further, the threshold can be set low enough to trigger stimulation during unambiguous inspiratory efforts, identified, for example, by recording of intratracheal pressure from a patient's tracheostoma or intercostal muscle EMG.

Figure 5 shows a series of oscillographic recordings from the external intercostal muscle (Figure 5A), PCA muscle Figure 5B), and phrenic nerve Figure 5C) in a canine model. The trace shown in Figure 5D provides the rectified and integrated recording of the phrenic nerve activity, which would be inputted into the threshold detector. The similarity in timing between the PCA and phrenic nerve activity confirms the applicability of measuring phrenic nerve action potentials as an appropriate inspiratory trigger signal.

Figure 6 shows stimulated abduction of the left vocal fold in a BVFP patient under the control of a chest wall expansion sensor and threshold detector circuit. While a chest wall expansion sensor may not be the preferred sensor in many BVFP patients for long-term treatment for the reasons previously stated, the figure demonstrates that stimulated glottal opening can be triggered and timed with inspiratory effort. For the phrenic nerve cuff embodiment, amplified-filtered, rectified-integrated signals can be substituted and inputted into the threshold detector to activate glottal opening. For the pressure transducer embodiment,signals from the dual-chambered pressure transducer can be fed into a differential amplifier, band-pass filtered, and inputted into the threshold detector.

In some embodiments, the sensor conditioning and trigger circuit parameters can have the flexibility to be changed telemetrically through the skin. Thus, threshold levels, amplifier gains, etc. can be changed by the external transmitter after implantation. This can be beneficial as it allows for variation in the sensor sensitivity across patients or over time in a given patient should, for example, partial encapsulation or migration of the sensor occur, weakening the signal.

To reiterate, in some embodiments, particularly those in which a subject suffers from airway obstruction due to for example BVFP, the respiratory sensor

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utilized in the presently disclosed laryngeal stimulation system can be selected based on detection specificity of compensatory changes in the respiration of the subject due to the airway obstruction. As previously noted, airway obstruction can result in compensatory respiration changes including increases in neuromuscular drive (*e.g.*, phrenic, diaphragm) and negative airway pressure. The sensors utilized in the laryngeal stimulation system disclosed herein can therefore include sensors which can detect a respiratory signal based on these compensatory respiration changes, including for example nerve cuff sensors (*e.g.*, phrenic nerve cuff sensor **34**) that measure action potentials in the monitored nerve and pressure sensor systems (*e.g.*, dual differential pressure transducer sensors **31**) that detect pressure differences between intrapleural pressures of the subject and atmospheric pressure.

I.C. Respiratory Signal Timer

In some embodiments of the presently disclosed system, laryngeal muscle stimulation continues even in the absence of a sensor signal. For example, a timer can be incorporated into the system that measures a time period between respiratory signals. If no signal is detected within a predetermined time interval, such as for example between about 5 seconds and about 10 seconds, the multiprogrammable stimulator (referred to as **22** in Figure 1) can default to a free run format until the sensor signaling falls again within the desired interval. This default feature can be a beneficial safety feature in case of failure of the sensor or loss of its capacity to detect inspiratory events.

II. Methods for Laryngeal Stimulation

The presently disclosed subject matter provides a laryngeal stimulation system as disclosed herein, which can be utilized for stimulation of one or more laryngeal muscles. The system has particular applicability for use with subjects suffering from airway obstruction due to muscular paralysis, such as resulting from for example impairment of mobility of the vocal folds, including bilateral impairment (*e.g.*, BVFP). As such, the presently disclosed subject matter provides methods for laryngeal stimulation.

In some embodiments, the method for laryngeal stimulation comprises

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detecting an occurrence of a respiratory signal in a subject and then stimulating one or more laryngeal muscles in response to detecting the occurrence of the respiratory signal. In some embodiments, for example, the respiratory signal comprises an inspiratory phase. In some embodiments, stimulation of the one or more laryngeal muscles abducts vocal folds of the subject, which in turn removes the obstruction and facilitates normal ventilation. In some embodiments, the one or more laryngeal muscles are one or more PCA muscles. Further, in some embodiments, the one or more laryngeal muscles are paralyzed, denervated, synkinetically reinnervated, or combinations thereof.

In some embodiments, detecting the occurrence of a respiratory signal comprises detecting action potentials of a nerve, such as for example a phrenic nerve, for indicating the occurrence of the respiratory signal. As discussed herein, the phrenic nerve facilitates control of the diaphragm, and nerve impulses through the phrenic nerves to the diaphragm are indicative signals of the inspiration phase of respiration. Therefore, in some embodiments of the method, detecting the respiratory signal comprises positioning a sensor, such as a nerve cuff, adjacent the nerve, for example a phrenic nerve, for detecting the action potentials of the nerve. In some embodiments, detecting the respiratory signal further comprises indicating the occurrence of an action potential when the action potential has a predetermined relationship with respect to a threshold, that is, when the action potential reaches a magnitude above a predetermined threshold that is indicative of a true respiratory signal.

In some embodiments, detecting the occurrence of a respiratory signal comprises detecting a pressure difference between intrapleural pressure of the subject and atmospheric pressure, wherein the difference indicates the occurrence of the respiratory signal. In some embodiments, a differential pressure transducer can be utilized to detect the pressure difference.

In some embodiments of the method, stimulating one or more laryngeal muscles comprises reanimating the one or more laryngeal muscles in response to detecting the occurrence of a respiratory signal. For example, in some embodiments, stimulating the one or more laryngeal muscles comprises electrically stimulating the one or more laryngeal muscles. In some embodiments, the laryngeal muscles are a first laryngeal muscle and a second

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laryngeal muscle, both of which are stimulated in response to detecting the occurrence of the respiratory signal. In some embodiments, an electrical signal (*e.g.*, electrical pulses) is emitted for stimulating the laryngeal muscles. Further, in some embodiments, the first and second laryngeal muscles are stimulated independently. In particular, in some embodiments, independent bilateral stimulation of the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal is provided.

In some embodiments of the method, the electrical signals emitted are electrical pulses, which are square-wave pulses. In some embodiments, the square-wave pulses include pulse durations from about 1 to about 2 milliseconds. In some embodiments, the electrical pulses are emitted at a frequency of ranging from about 30 to about 40 pulses per second and in some embodiments, the pulses have an amplitude ranging from about 2 milliamps to about 20 milliamps, in some embodiments from about 5 milliamps to about 15 milliamps, and in some embodiments from about 8 milliamps to about 12 milliamps.

In some embodiments, the method further comprises determining whether the respiratory signal is detected by a timer within a predetermined time interval. If the signal is not detected within the time interval, then the method further comprises stimulating the laryngeal muscle in response to the timer not detecting the occurrence of the respiratory signal within the predetermined time interval.

REFERENCES

The references listed below, as well as all references cited in the specification, are incorporated herein by reference to the extent that they supplement, explain, provide a background for, or teach methodology, techniques, and/or compositions employed herein.

1. Dedo H. The paralyzed larynx: An electromyographic study in dogs and humans. Laryngoscope 1970, 80:1455-1517.

2. Holinger L, Holinger PC, Holinger PH. Etiology of the bilateral abductor vocal

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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cord paralysis. Ann Otol 85:428-36.

3. Viau F, Ledente A, Le Tinier JY. Complications of tracheotomy. Rev Pneumol Clin 1988, 44(1):24-32.

4. Goldenberg D, Ari EG, Golz A, Danino J, Netzer A, Joachims HZ. Tracheotomy complications: a retrospective study of 1130 cases. Otolaryngol Head Neck Surg 2000, 123(4):495-500.

5. Norwood S, Vallina VL, Short K, Saigusa M, Fernandez LG, McLarty JW. Incidence of tracheal stenosis and other late complications after percutaneous tracheostomy. Ann Surg 2000, 232(2):233-41.

6. Maurizi M, Paludetti F, Galli J, Cosenza A, Di Girolamo S, Ottaviani F. CO2 laser subtotal arytenoidectomy and posterior true and false cordotomy in the treatment of post-thyroidectomy bilateral laryngeal fixation in adduction. Eur Arch Otorhinolaryngol 1999, 256(6):291-5.

7. Eckel HE, Thumfart M, Wassermann K, Vossing M, Thumfart WF. Cordectomy versus arytenoidectomy in the management in bilateral vocal cord paralysis. Ann Otol Rhinol Laryngol 1994, 103(11):852-7.

8. Lawson G, Remacle M, Hamoir M, Jamart J. Posterior cordectomy and subtotal arytenoidectomy for the treatment of bilateral vocal fold immobility: functional results. J Voice 1996, 10(3):314-9.

9. Pia F, Pisani P, Aluffi P. CO2 laser posterior ventriculocordectomy for the treatment of bilateral vocal fold paralysis. Eur Arch Otorhinolaryngol 1999, 256(8):403-6.

10. Zealear DL, Dedo H. Control of paralyzed axial muscles by electrical stimulation. Acta Otolaryngol 1977, 83:514-27.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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11. Dedo H. Studies of larynx and pharynx physiology. NIH Grant Application NS06527, 1973.

12. Obert PM, Young KA, Tobey DN. Use of direct posterior cricoarytenoid stimulation in laryngeal paralysis. Arch Otolaryngol 1984, 110:88-92.

13. Bergmann K, Warzel H, Eckhardt H-U, Gerhardt H-J. Respiratory rhythmically regulated electrical stimulation of paralyzed laryngeal muscles. Laryngoscope 1984, 94:1376-80.

14. Zealear DL, Herzon GD. Progress toward the development of a chronically implantable laryngeal pacemaker. In: Fujimura O, ed. Vocal physiology: voice production, mechanisms and functions. New York, NY: Raven Press, 1988, p. 443-8.

15. Kim GR, Choi HS, Kim GR, Hong WP, Chun YM, Park YJ. Laryngeal pacemaker using a temperature sensor in the canine. Laryngoscope 1987, 97:1207-10.

16. Otto RA, Temper J, Davis W, Homeyer D, Stroble M. Coordinated electrical pacing of vocal cord abductors in recurrent laryngeal nerve paralysis. Otolaryngol Head Neck Surg 1985, 93:634-8.

17. Broniatowski M, Kaneo S, Jacobs G, Nose Y, Tucker HM. Laryngeal pacemaker II. Electronic pacing of the posterior cricoarytenoid muscles in the canine, Laryngoscope 1985, 95:1194-8.

18. Ransom SA, Herzon GD, Troyk PR, Schwan MAK. Development of an inspiratory pressure-triggered laryngeal pacer. IEEE Trans Rehab Eng 1995, 3(4):318-23.

19. Sanders I. Electrical stimulation of laryngeal muscle. Otolaryngol Clin North Am 1991, 24:1253-74.

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20. Zrunek M, Streinzer W, Mayr W, Burian K, Thoma H, Gruber H. Experiments of acute and chronic direct electrical stimulation of glottis opening muscles. Eur Arch Otorhinolaryngol 1991, 248:445-8.

21. Zealear DL, Billante CL, Chongkolwatana C, Rho YS, Hamdan AL, Herzon GD. The effects of chronic electrical stimulation on laryngeal muscle physiology and histochemistry. J. Oto-Rhino-Laryngology & Related Specialties 2000, 62(2):81-86.

22. Zealear DL, Rainey CL, Herzon GD, Netterville JL, Ossoff RH. Electrical pacing of the paralyzed human larynx. Ann Otol Rhinol Laryngol 1996;105(9):689-93.

23. Zealear DL, Billante CR, Courey MS, Netterville JL, Paniello RC, Sanders I, Herzon GD, Goding GS, Mann W, Ejnell H, Herzon GD, Habets AMMC, Testerman R, Van de Heyning P. Reanimation of the paralyzed human larynx with an implantable electrical stimulation device. Laryngoscope 2003 Jul;113(7):1149-56.

24. Billante CR, Zealear DL, Courey MS, Netterville JL. Effect of chronic electrical stimulation of laryngeal muscle on voice. Ann Otol Rhinol Laryngol 2002;111:328-32.

25. Zealear DL, Swelstad MR, Sant'anna GD, Bannister RA, Billante CR, Rodriguez RJ, Garren KC, Billante MJ, Champney MS. Determination of the optimal conditions for laryngeal pacing with the Itrel II implantable stimulator. Otolaryngol Head Neck Surg 2001;125(3):183-92.

26. Zealear DL, Billante CR, Courey MS, Sant'anna GD, Netterville JL. Electrically stimulated glottal opening combined with adductor muscle botox blockade restores both ventilation and voice in a patient with bilateral laryngeal paralysis. Ann Otol Rhinol Laryngol. 2002; 111(6):500-6.

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27. Sanders I. Method of relieving airway obstruction in patients with bilateral vocal fold impairment. U.S. Patent No. 5,897,579; April 27, 1999.

It will be understood that various details of the presently disclosed subject matter may be changed without departing from the scope of the present subject matter. Furthermore, the foregoing description is for the purpose of illustration only, and not for the purpose of limitation.

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CLAIMS

What is claimed is:

1. A laryngeal stimulation system comprising:

(a) a sensor for detecting an occurrence of a respiratory signal in a subject; and

(b) a laryngeal stimulator adapted for coupling to a laryngeal muscle and operable to stimulate the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

2. The laryngeal stimulation system of claim 1, wherein the respiratory signal comprises an inspiratory phase.

3. The laryngeal stimulation system of claim 1, wherein the sensor is adapted for positioning adjacent to an intrapleural space of the subject.

4. The laryngeal stimulation system of claim 1, wherein the sensor is adapted for positioning within a mediastinum of the subject.

5. The laryngeal stimulation system of claim 1, wherein the sensor is adapted for positioning within a manubrium of the subject.

6. The laryngeal stimulation system of claim 1, wherein the sensor comprises a nerve cuff adapted for attachment to a nerve of the subject and operable to detect action potentials of the nerve and transmit a signal to the laryngeal simulator for indicating the occurrence of an action potential.

7. The laryngeal stimulation system of claim 6, wherein the nerve is a phrenic nerve.

8. The laryngeal stimulation system of claim 6, wherein the nerve cuff comprises a plurality of electrodes for detecting the action potentials of the nerve.

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9. The laryngeal stimulation system of claim 6, comprising electrical circuitry coupled to the sensor for amplifying and conditioning the signal indicating the action potential.

10. The laryngeal stimulation system of claim 6, wherein the sensor is adapted to indicate the occurrence of an action potential in response to the action potential having a predetermined relationship with respect to a threshold.

11. The laryngeal stimulation system of claim 1, wherein the sensor comprises a differential pressure transducer adapted to detect a pressure difference between intrapleural pressure of the subject and atmospheric pressure, wherein the difference indicates the occurrence of the respiratory signal.

12. The laryngeal stimulation system of claim 1, wherein the laryngeal muscle is a posterior cricoarytenoid (PCA) muscle.

13. The laryngeal stimulation system of claim 1, wherein the stimulator is operable to reanimate the laryngeal muscle.

14. The laryngeal stimulations system of claim 1, wherein the laryngeal muscle is one of paralyzed, denervated, synkinetically reinnervated, and combinations thereof.

15. The laryngeal stimulation system of claim 1, wherein the stimulator is operable to provide electrical stimulation to the laryngeal muscle.

16. The laryngeal stimulation system of claim 1, wherein the laryngeal muscle is a first laryngeal muscle, the stimulator is adapted for attachment to a second laryngeal muscle, and the stimulator is operable to stimulate the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

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17. The laryngeal stimulation system of claim 1, wherein the laryngeal muscle is a first laryngeal muscle, and wherein the stimulator is operable to independently stimulate the first laryngeal muscle and a second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

18. The laryngeal stimulation system of claim 17, wherein the stimulator is operable to provide independent bilateral stimulation of the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal with respect to each muscle.

19. The laryngeal stimulation system of claim 1, wherein the stimulator comprises a plurality of electrodes operable to emit an electrical signal for stimulating the laryngeal muscle.

20. The laryngeal stimulation system of claim 1, wherein the stimulator comprises an electrode array operable to emit an electrical signal for stimulating the laryngeal muscle.

21. The laryngeal stimulation system of claim 20, wherein the stimulator comprises a paddle-shaped body including a first side, and wherein the electrode array is arranged on the first side of the paddle-shaped body.

22. The laryngeal stimulation system of claim 21, wherein the electrode array is arranged in a plurality of columns.

23. The laryngeal stimulation system of claim 1, wherein the stimulator comprises a pulse generator for emitting electrical pulses to stimulate the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

24. The laryngeal stimulation system of claim 23, wherein the emitted electrical pulses are square-wave pulses.

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25. The laryngeal stimulation system of claim 24, wherein the square-wave pulses include pulse durations from about 1 to about 2 milliseconds.

26. The laryngeal stimulation system of claim 24, wherein the emitted electrical pulses are emitted at a frequency from about 30 to about 40 pulses per second.

27. The laryngeal stimulation system of claim 24, wherein the pulses have an amplitude ranging from about 2 to about 20 milliamps.

28. The laryngeal stimulation system of claim 1, comprising a timer for determining whether the respiratory signal is detected within a predetermined time interval, and the laryngeal stimulator is adapted to stimulate the laryngeal muscle in response to the timer not detecting the occurrence of the respiratory signal within the predetermined time interval.

29. The laryngeal stimulation system of claim 1, wherein the stimulation of the laryngeal muscle abducts vocal folds of the subject.

30. The laryngeal stimulation system of claim 1, wherein all or part of the system is implantable within the subject.

31. The laryngeal stimulation system of claim 30, wherein the subject suffers from bilateral vocal fold paralysis.

32. A method for laryngeal stimulation, the method comprising:

(a) detecting an occurrence of a respiratory signal in a subject; and

(b) stimulating a laryngeal muscle in response to detecting the occurrence of the respiratory signal.

33. The method of claim 32, wherein the respiratory signal comprises an inspiratory phase.

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34. The method of claim 32, comprising detecting action potentials of a nerve for indicating the occurrence of the respiratory signal.

35. The method of claim 34, wherein the nerve is a phrenic nerve.

36. The method of claim 34, comprising positioning a sensor adjacent the nerve for detecting the action potentials of the nerve.

37. The method of claim 34, comprising indicating the occurrence of an action potential when the action potential has a predetermined relationship with respect to a threshold.

38. The method of claim 32, comprising detecting a pressure difference between intrapleural pressure of the subject and atmospheric pressure, wherein the difference indicates the occurrence of the respiratory signal.

39. The method of claim 32, wherein the laryngeal muscle is a posterior cricoarytenoid (PCA) muscle.

40. The method of claim 32, wherein the laryngeal muscle is one of paralyzed, denervated, synkinetically reinnervated, and combinations thereof.

41. The method of claim 32, comprising reanimating the laryngeal muscle in response to detecting the occurrence of the respiratory signal.

42. The method of claim 32, comprising electrically stimulating the laryngeal muscle.

43. The method of claim 32, wherein the laryngeal muscle is a first laryngeal muscle, and comprising stimulating a second laryngeal muscle in response to detecting the occurrence of the respiratory signal.

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44. The method of claim 43, comprising emitting an electrical signal for stimulating the first and second laryngeal muscles.

45. The method of claim 32, wherein the laryngeal muscle is a first laryngeal muscle, and comprising stimulating a second laryngeal muscle independent of the first laryngeal muscle and in response to detecting the occurrence of the respiratory signal.

46. The method of claim 45, comprising providing independent bilateral stimulation of the first laryngeal muscle and the second laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal with respect to each muscle.

47. The method of claim 32, comprising emitting electrical pulses for stimulating the laryngeal muscle in response to the sensor detecting the occurrence of the respiratory signal.

48. The method of claim 47, wherein the emitted electrical pulses are square-wave pulses.

49. The method of claim 47, wherein the square-wave pulses include pulse durations from about 1 to about 2 milliseconds.

50. The method of claim 47, wherein the emitted electrical pulses are emitted at a frequency of ranging from about 30 to about 40 pulses per second.

51. The method of claim 47, wherein the pulses have an amplitude ranging from about 2 to about 20 milliamps.

52. The method of claim 32, comprising determining whether the respiratory signal is detected by a timer within a predetermined time interval, and comprising stimulating the laryngeal muscle in response to the timer not detecting the occurrence of the respiratory signal within the predetermined time

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interval.

53. The method of claim 32, wherein the stimulation of the laryngeal muscle abducts vocal folds of the subject.

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54. The method of claim 32, wherein the subject suffers from bilateral vocal fold paralysis.

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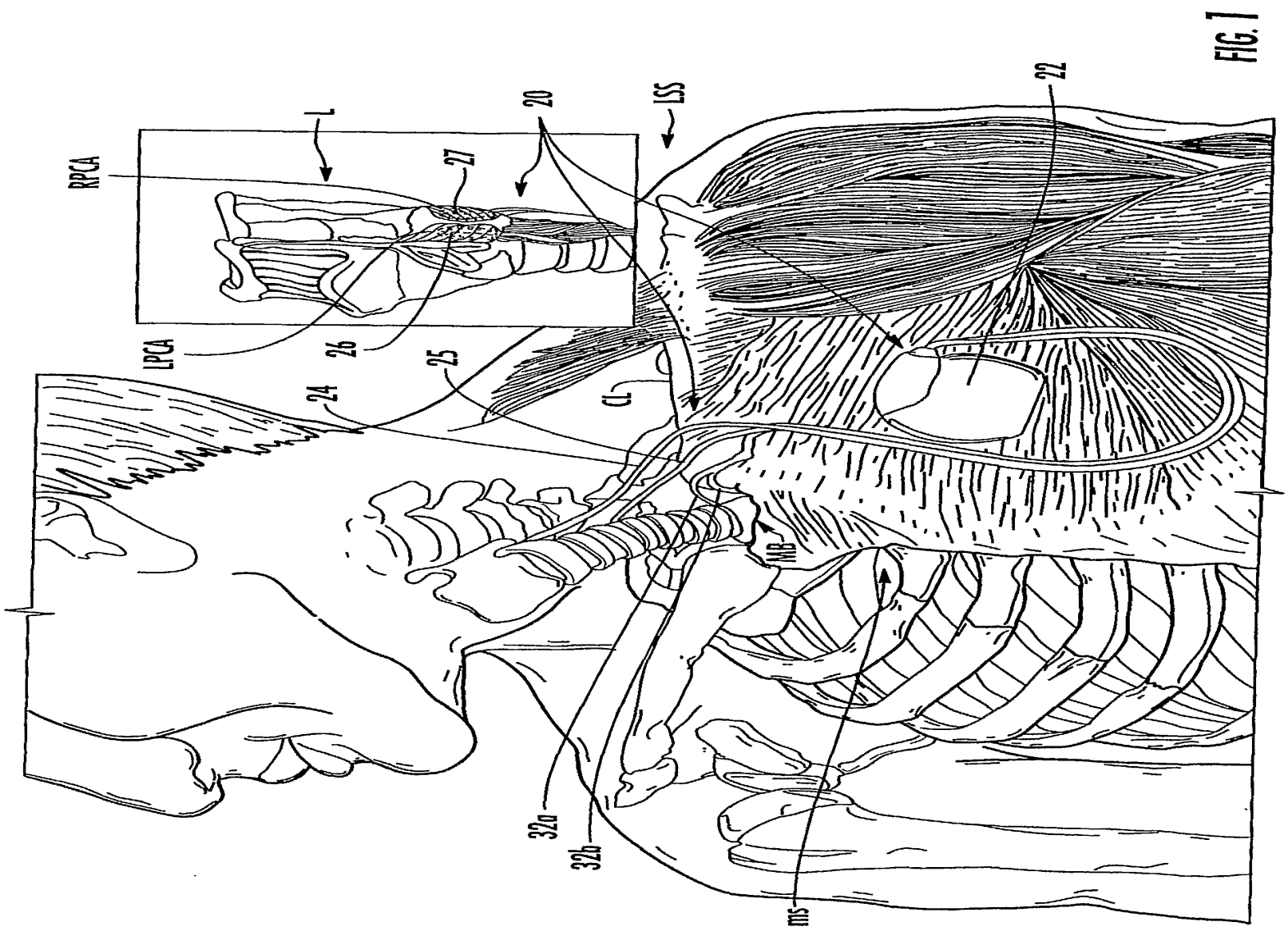


FIG. 1

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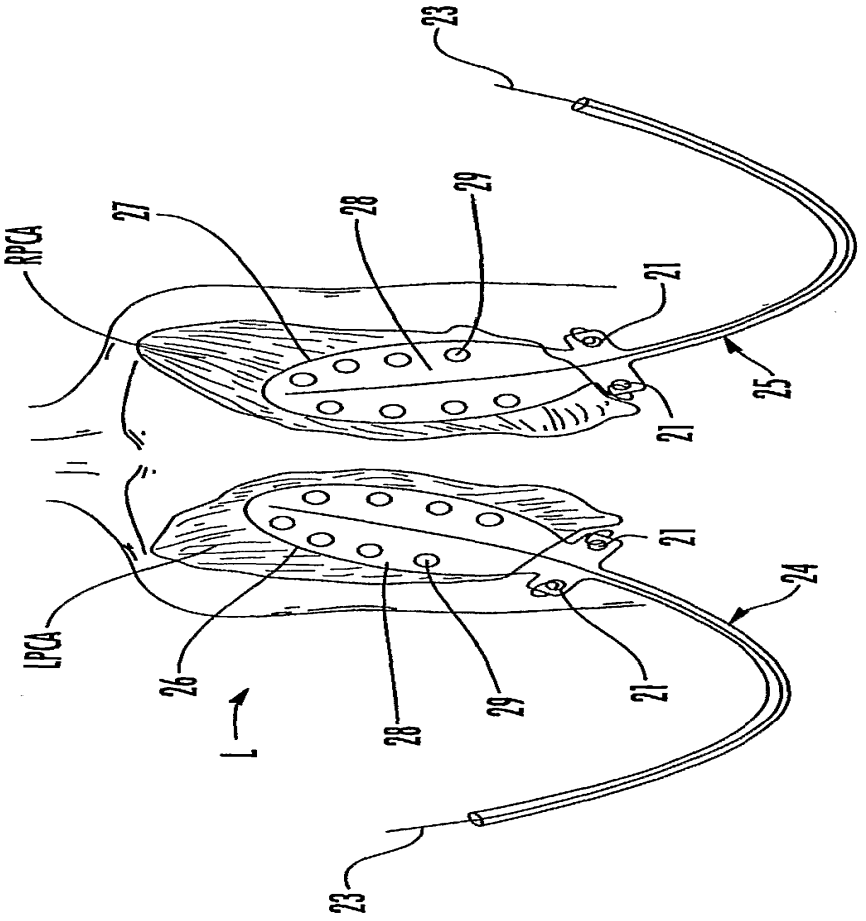


FIG. 2

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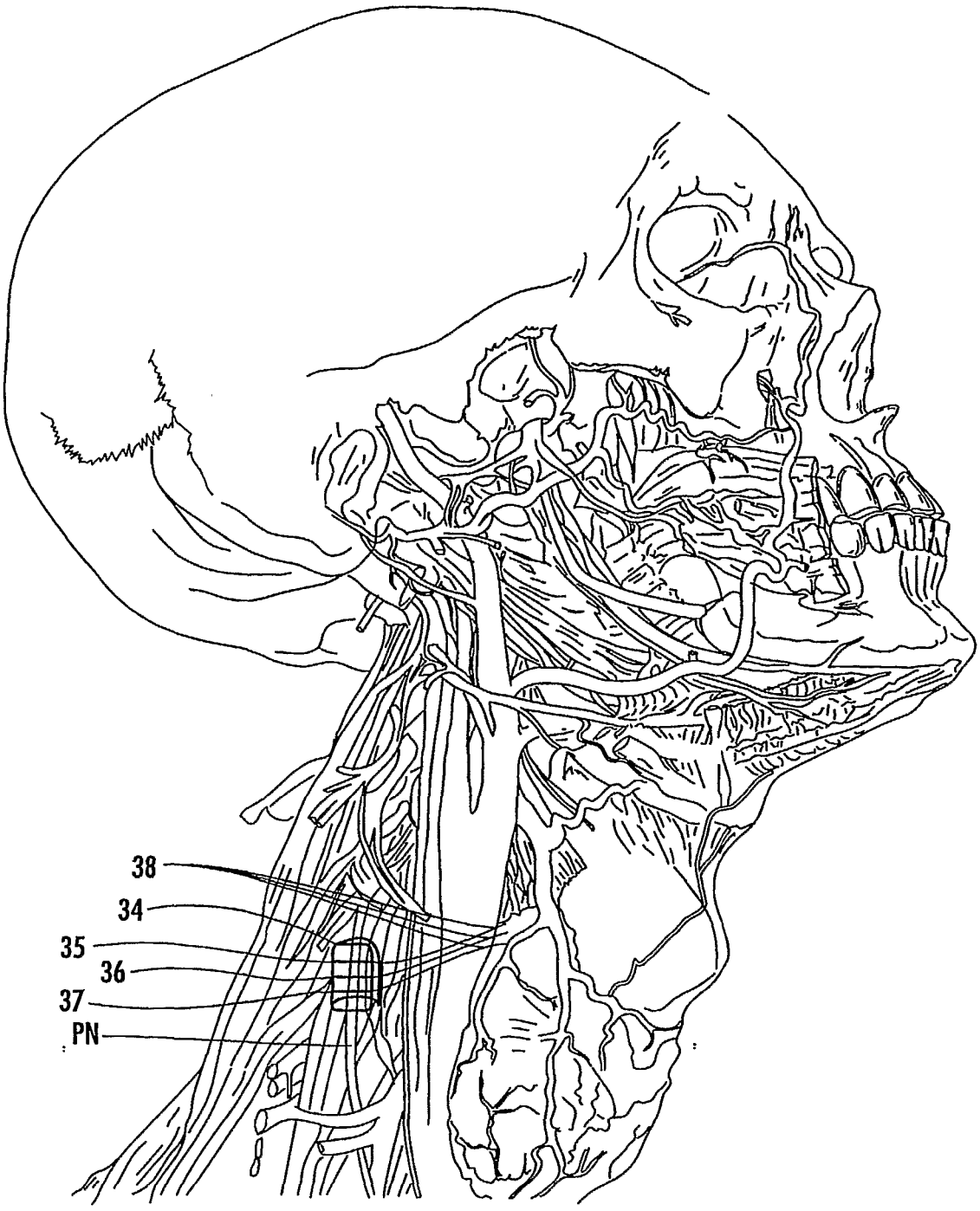


FIG. 3

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SUBSTITUTE SHEET (RULE 26)

PHRENIC NERVE TRIPOLAR CUFF

FIG. 4A

TRUE TRIPOLE AMPLIFIER

FIG. 4B

PRESSURE TRANSDUCER CHAMBER

FIG. 4C

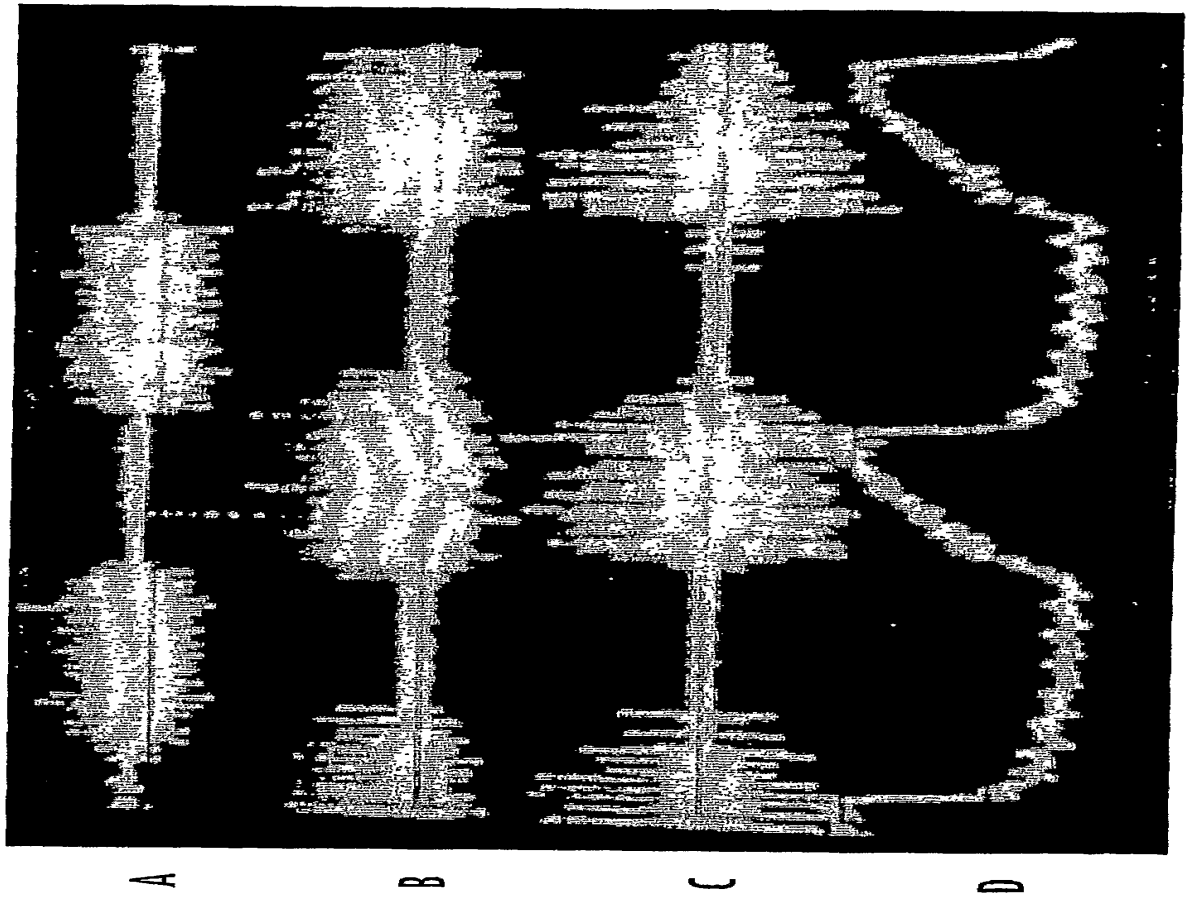


FIG. 5

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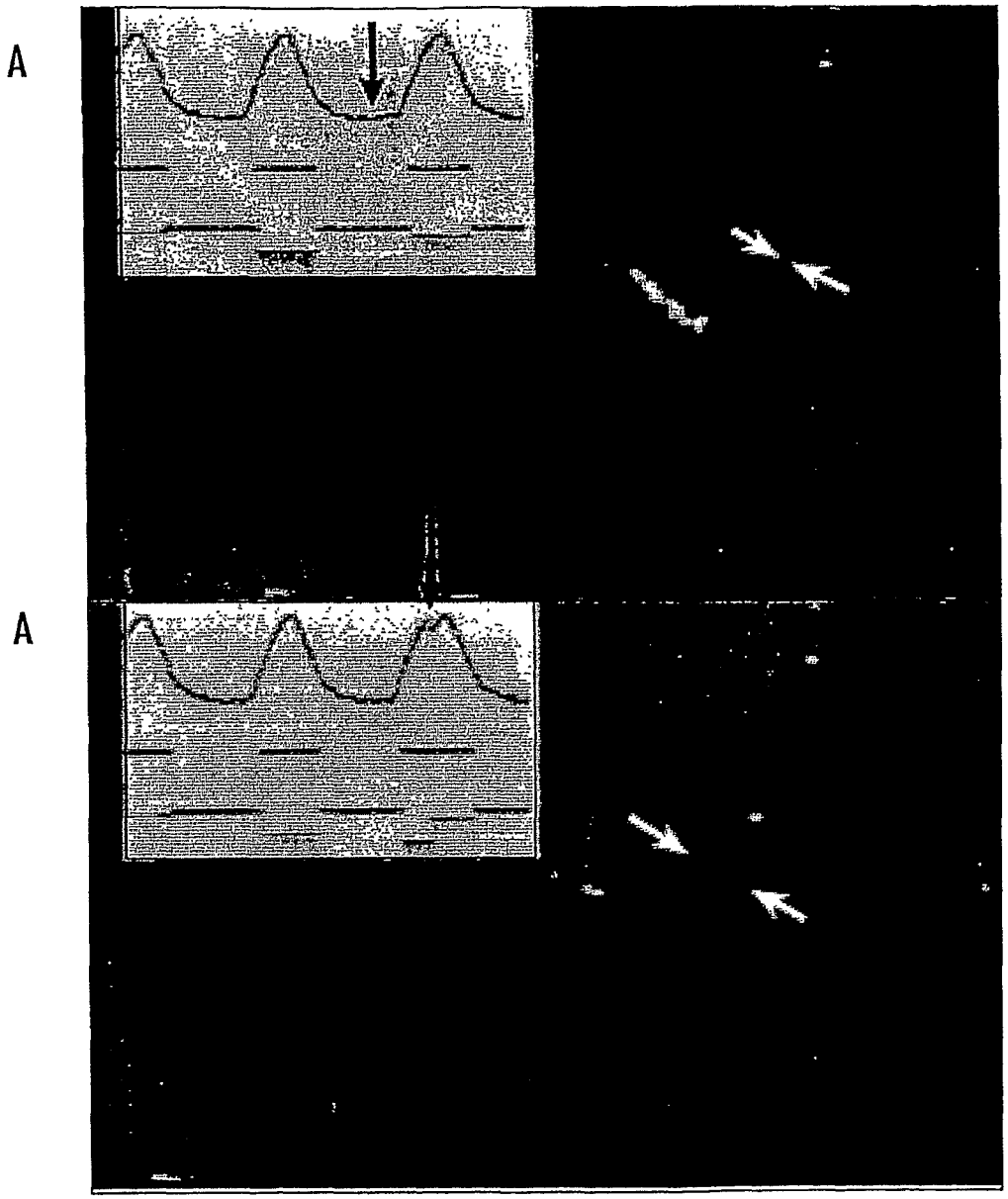


FIG. 6

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 June 2007 (21.06.2007)

PCT

(10) International Publication Number
WO 2007/068284 A1

(51) International Patent Classification:
A61N 1/365 (2006.01) *A61N 1/378* (2006.01)

(21) International Application Number:
PCT/EP2005/056700

(22) International Filing Date:
12 December 2005 (12.12.2005)

(25) Filing Language: English

(26) Publication Language: English

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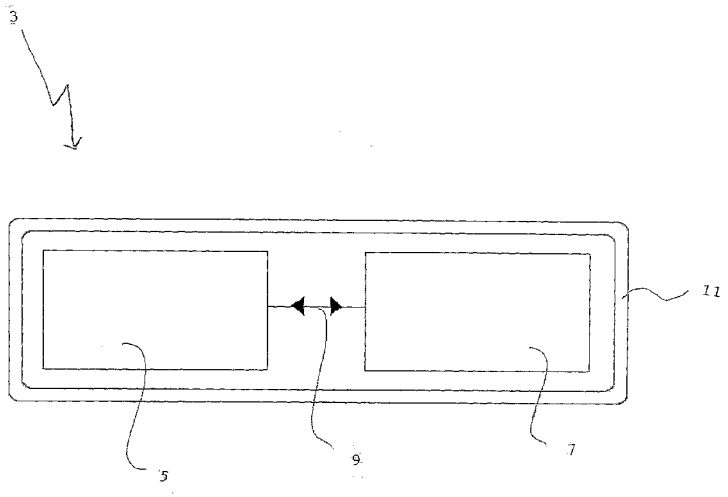
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(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INTRA CARDIAC DEVICE, SYSTEM AND METHODS



(57) **Abstract:** An intra cardiac device is disclosed. The device comprises means for transforming kinetic energy from heart tissue movement into electrical energy in use, from which electrical energy information in respect of heart function is obtainable. Furthermore, a system is disclosed, comprising one such intra cardiac device and at least one receiver, wherein the intra cardiac device comprises means of communication, through which said at least one device communicates with the receiver(s) wirelessly. In this way energy from heart movement provides self contained intra cardiac devices for conveniently monitoring or stimulating a patient's heart.

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INTRA CARDIAC DEVICE, SYSTEM AND METHODS

Field of the Invention

The present invention refers to an intra cardiac device and methods for heart function intervention, such as monitoring and controlling of said heart function.

Background of the Invention

Congestive heart failure (CHF) is a condition where the heart is not able to pump enough blood to supply the body with energy and oxygen. There are multiple causes for the heart to fail, such as ischemic heart disease caused by clogged arteries, cardiomyopathy of unknown reasons or end stage after congenital heart diseases or heart valve diseases. With an increasing aging of the population today, the problem of CHF is increasing and is now the most common cause of heart disease mortality. According to the American Heart Association 5 million people in the United States experience CHF, increasing in number by half a million every year. 1% of the population over 50 years of age or 5% of the more than 75 years old are affected by the condition of CHF. Worldwide the number of people suffering from CHD is estimated around 20 million. Independent of what the reason for CHD, the symptoms and the treatment are the same. The failing pump function causes low blood pressure and low cardiac output resulting in renal failure, and a lower urine production causes fluid retention in the body.

A failing left ventricle of the heart causes the blood to be stagnant in the lungs, causing slow flow and high pressures in the blood stream of the lungs. As a result thereof, fluid will be pressed from the blood vessels into the lung tissue resulting in a decreased gas exchange in the lungs, a condition that worsens the heart condition.

A right heart failure on the other hand causes slow flow and stagnation of blood in the vein system of the

body. As a result thereof, fluid is pressed from the small blood vessels, the capillaries, into the various organ tissues including the fatty tissue under the skin. This fluid retention causes for instance weight gain, swollen organs and legs and shortness of breath.

The treatment of CHF is first of all a correction of the underlying causes such as valvular disease or coronary artery blocks. However, for the majority of patients this treatment is too late. Surgically, only heart transplantation and implantation of mechanical heart assist devices are available. However, only 2-3000 heart transplants are made worldwide in the youngest population, due to lack of donor organs. Also, mechanical assist devices are still experimental. Therefore the majority of the patients are left with symptomatic medical treatment. First of all fluid restriction and treatment with diuretics are used. Other drugs are Angiotensin-converting Enzyme (ACE) inhibitors, beta-blockers and digitalis. Most of CHF patients live for a long time before dying and are readmitted again and again in order to adjust medication or get diuretics injected. Changes in the heart movements, the volumes and the pressures occur fast. The symptoms, however, appear slowly, resulting in treatment too late.

Previously, Medtronic Inc. has introduced the Chronicle device, an implantable Hemodynamic Monitor. That system contains a Lithium battery and a computing element to be implanted under the skin, remote from the heart. Further, this unit has a lead with a pressure transducer that extends into the heart where it can measure intra cardiac pressure, an indirect indicator when diagnosing a heart condition. The Chronicle unit is capable of using several algorithms to present curves and trends that can be detected in a receiver outside the body.

Savacor Inc. has developed the HeartPOD™, a very similar product to the Chronicle device, the major

difference being that the transducer located at the tip of a lead is implanted in the atrial septum wall measuring the pressure in the left atrium. A handheld computer serves as a patient monitor receiving physiological signals from an implant by wireless transmission. Savacor's technology is based on apparatus and methods as described in US 6,328,699.

US 6,328,699 discloses an apparatus for treating congestive heart failure in a patient. However, this apparatus is provided with a pressure transducer lead that is permanently implanted in the left atrium of the patients heart. This pressure transducer lead is connected to an electrical circuitry for processing electrical signals. Thus, the apparatus according to US 6,328,699 has the disadvantage of presenting a lead (or wire) inside the body (and inside the heart) of the patient, rendering the apparatus inferior in respect of a device in no need of such a lead, said device being fully implantable in the body of the patient. Moreover, the device according to US 6,328,699 receives energy from a battery, which renders it inferior inn comparison to a device in no need of a battery.

Remon Medical Technologies Inc. has introduced a device for non-invasive assessment of pulmonary artery pressure. A pressure transducer is inserted into the pulmonary artery and fixed there. The pressure transducer is connected to an implanted remote device collecting data from the implanted transducer. Ultrasound energy is applied from outside the body in order to activate and energize the device. Wireless communication to an external unit is also supported when the device is powered-up.

CardioMEMS Inc. on the other hand has developed a similar system that can measure pressure by means of an un-powered, permanently implantable pressure sensor, which is energized by means of high frequency radio waves from

outside the body. The pressure sensor is intended for measuring intrasac pressure during endovascular abdominal aortic aneurysm (AAA) repair.

Disturbances of the heart rhythm

Pacemakers (PM) are electronic devices to be implanted in a human body with the purpose to regulate the heart beat and the heart rhythm by means of electrical stimuli in patients that have lost the ability to regulate the heart rhythm, e.g. a heart block is such a condition. A PM 36, e.g. shown in Fig. 2, is a hermetically sealed metal can 38 that contains a battery 40 and an electronic circuit. The PM can is implanted in the body under the skin at a remote site from the heart. The PM delivers electrical stimuli to the heart by means of an electrical lead 42, or multiple electrical leads 42, extending from the PM can 38 in one end to a heart tissue and in the other end having an un-insulated electrode tip 44 or another form of transducer at tip 44, respectively.

Rune Elmqvist, a Swedish engineer designed the first implantable PM, and Dr. Aake Senning implanted the device into the body of the patient Arne Larsson in 1958. The patient lived for 43 years after the first implant and had additionally 23 different PMs implanted during his lifetime. This first PM had a battery that was rechargeable, the first non rechargeable PM was developed simultaneously by Dr. Greatbach in USA and was implanted for the first time in 1960. Today only non-rechargeable PMs are used. The PM industry today is among the most profitable in the medical device area, more than 600,000 PMs are produced yearly. Some modern PMs are able also to detect irregular, sometimes life-threatening irregularities in the heart rhythm, also known as arrhythmia. Over time, PMs were combined with a defibrillator, called an implantable cardioverter defibrillator (ICD), to correct such arrhythmia by means of an electrical shock.

Generally, there are two main problems with PM treatment today, related to the leads and to the battery.

The leads are insulated cables, connected hermetically sealed to the electronic circuit in the PM can in one end and connected to the heart tissue with an un-insulated end, the electrode tip, in the other end. The tip is made of material that facilitates in-growth in the heart tissue. The insulation is made of medical quality polymers, usually polyurethane and is made as thin as possible in order to save space. The insulation must be absolutely impermeable. If not, electrical leak currents will occur and the PM will not function. The core of the lead, the electrically conducting part, is made of a metal that is a good electrical conductor. Since the heart is constantly bending and twisting, the metal in the conductor has to be very tolerant to bending without fracturing, a fracture occurs frequently and stops the electron transfer and the PM does not function. Lead infection is another large problem. Furthermore, the leads are immersed in the blood stream, a perfect environment for bacteria, and in contact with subcutaneous tissue, a common site for infections, especially from the PM can pocket. Bacteria easily migrate from the skin to subcutaneous tissue and into the blood stream along the leads. Finally lead tips often dislocate from the heart tissue, loosing contact to the heart cells, and thereby no electron transfer to the heart tissue is possible. Insulation defects, conductor fracture, infections, and tip dislocations are some of the PM related issues that result in recurrent surgical operations, usually including additional leads being put in, since retrieval of previously implanted leads is very difficult if not impossible in many cases. Thus patients normally end up having many leads, most of them not in use. When more complex devices are used, like an ICD or a PM that stimulates and detects at different sites in the heart

(e.g. atrium and ventricle) a system may consist of up to four leads at implant, each of them prone to the problems described above.

The battery

Different energy sources have been explored for batteries, inclusive nuclear. However, only Lithium (Li) batteries have proven to function well in PMs and today this energy source is exclusively used. Like all batteries the main problem is durability. The electrons will only flow through a closed circuit, from the negative pole of a battery through the load, i.e. the body, back to the positive pole of a battery, and then through the battery (electrical current is described in the opposite direction). Electrons returning to the battery join with Iodine and then with Lithium to Lithium-Iodine (LiI), which is not a good electron conductor. Buildup of LiI increases the internal resistance in a Li battery. Increasing internal resistance causes a decreasing battery voltage and finally the available voltage becomes insufficient to stimulate the heart and the battery is useless. A Li battery will deliver at its beginning-of-life around 2.8 V and in the best case it will have a linear output for 5 years. From this time the internal resistance increases exponentially, and when the voltage comes down to close to the heart stimulation threshold, the battery has to be replaced. A Li battery will normally contain 2 Ah (ampere-hours) of capacity, the drain is typically 25 microamperes, giving a battery a theoretical lifetime of 80 000 hours. In reality, however, they seldom last longer than 5 years.

As one may see, the main problems related to PM treatment are related to the battery and to the leads.

Several attempts have been made to solve these problems.

For instance, W.H. Ko, in US 03,456,134, as published July 15, 1969, discloses a piezoelectric converter for

converting body motion to electrical energy for driving electrical implants, such as a PM. Ko found that this piezoelectric system may deliver enough energy to run a PM when driven at a mechanical pulse rate and with a motion similar to the heart motion of an animal, upon which it was tested. However he did neither suggested to integrate a piezoelectric system in a PM itself nor to implant such a conversion device in a heart. As nearly 40 years have passed since the disclosure of Ko, and no commercially available PMs using Kos principle have become available, it is regarded that the skilled person in the field of implanted devices does not regard that it is feasible to carry out Kos piezoelectric system with implantable devices.

US 6,654,638 discloses ultrasonically activated electrodes that generally use a piezoelectric energy converter to convert energy from an external energy source, e.g. an ultrasonic element. This energy is stored within the electrode. It is also mentioned that the electrodes may use the contracting heart to produce energy by compressing or deflecting a piezoelectric element. However, the electrodes disclosed in US 6654638 are always controlled by an external device. That means pacing action is not possible by the electrode itself without the interaction with an external control unit. Furthermore, also the piezoelectric element is integrated into the housing of the electrode, whereby the piezoelectric element uses valuable space of the housing's surface that no longer is available for use as an electrode surface.

Hence, there is a need for a device which alleviates or avoids problems such as, but not limited to, those mentioned above, and which device is fully implantable in the body, such as in the vicinity of, or inside, the heart, of a patient, which device may be used for instance for CHF cases, but also in acute situations in the intensive care

unit for patients suffering from acute heart failure, for instance after large myocardial infarctions, after catheter based coronary artery operation or after cardiac surgery, which device is in no need of battery (or batteries) or lead(s), which device may continuously monitor the heart function and may initiate early medical counter measures.

Summary of the Invention

Accordingly, the present invention preferably seeks to mitigate, alleviate or eliminate one or more of the deficiencies in the art and disadvantages, such as the above-identified, but not limited to, singly or in any combination, and solves problems, such as the above-identified, but not limited to, by providing a device according to the appended patent claims.

For this purpose an intra cardiac device of this kind according to claim 1, is characterized by means for transforming kinetic energy from heart muscle movement into electrical energy in use, from which electrical energy information in respect of heart function is obtainable.

Advantageous features of the invention are defined in the dependent claims.

More specifically, according to a first aspect of the invention, an intra cardiac device for heart function intervention is provided that comprises means for transforming kinetic energy from heart tissue movement into electrical energy in use, from which electrical energy information in respect of heart function is obtainable.

The means for transforming kinetic energy into electrical energy may be a magnet, movable relative a coil.

The means for transforming kinetic energy into electrical energy may be a rotatable pendulum, communicating with a magnet, rotatable relative a coil.

The means for transforming kinetic energy into electrical energy may be a piezo-electric energy converter.

The intra cardiac device may comprise an energy storage means, such as a capacitor, adapted to store the transformed electrical energy for use by the intra-cardiac device.

The intra cardiac device may comprise a wireless transmitter or transceiver.

The intra cardiac device may comprise fixation means, for attachment of said device in or at the heart, such as a stent, tines or hooks, or a screw.

The intra cardiac device may comprise elutionable steroids.

The intra cardiac device may be configured to provide device function related data, such as administrative data, programmed data like mode, cardiac stimulation pacing rate, defibrillation energy, power unit condition.

The information may be information in respect of heart function such as measured data like heart rate, heart movement amplitude, heart movement acceleration, electrical heart rate, electrical signal amplitude, or data related to previous cardiac events stored in the intra cardiac device.

The intra cardiac device may be an electrical cardiac stimulator device, such as an implantable pacemaker, a cardioverter defibrillator or a defibrillator.

The intra cardiac device may comprise at least one electronic circuit.

The electronic circuit may comprise pacing algorithms and/or defibrillating algorithms.

The intra cardiac device may comprise a positive and a negative electrode.

The positive and a negative electrode may be configured to obtain electrical heart signals.

The electrical energy may in use of the intra cardiac device be stored in an energy storage means, wherein the energy storage means may be configured to provide energy stored therein for cardiac stimulation via said positive

and negative electrode when electrical heart signals are not obtained via said positive and negative electrode.

The poles may be made of good electrically conducting material.

The poles may be made of copper or steel or a polymer.

At least one of said poles may be covered with porous material.

The porous material may be activated carbon, sintered platinum-iridium or sputtered titanium-nitride.

The heart tissue may be a heart muscle.

The intra cardiac device may be a leadless (no external lead as conventionally known) and batteryless self-contained intra cardiac monitoring and/or intra cardiac stimulating heart device capable of wireless communication with other intra cardiac or extracorporeal devices.

According to a second aspect of the invention, a system is provided. The system comprises at least one intra cardiac device according to the first aspect of the invention, and at least one receiver, wherein the at least one intra cardiac device comprises means of communication, through which said at least one device may communicate wirelessly with said at least one receiver.

The at least one receiver may be an extracorporeal receiver located outside a patients body in use of said system having said at least one intra cardiac device implanted therein.

The at least one receiver may be located in a mobile terminal such as a mobile telephone, a fix-net telephone, an intensive care monitor, a pacemaker, a defibrillator, an infusion pump, or a transceiver of a telemetry system.

The system may comprise a plurality of said intra cardiac devices and a first intra cardiac device of said plurality of intra cardiac devices may be configured to

communicate with a receiver located in a second intra cardiac device of said plurality of intra cardiac devices.

The intra cardiac device of the system may be configured to communicate information in respect of heart function derived from electrical energy information originated during conversion from kinetic heart movement energy to electrical energy to the receiver.

The means of communication may be wireless communication selected from the group comprising of wireless radio transmission including Bluetooth or ZigBee, and ultrasound communication, or combinations thereof.

The system may further comprise a delivery system for an intra cardiac device, wherein the delivery system comprises an intra cardiac device according to the first aspect of the invention, an introducer sheath (78), a guide wire (76), a diagnostic catheter (102), and a delivery catheter (94).

According to another aspect of the invention, a method of communication between a first intra cardiac device according to the first aspect of the invention and a receiver is provided. The method comprises transforming kinetic energy from heart tissue movement into electrical energy, deriving information obtained from said transformed electrical energy related to said heart movement, and communicating said information to said receiver wirelessly.

The method may further comprise using said information to electrically instruct a second intra cardiac device.

The method may further comprise using said information in an external data assembly equipment for monitoring said heart movement.

According to yet another aspect of the invention, a method for monitoring heart function is provided. The method comprises converting kinetic energy from heart tissue movement to electrical energy, and using information

related to said electrical energy as an indicator of said heart function.

The method may further comprise wirelessly communicating said information related to the electrical energy to a receiver for interpretation.

The receiver may be located in an external data assembly equipment outside of the patient body.

The external data assembly equipment may be a mobile terminal such as a mobile telephone, or a fix-net telephone line, an intensive care monitor, an infusion pump or a transceiver of a telemetry system.

According to still another aspect of the invention, a method of treatment of heart blocks and arrhythmias is provided. The method comprises transforming kinetic energy from heart tissue movement into electrical energy, and deriving information obtained from said transformed electrical energy related to said heart movement, by the use of at least one intra cardiac device according to a first aspect of the invention; and obtaining electrical heart signals from said at least one intra cardiac device, and stimulating the heart electrically by at least one intra cardiac device with at least a part of the transformed electrical energy.

The first intra cardiac device may communicate with at least a second intra cardiac device.

The first intra cardiac device may act as a master device and the at least second intra cardiac device may act as a slave device.

According to yet a further aspect of the invention, a method of monitoring congestive heart failure is provided. The method comprises transforming kinetic energy from heart tissue movement into electrical energy by the use of at least one intra cardiac device according to a first aspect of the invention, deriving information obtained from said transformed electrical energy related to said heart

movement, and communicating said information to a receiver wirelessly.

According to yet another aspect of the invention, a method for positioning a system comprising any of the intra cardiac devices according a first aspect of the invention is provided. The method comprises positioning said intra cardiac device in the right ventricle (RV), in the middle cardiac vein or in the coronary sinus, positioning a second intra cardiac device inside the LV from the aorta, in the lateral marginal veins, in the great cardiac vein or in the coronary sinus, and positioning a third intra cardiac device inside the wall of the right atrium or right atrium appendage, wherein each of these intra cardiac devices implemented as units in a system will communicate with each other.

The method may further comprise positioning a fourth intra cardiac device, implemented as a defibrillator, inside the RV, the marginal veins, the great cardiac vein 4, the coronary sinus 2 or in the middle cardiac vein 10, which fourth intra cardiac device also will communicate with said first, second, and/or third intra cardiac device.

The intra cardiac devices may be attached to the heart surface directly for optimizing positioning, according to the method.

Brief Description of the Drawings

These and other aspects, features and advantages of which the invention is capable of will be apparent and elucidated from the following description of embodiments of the present invention, reference being made to the accompanying drawings, in which

Fig. 1 is a schematic illustration showing a human heart;

Fig. 2 is a schematic illustration showing a pacemaker or prior art monitoring device 36 like a HeartPod

from Savacor Inc., a Chronicle system from Medtronics or a Pacemaker implanted at a patients shoulder area, remote from the heart. A lead for transportation of electrons runs from the implant can to the pressure transducer and back or in the case of a pacemaker to the heart tissue where the electron transfer takes place from the lead tip. These devices have a battery in the can;

Fig. 3 is a schematic block diagram showing an intra cardiac device according to an embodiment of the present invention, wherein the device is capable of communicating with an external communication unit, e.g. outside the patient, via an integrated communication unit;

Fig. 4 a) is a schematic illustration showing an intra cardiac device producing electricity by means of induction;

Fig. 4 b) is a schematic illustration showing another intra cardiac device producing electricity by means of induction;

Fig. 5 a) is a schematic illustration showing tines as fixation means for an intra cardiac device;

Fig. 5 b) is a schematic illustration showing a screw as fixation means for an intra cardiac device;

Fig. 5 c) is a schematic illustration showing a stent as fixating means for an intra cardiac device, the stent pushing the device against a vessel wall and still leaving the lumen open for sufficient flow;

Fig. 6 a) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention implemented with fixation tines;

Fig. 6 b) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention having a fixation screw;

Fig. 7 a) is a schematic illustration showing an intra cardiac device according to an embodiment of the

invention delivered and fixed in the anterior inter-ventricular vein;

Fig. 7 b) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered and fixed in the lateral marginal vein;

Fig. 7 c) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered and fixed in the middle cardiac vein;

Fig. 7 d) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered and fixed in the right ventricle;

Fig. 7 e) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered and fixed in the left ventricle;

Fig. 7 f) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered and fixed on the heart surface;

Fig. 8 is a schematic block diagram of showing an intra cardiac device according to an embodiment of the invention having an energy unit powering a cardiac stimulator in the form of a pacemaker;

Fig. 9 is a schematic illustration showing a complete pacemaker system implemented with four intra cardiac device according to embodiments of the invention implemented as pacemaker units are implanted in the lateral marginal vein, the middle cardiac vein, in the right ventricle and in the right atrium appendage, respectively, and a further intra cardiac device according to an embodiment of the invention implemented as a defibrillation unit is located in the great cardiac vein, wherein the devices may communicate with each other and outside the patient by means of the built in communication units;

Fig. 10 a) is a schematic illustration showing access to the vein system through the internal Jugular vein;

Fig. 10 b) is a schematic illustration showing access to the vein system through the femoral vein;

Fig. 10 c) is a schematic illustration showing access to the left ventricle through the femoral artery;

Fig. 11 is are schematic illustrations showing a delivery system for fixation with tines and a screw respectively;

Fig. 12 is a schematic illustration showing a delivery system for fixation with stent;

Fig. 13 is a schematic illustration showing the insertion of a guide wire into the coronary sinus through the internal Jugular vein;

Fig. 14 a) is a schematic illustration showing a guide wire and a guiding catheter introduced through the coronary sinus, the great cardiac vein and into the anterior inter-ventricular vein;

Fig. 14 b) is a schematic illustration showing an intra cardiac device according to an embodiment of the invention delivered in the great cardiac vein by means of a stent; and

Fig. 15 is a schematic illustration showing a complete heart function monitoring system according to an embodiment of the invention with an external communication unit.

Embodiments of the Invention

The following description focuses on embodiments of the present invention applicable to a device, and in particular to a method of using said device, for transforming kinetic energy of a heart 1 into electrical energy. The device may transmit data outside the body. However, it will be appreciated that the invention is not limited to this application but may be applied to many other embodiments.

It will be understood that the Figures are merely schematic and are not drawn to scale. For clarity of illustration, certain dimensions may have been exaggerated while other dimensions may have been reduced. Also, where appropriate, the same reference numerals and letters are used throughout the Figures to indicate the same parts and dimensions.

In one embodiment the device according to the present invention is an intra cardiac device for heart function intervention. This device has the capability to transform kinetic energy obtained from heart muscle movement into electrical energy in use. This electrical energy may then be used to obtain information in respect of heart function.

The term "intervention" is, in this context, meant to be interpreted as monitoring, modifying, surveying, and/or controlling heart function and action.

In one embodiment of the present invention the herein presented device is designed to be implanted totally in the heart itself. Since the heart is constantly moving vigorously in all three dimensions, a device provided in the heart has a certain potential kinetic energy. With modern technology, e.g. micro mechanical systems, such kinetic energy may be detected and transformed into electrical energy. Since the heart never stops, it is not necessary to save any energy in batteries, if necessary possibly only momentarily in a capacitor. The electrical drain of 25 microamperes according to the prior art mentioned above includes the energy loss in the lead, thus the energy needed in a leadless system is much lower than that with a lead.

Modern technology permits new solutions for transforming kinetic energy into electrical energy by means of Micro Electro Mechanical Systems, also called MEMS. These new solutions may be implemented in respect of the embodiments according to the present invention. There are

different methods to transform kinetic energy into electrical energy, by using an energy conversion unit 5.

Electrical energy may be obtained by means of unit 5 by inductive conversion from kinetic energy. In this case, a magnet 52 is moving relative a coil 50, whereupon a voltage and current is generated in the coil 50. Magnet 52 for instance may be connected via a connection means such as a rod 48 and a gearbox to a pendulum 46 for converting heart tissue movements in three dimensions to a suitable movement of the magnet 52 relative coil 50. This may be achieved by moving a magnet 52 back and forth through the coil 50, as suggested by Lee et al 2003, in "AA Size micro Resonators". Lee demonstrated that up to 830 microwatts could be achieved with such a conversion device.

Therefore, in one embodiment of the present invention, electrical energy is achieved by moving a magnet 52 back and forth relative a coil 50.

Another energy conversion solution is to transform movements of a magnetic pendulum 46 in another embodiment of energy conversion unit 5 into rotation and then have the magnet 52 to rotate in the coil 50. The Seiko watch, a self winding electric watch, is an example that may produce up to 1 mW. A spring like in a self winding wrist-watch and a gear system might accelerate the rotational speed to 15000 rev/min, an optimal rate. Kula and Najafi could achieve 2.5 microwatt at 10 Hz in a MEMS. Hence, a pendulum of 2 g is sufficient to convert enough energy to supply a pacemaker, such as a pacemaker unit 70. In this respect, one embodiment of the present invention transforms movements of a magnetic pendulum 46 into rotation, and then have the magnet to rotate in a coil 50 to obtain electrical energy.

Piezo-electrical materials may produce an electrical current with no mechanical parts moving. Pressure on a piezo-electrical material produces a voltage. Roundy, 2003, produced 0.2 mW on a 1cm cube @ 120 Hz. Capacitive or

electrostatic methods might also be used . The housing of the intra cardiac device may comprise piezo electric elements for the energy conversion. However, in this case a part of the housing area is blocked for other use, e.g. as electrode surface. As the intra cardiac device is very compact, housing surface is rather limited. Moreover, the housing itself has to be exposed to a pressure from the moving heart tissue. When the device is attached to the tissue, this is difficult to implement. Therefore, it is proposed to have a piezo electric conversion means inside the housing, which is exposed to a mechanical pressure when the heart tissue accelerates. For instance, a T-bar like element which generates a lever on a piezo electric element due to resulting inertia of a lever perpendicularly arranged to the piezo element may be used for piezo electric energy conversion. Accordingly, some embodiments of the invention are implemented by using piezo-electrical, capacitive or electrostatic energy conversion methods in embodiments of energy conversion unit 5.

Hence, a self-contained implantable intra cardiac device may be provided according to some embodiments.

The device according to some embodiments of the present invention provides the possibility to continuously monitor the heart function and initiate early intervention, if the heart condition of a patient is deteriorating. An energy device fully implantable monitors in use the kinetic energy of a heart 1 and continuously transmit a report of the condition of the heart 1 to a receiver outside the body or to another device inside the body, for instance a pacemaker, such as a pacemaker unit 70, a defibrillator or an infusion pump able to adjust the amount of diuretics to be injected. For this purpose, energy conversion unit 5 is via communication element 9, e.g. by wires or wirelessly, connected to a communication unit 7 inside a housing 11 of the intra cardiac device 3, as shown in Fig. 3.

According to a specific embodiment, the device is self-contained and does not communicate with an extracorporeal device. The device according to this embodiment continuously monitors the heart function and initiate early intervention, if the heart condition of a patient is deteriorating. The device is in use fully implanted in the heart 1 and converts kinetic energy from heart movements into electric energy. The conversion signal provides information to monitor the kinetic energy of the heart 1 and continuously analyzes this information in order to activate a pacing circuitry if required.

A device according to one embodiment of the present invention may also be used in acute situations in the intensive care unit for patients suffering from acute heart failure, for instance after large myocardial infarctions, after catheter based coronary artery intervention or after cardiac surgery. By means of the device according to the embodiment of the present invention, the kinetic energy of the heart 1 is transformed into electricity; the amount of electrical energy achieved is related to the force of movement of the heart 1, an indicator of the heart condition. More specifically, an electrical signal is obtained when converting the heart movement kinetic energy into electrical energy. The electrical signal has a characteristic electrical voltage and current over time. For instance, the maximum amplitude of the electrical signal may deliver information how fast the heart 1 is accelerating. The curve form may give information how the muscle exactly is accelerating, etc. Furthermore, no energy is transferred to the herein presented inventive device from outside the heart 1.

In respect of the PM's according to the prior art, the herein presented device, according to some embodiments of the present invention, eliminates among others the problems related to batteries and leads, since there is no

battery and there are no leads comprised in the herein presented PM.

In a first embodiment an energy unit is utilizing induction for creating electricity electromagnetic, by transforming the kinetic energy of the heart movements. This is achieved either by moving a magnet back and forth relative a coil 50, e.g. through the coil 50, or by rotating a magnet 52 relative a coil 50, e.g. by rotating a magnet 52 in a coil 50 or by rotating a coil 50 around a magnet 52, e.g. by means of a pendulum effect.

In a second embodiment electric current unit is utilizing a piezo-electric material, i.e. a material that creates an electric current when deformed.

In still another embodiment an energy unit is created utilizing electrostatic or capacitive technology.

The amount of electricity produced is an indicator of the kinetic energy of the heart 1 reflecting acceleration and movement of the site where the device is implanted. Acceleration and movements are indicators of the heart muscle condition at a given time. According to some embodiments, the device has a transmitter emitting a signal to a receiver, e.g. outside the body. Thus, the device according to some embodiments comprises an energy unit, an electronic control unit, a transmitting unit and fixation means. Some embodiments of the device may also comprise a transmitting and receiving unit (also called transceiver unit) instead of only a transmitting unit.

The receiver may also be incorporated in another device according to another embodiment of the invention. Thus, one implanted device may communicate with another implanted device, e.g. to give the other implanted device instructions in respect of when and how to act. For instance, a first implanted device may convert kinetic energy, analyze heart condition, and send a signal to a second implanted device if a heart failure is detected. The

second device also converts kinetic energy for powering a receiver and a pacing circuit. When the second implanted device receives a signal from the first implanted device, e.g. that pacing is necessary, the second implanted device takes appropriate action.

In one embodiment wireless communication is provided by means of radio frequency (RF) transmission which may be digitally coded.

In one embodiment the means of communication is provided by so called Bluetooth technology.

The new ZigBee technology might also be used in other embodiments. ZigBee is a published specification set of high level communication protocols designed to use small, low power digital radios based on the IEEE 802.15.4 standard for wireless personal area networks (WPANs). The technology is designed to be simpler and cheaper than other WPANs such as Bluetooth. The most capable ZigBee node type is said to require only about 10% of the software of a typical Bluetooth or Wireless Internet node, while the simplest nodes are about 2%. ZigBee provides an inexpensive self-organizing mesh network. However, it has not yet been envisaged for use in implanted medical devices. ZigBee is designed to use very small amounts of power. This makes ZigBee perfectly suited for use in the implantable cardiac devices of the present invention.

In still another embodiment ultrasound may be used for wireless communication with the intra cardiac device(s).

The data retrieved outside may be exact numeric data of a current status or may also only comprise trends.

In another embodiment a device and a method for treatment of heart blocks and arrhythmias by means of an electrical cardiac stimulator without battery and leads are presented. The device is designed to be completely implanted in a heart 1 or on a heart surface. In this

embodiment the device comprises five main components: an energy unit, an electronic control circuit, an electric contact surface towards the heart tissue, a communication unit 7 and finally means for attachment or fixation in or to the heart 1.

In one embodiment of the intra cardiac device according to the present invention in the form of an electrical cardiac stimulator, an energy unit is utilizing induction for creating electricity by means of electro-magnetically converting kinetic energy from heart movement into electrical energy. This is achieved either by moving a magnet 52 back and forth relative a coil 50 or by rotating a magnet 52 relative a coil 50, e.g. by rotating a magnet 52 in a coil 50 or by rotating a coil 50 around a magnet 52, e.g. by means of a pendulum effect.

In another embodiment of the electrical cardiac stimulator according to the present invention, an energy conversion unit is utilizing piezo-electric material, a material that creates an electric current when deformed.

In still another embodiment of the electrical cardiac stimulator according to an embodiment of the present invention, an energy conversion unit is based on electrostatic or capacitive conversion technology.

According to one embodiment, the electrical cardiac stimulator's electronic circuit utilizes traditional PM algorithms on an electronic chip. The chip may for instance be of rectangular or square surface area, and by estimation the complete area is with current technology less than approximately one square centimeter in size. Further miniaturization is envisaged with emerging technologies. The device has two electrode contact surfaces, preferably one at each end of the implant, one positive pole receiving the electrons and one negative emitting electrons into the heart tissue. The electrode contact surfaces are made of good electrically conducting metal material like copper or

steel or other alloys. They may be covered with porous material like activated carbon, sintered platinum-iridium or sputtered titanium-nitride. The current is concentrated in a small area of contact with the myocytes by means of designing the geometrical surface area of contact of the electrodes as small as is optimal. The surface may also be eluting stereoids like dexamethasone from the surface initially in order to limit inflammation during healing in. The electrical cardiac stimulator device has a unit of communication. The communication unit 7 may communicate with communication units in other devices implanted in the same heart 1, e.g. one in an atrium and one in a ventricle, or one electrical cardiac stimulator in the implementation of a PM unit and one electrical cardiac stimulator in the implementation of an ICD unit. Thus, one unit may serve as a master and the others are slaved to the master. Thus, one device may communicate with another device, e.g. to give the other device instructions in respect of when and how to act. The communication unit 7 may also be designed to communicate outside of the patient. Communication may occur one-way out of the device in order to deliver information from the implanted device (in this case the device has a transmitter only), or two-way so that the implanted device also may receive information (in this case the device has a transceiver). In either case information that is transmitted may comprise information related to follow up of the device's function and for adjustments of it's mode of operation, for instance administrative data, programmed data like mode, rate etc., measured data like heart rate, mechanical cardiac function values, like local acceleration at the implanted devices location, or the electrical pulse rate, electrical pulse amplitude, power unit condition etc., or stored data. The means of communication is based on wireless transmission technologies. In one embodiment the means of communication is by means of radio frequency

(RF) waves. Communication may be digitally coded and/or authenticated in order to provide a secure and reliable data transmission to and/or from implanted device(s).

In another embodiment of the electrical cardiac stimulator device according to the present invention the means of communication is based on so called Bluetooth™ technology. The new ZigBee technology may also be used in respect of the presently described electrical cardiac stimulators.

In still another embodiment of the electrical cardiac stimulator device according to the present invention ultrasound transmissions through the body may be used for wireless communication to/from the implanted device(s).

Again Nanotechnology and MEMS may be utilized for minimizing the communication unit 7 in the device.

In yet another embodiment the intra cardiac device according to the present invention is a congestive heart failure monitoring device 3. The congestive heart failure monitoring device 3 is intended to be inserted and fixated adjacent to the left ventricle of the heart 1. Preferably the device is inserted in the vein system through the coronary sinus 2 and the great cardiac vein 4 into smaller branches along the lateral wall of the left ventricular wall 26. Other positions in the vein system are in the anterior inter-ventricular vein on the front of the heart 1 or in the middle cardiac vein 10 behind the heart 1 between the left and the right ventricle, or in the great cardiac vein 4. In cases of right heart failure separately, the device is placed close to the right ventricle, in case only one embodied device is implanted.

In the Figures, e.g. Fig. 1, furthermore the following elements are illustrated for a better understanding of the present invention: anterior inter-ventricular vein 8, left atrium appendage 14, pulmonary artery 16, superior vena cava (SVC) 20, right ventricular

wall 24, tricuspid valve 32, mitral valve 34, right atrium appendage cavity 74, the femoral artery 84, the iliac artery 86, the aorta 88 and the inferior vena cava (IVC) 90.

The positioning of electrical cardiac stimulator devices, such as pacemaker (PM) devices, for example a pacemaker unit 70, according to embodiments of the present invention may also be more diverse or distributed over the heart 1, depending on the function of the different components of a electrical cardiac stimulator system. For instance a first intra cardiac device implemented as a PM for stimulation of the right ventricle (RV) may be positioned inside the RV, in the middle cardiac vein 10 or in the coronary sinus 2. A second intra cardiac device implemented as PM for stimulation of the left ventricle (LV) may additionally be positioned inside the LV from the aorta 18, in the lateral marginal veins 6, in the great cardiac vein 4 or in the coronary sinus 2. A third intra cardiac device implemented as a PM for stimulation of the right atrium 22 may additionally be positioned inside the right atrium wall or right atrium appendage 12. An intra cardiac device implemented as a defibrillator may additionally be positioned inside the RV, the marginal veins, the great cardiac vein 4, the coronary sinus 2 or in the middle cardiac vein 10. Each of these intra cardiac devices implemented as a units will communicate with each other. For instance during open chest surgery, the devices are attached to the heart surface directly, a technique that optimizes positioning.

An embodiment of the method according to the present invention is now described. The method provides for monitoring of the heart function by means of converting kinetic energy from the heart 1 to electrical energy and using information related to the electrical energy, e.g.

the amount of electricity produced over time, as an indicator of the heart function.

Initially access to the circulatory system is established. More precisely, one specific way is to first establish access to the vein system by means of puncturing a large vein with a needle, wherein such veins might be the cubital arm vein, the cephalic vein, the internal jugular vein 78, the subclavian vein, the femoral vein 82 or any other vein large enough. Subsequently, a guide wire 76 is inserted and an introducer sheath 78 with a hemostatic valve is placed over the wire. The guide wire 76 is then withdrawn. A diagnostic catheter 102 is inserted in the introducer sheath 78 to the location intended for positioning the device in the body. Preferably the catheter is inserted in the vein system through the coronary sinus 2 and the great cardiac vein 4 into smaller branches along the lateral wall of the left ventricular wall 26, the lateral marginal branches. Other suitable positions in the vein system are for instance in the anterior inter-ventricular vein on the front of the heart 1 or in the middle cardiac vein 10 behind the heart 1 between the left and the right ventricle. Once the diagnostic catheter 102 is in position an angiogram of the vein system is achieved using contrast dye. By interpreting the image from the angiogram of the vein, the proper position for the device is determined. A guide wire 76 is now advanced to the selected position in the vein and beyond, whereupon the diagnostic catheter 102 is withdrawn, leaving the guide wire 76 in position. Over the guide wire 76 a guiding catheter is advanced to the deployment site or adjacent. Now the delivery system 92 is advanced over the guide wire 76 but inside the guiding catheter to the desired site. If the device is kept inside the delivery system 92 by means of a restraining catheter, this is now retracted, thereby exposing the device that is expanding inside the vein, e.g.

by a shape memory effect. This shape memory effect may for example be accomplished by polymers that present this feature, or with other suitable materials such as nitinol, which is a nickel-titanium alloy presenting this feature. The device may thus fixate itself at the selected position, or in case the device has tines 56 the tines 56 will attach into the vein wall, keeping the device strongly fixated. In case the device has a screw 58 for fixation in the tissue, the delivery system 92 is rotated in the proper direction until the screw 58 is solidly attached in the heart tissue. In case the fixation means is a stent 60 made of stainless steel, or another alloy, without shape memory, the fixation in the vessel is made by inflating a balloon inside the stent 60 for stent expansion. A pushing rod 96, a pushing catheter 98, and an X-ray marker 100 are further elements used for certain of the herein described procedures.

If the device is to be deployed in a cavity like the RV 62, LV 64 or the right atrium 22, the same actions as above are executed until the guiding catheter and the delivery system 92 is in position inside the cavity. The device is advanced and in case of a screw attachment the delivery system 92 is rotated in the proper direction until the device has a strong attachment in the heart tissue wall. In case the device has fixation tines 56 on the outside a place between the papillary muscles 28 or between the trabecles of the heart muscle 30 is located where the tines 56 get a good attachment and then the device is released from the delivery system 92 by retracting the delivery catheter 94 from over the device.

Other fixation means are for instance eyelets 66or a suture 68, as shown in Fig. 7f.

Once the intra cardiac energy and monitoring device 3 is in the proper position the movements of the heart 1 produce a certain amount of electricity in the device. This

is done by converting kinetic energy from the heart movement into electric energy, as described above.

The communication unit 7 of the intra cardiac device may transmit information to a receiver or an external communication unit 104, e.g. outside of the body or in other implanted intra-cardiac devices. The information may be used for interpretation of the current or previous heart condition. The external communication unit 104 may comprise an antenna 106, which may be integrated inside a housing of unit 104, and a display 108 for visualization of information.

The receiver outside of the body may be part of or connected to a mobile telephone or a fix-net telephone line for direct communication to a physician or a nurse for monitoring purposes and for taking the right actions. The receiver might also be a part of or connected to intensive care monitors. The receiver might be a handheld unit and also have an algorithm and display suggesting to the patient directly the current status and which actions to take.

A method according to another embodiment of the present invention is described for insertion of and establishing a electrical cardiac stimulator system, such as a pacemaker (PM) system, without leads or battery by means of converting kinetic energy from the heart 1 to electricity and using the a certain amount of the electricity produced for stimulating the heart 1 electrically securing a safe heart rhythm. The same method is applied for positioning of electrical cardiac stimulator devices implemented as defibrillation devices.

First access to the vein system is established by means of puncturing a large vein with a needle, such veins might be the cubital arm vein, the cephalic vein, the internal jugular vein 80, the subclavian vein, the femoral vein 82 or any other vein large enough. A guide wire 76 is

then inserted and an introducer sheath 78 with a hemostatic valve is placed over the guide wire 76. Subsequently the guide wire 76 is withdrawn. Then a diagnostic catheter 102 is inserted to a location intended for positioning the device. For instance for LV pacing, the catheter may be inserted in the vein system through the coronary sinus 2 and the great cardiac vein 4 into smaller branches along the lateral wall of the left ventricular wall 26, the marginal branches. Other positions in the vein system would be in the anterior inter-ventricular vein on the front of the heart 1 or in the middle cardiac vein 10 behind the heart 1 between the left and the right ventricle.

Once the diagnostic catheter 102 is in position an angiogram of the vein system is achieved using contrast dye. By interpreting the image from the angiogram of the vein, the proper position for the device is decided. A guide wire 76 is now advanced to the selected position in the vein and beyond, whereupon the diagnostic catheter 102 is withdrawn, leaving the guide wire 76 in position. Over the guide wire 76 a guiding catheter is advanced to the deployment site or adjacent. Now the delivery system 92 is advanced over the guide wire 76 but inside the guiding catheter to the desired site. If the device is kept inside the delivery system 92 by means of a restraining catheter, this is now retracted, exposing the device that is expanding inside the vein and fixating itself there, or in case the device has tines 56 the tines 56 will attach to the vein wall, keeping the device strongly fixated. In case the device has a screw 58 for fixation in the tissue, the delivery system 92 is rotated in the proper direction until the screw 58 is solidly attached to the tissue. If the device has tines 56 for fixation they will engage the vein wall for secure anchoring. If the device is to be deployed in a cavity like the RV 62, LV 64, the right atrium 22 or the appendage of the right atrium 12, the same actions as

above are executed until the guiding catheter and the delivery system 92 is in position inside the cavity. The device is advanced and in case of a screw attachment the delivery system 92 is rotated in the proper direction until the device has a strong attachment in the wall. In case the device has fixation tines 56 on the outside a place between the papillary muscles 28 or the muscular trabecles is located where the tines 56 get a good attachment and then the device is released from the delivery system 92 by retracting the delivery catheter 94 from over the device. In case the electrical cardiac stimulator system comprises several electrical cardiac stimulator devices, the procedure described above is repeated for each of the device members of the system by means of repositioning the guide catheter in the desired positions until all the devices in the system have been deployed. Once all electrical cardiac stimulator device, such as pacemaker, for example pace maker unit 70, and defibrillator devices, are in the proper positions the movements of the heart 1 will induce a certain amount of electricity in each of the devices. The devices are now able to communicate with the others. One of the devices, for instance an electrocardiogram detecting device may take the lead and run the operation of the system. The transmitting system of each of the devices or the leading device only will send the information to a receiver or a communication unit 7 outside of the body for interpretation and setting mode of operation by means of transmitting back to the device(s). The receiver outside of the body may be part of or connected to a mobile terminal or a fix-net telephone line for direct communication to a physician or a nurse for monitoring purposes and for taking the right actions. For instance most mobile terminals in the form of mobile telephones have an integrated Bluetooth wireless communication port. Embodiments of the intra cardiac device

having a Bluetooth transmitter or transceiver may directly connect to such a mobile telephone according to a simple pairing routine matching the phone and the implanted device for communication. Once this link is established, data communicated via the Bluetooth link may easily be forwarded to or received via the mobile networks connection of the mobile phone enabling a multitude of operations including maintenance actions or reprogramming of the implanted devices.

The external receiver communicating wirelessly with the implanted intra cardiac device may also communicate information via a distributed network, like the Internet, e.g. to a physician for examination.

The external receiver might also be a part of or connected to intensive care monitors or telemetry systems. In the first case data from the intra cardiac devices may be displayed on the intensive care monitor. Often intensive care monitors are embedded in a network providing e.g. data storage, print outs etc., or even access to and from a Hospital Information System.

Connecting intra cardiac devices of embodiments of the invention wirelessly to telemetry systems provides a number of advantages compared with today's telemetry systems. Especially the patient telemetry units do no longer need ECG electrodes taped to the patient. Existing telemetry systems may be used with a simple transceiver outside the patient body managing communication both with the implanted intra cardiac device(s) and the fixed installed telemetry system. In this manner a convenient continuous monitoring of a patient is provided right away from the end of implantation. This may contribute to cost saving in healthcare as patients that have undergone cardiac surgery may be directly submitted to non-critical care units.

The invention may be implemented in any suitable form, and the elements and components of an embodiment of the invention may be physically, functionally and logically implemented in any suitable way. Indeed, the functionality may be implemented in a single unit, in a plurality of units or as part of other functional units. As such, the invention may be implemented in a single unit, or may be physically and functionally distributed between different units.

Although the present invention has been described above with reference to specific embodiments, it is not intended to be limited to the specific form set forth herein. Rather, the invention is limited only by the accompanying claims, and other embodiments than the specific above are equally possible within the scope of these appended claims.

In the claims, the term "comprises/comprising" does not exclude the presence of other elements or steps. Furthermore, although individually listed, a plurality of means, elements or method steps may be implemented. Additionally, although individual features may be included in different claims, these may possibly advantageously be combined, and the inclusion in different claims does not imply that a combination of features is not feasible and/or advantageous. In addition, singular references do not exclude a plurality. The terms "a", "an", "first", "second" etc do not preclude a plurality. Reference signs in the claims are provided merely as a clarifying example and shall not be construed as limiting the scope of the claims in any way.

CLAIMS

1. An intra cardiac device for heart function intervention,
c h a r a c e r i z e d by
means for transforming kinetic energy from heart tissue movement into electrical energy in use, from which electrical energy information in respect of heart function is obtainable.

2. Intra cardiac device according to claim 1, wherein said means for transforming kinetic energy into electrical energy is a magnet (52), movable relative a coil (50).

3. Intra cardiac device according to claim 1, wherein said means for transforming kinetic energy into electrical energy is a rotatable pendulum (46), communicating with a magnet (52), rotatable relative a coil (50).

4. Intra cardiac device according to claim 1, wherein said means for transforming kinetic energy into electrical energy is a piezo-electric energy converter.

5. Intra cardiac device according to claim 1, further comprising an energy storage means, such as a capacitor, adapted to store said electrical energy for use by the intra-cardiac device.

6. Intra cardiac device according to claim 1, comprising a wireless transmitter or transceiver.

7. Intra cardiac device according to claim 1, comprising fixation means, for attachment of said device in

or at the heart (1), such as a stent (60), tines (56) or hooks, or a screw (58).

8. Intra cardiac device according to claim 1, comprising elutionable steroids.

9. Intra cardiac device according to any preceding claim, wherein said intra cardiac device is configured to provide device function related data, such as administrative data, programmed data like mode, cardiac stimulation pacing rate, defibrillation energy, power unit condition.

10. Intra cardiac device according to claim 1, wherein said information is information in respect of heart function such as measured data like heart rate, heart movement amplitude, heart movement acceleration, electrical heart rate, electrical signal amplitude, or data related to previous cardiac events stored in the intra cardiac device.

11. Intra cardiac device according to any previous claim, wherein said device is a electrical cardiac stimulator device, such as an implantable pacemaker (70), cardioverter defibrillator or defibrillator.

12. Intra cardiac device according to claim 1 or 11, comprising at least one electronic circuit.

13. Intra cardiac device according to claim 11, wherein said electronic circuit comprises pacing algorithms and/or defibrillating algorithms.

14. Intra cardiac device according to any previous claim, comprising a positive and a negative electrode.

15. Intra cardiac device according to claim 14, wherein said positive and a negative electrode are configured to obtain electrical heart signals.

16. Intra cardiac device according to claim 14 or 15, wherein said electrical energy in use is stored in an energy storage means, and wherein said energy storage means is configured to provide energy stored therein for cardiac stimulation via said positive and negative electrode when electrical heart signals are not obtained via said positive and negative electrode .

17. Intra cardiac device according to claim 14, wherein said poles are made of good electrically conducting material.

18. Intra cardiac device according to claim 14, wherein said poles are made of copper or steel or a polymer.

19. Intra cardiac device according to any of claims 14-18, wherein at least one of said poles is covered with porous material.

20. Intra cardiac device according to claim 19, wherein said porous material is activated carbon, sintered platinum-iridium or sputtered titanium-nitride.

21. Intra cardiac device according to any preceding claim, wherein said heart tissue is a heart muscle.

22. Intra cardiac device according to any preceding claim, wherein said intra cardiac device is a leadless and batteryless self-contained intra cardiac monitoring and/or intra cardiac stimulating heart device capable of wireless

communication with other intra cardiac or extracorporeal devices.

23. A system, comprising at least one intra cardiac device according to any of claims 1 to 22 and at least one receiver,

c h a r a c e t i z e d by

said at least one intra cardiac device comprising means of communication, through which said at least one device communicates with said at least one receiver wirelessly.

24. System according to claim 23, wherein said at least one receiver is an extracorporeal receiver located outside a patients body in use of said system having said at least one intra cardiac device implanted therein.

25. System according to claim 23, wherein said at least one receiver is located in a mobile terminal such as a mobile telephone, a fix-net telephone, an intensive care monitor, a pacemaker (70), a defibrillator, an infusion pump, or a transceiver of a telemetry system.

26. System according to claim 23, wherein said system comprises a plurality of said intra cardiac devices and wherein a first intra cardiac device of said plurality of intra cardiac devices is configured to communicate with a receiver located in a second intra cardiac device of said plurality of intra cardiac devices.

27. System according to claim 23, wherein said intra cardiac device is configured to communicate information in respect of heart function derived from electrical energy information originated during conversion from kinetic heart movement energy to electrical energy to said receiver.

28. System according to any of claims 23-27, wherein said means of communication is wireless communication selected from the group comprising of wireless radio transmission including Bluetooth or ZigBee, and ultrasound communication, or combinations thereof.

29. A system according to any of claims 23-28, further comprising a delivery system (92) for an intra cardiac device, said delivery system (92) comprising
an intra cardiac device according to any of claims 1 to 22,
an introducer sheath (78),
a guide wire (76),
a diagnostic catheter (102), and
a delivery catheter (94).

30. A method of communication between a first intra cardiac device according to any of claims 1 to 22 and a receiver,
c h a r a c t e r i z e d in
transforming kinetic energy from heart tissue movement into electrical energy,
deriving information obtained from said transformed electrical energy related to said heart movement, and
communicating said information to said receiver wirelessly.

31. Method according to claim 30, further comprising using said information to electrically instruct a second intra cardiac device according to any of claims 1 to 22.

32. Method according to claim 30, further comprising using said information in an external data assembly equipment for monitoring said heart movement.

33. A method for monitoring heart function,
c h a r a c t e r i z e d in
converting kinetic energy from heart tissue movement to electrical energy,
using information related to said electrical energy as an indicator of said heart function.

34. Method according to claim 33, further comprising wirelessly communicating said information related to said electrical energy to a receiver for interpretation.

35. Method according to claim 33, wherein said receiver is located in an external data assembly equipment outside of the patient body.

36. Method according to claim 35, wherein said external data assembly equipment is a mobile terminal such as a mobile telephone, or a fix-net telephone line, an intensive care monitor, an infusion pump or a transceiver of a telemetry system.

37. A method of treatment of heart blocks and arrhythmias,
c h a r a c e r i z e d in
transforming kinetic energy from heart tissue movement into electrical energy, and
deriving information obtained from said transformed electrical energy related to said heart movement, by the use of at least one intra cardiac device according to claims 1 to 22; and
obtaining electrical heart signals from said at least one intra cardiac device,

and stimulating the heart electrically by at least one intra cardiac device according to claims 1-22 with at least a part of said transformed electrical energy.

38. Method according to claim 37, wherein a first intra cardiac device communicates with at least a second intra cardiac device.

39. Method according to claim 38, wherein said first intra cardiac device acting as a master device and the at least second intra cardiac device acting as a slave device.

40. A method of monitoring congestive heart failure, c h a r a c e r i z e d in
transforming kinetic energy from heart tissue movement into electrical energy by the use of at least one intra cardiac device according to claims 1 to 22,
deriving information obtained from said transformed electrical energy related to said heart movement, and
communicating said information to a receiver wirelessly.

41. A method for positioning a system of any of the intra cardiac devices according to claims 1 to 22, c h a r a c t e r i z e d by
positioning said intra cardiac device in the right ventricle (RV), in the middle cardiac vein (10) or in the coronary sinus (2),
positioning a second intra cardiac device inside the LV from the aorta (18), in the lateral marginal veins (6), in the great cardiac vein (4) or in the coronary sinus (2),
positioning a third intra cardiac device inside the wall of the right atrium (22) or right atrium appendage (12),

wherein each of these intra cardiac devices implemented as units in a system will communicate with each other.

42. The method according to claim 41, comprising positioning a fourth intra cardiac device, implemented as a defibrillator, inside the RV, the marginal veins, the great cardiac vein (4), the coronary sinus (2) or in the middle cardiac vein (10), which fourth intra cardiac device also will communicate with said first, second, and/or third intra cardiac device.

43. The method according to claim 41 or 42, wherein said intra cardiac devices are attached to the heart surface directly for optimizing positioning.

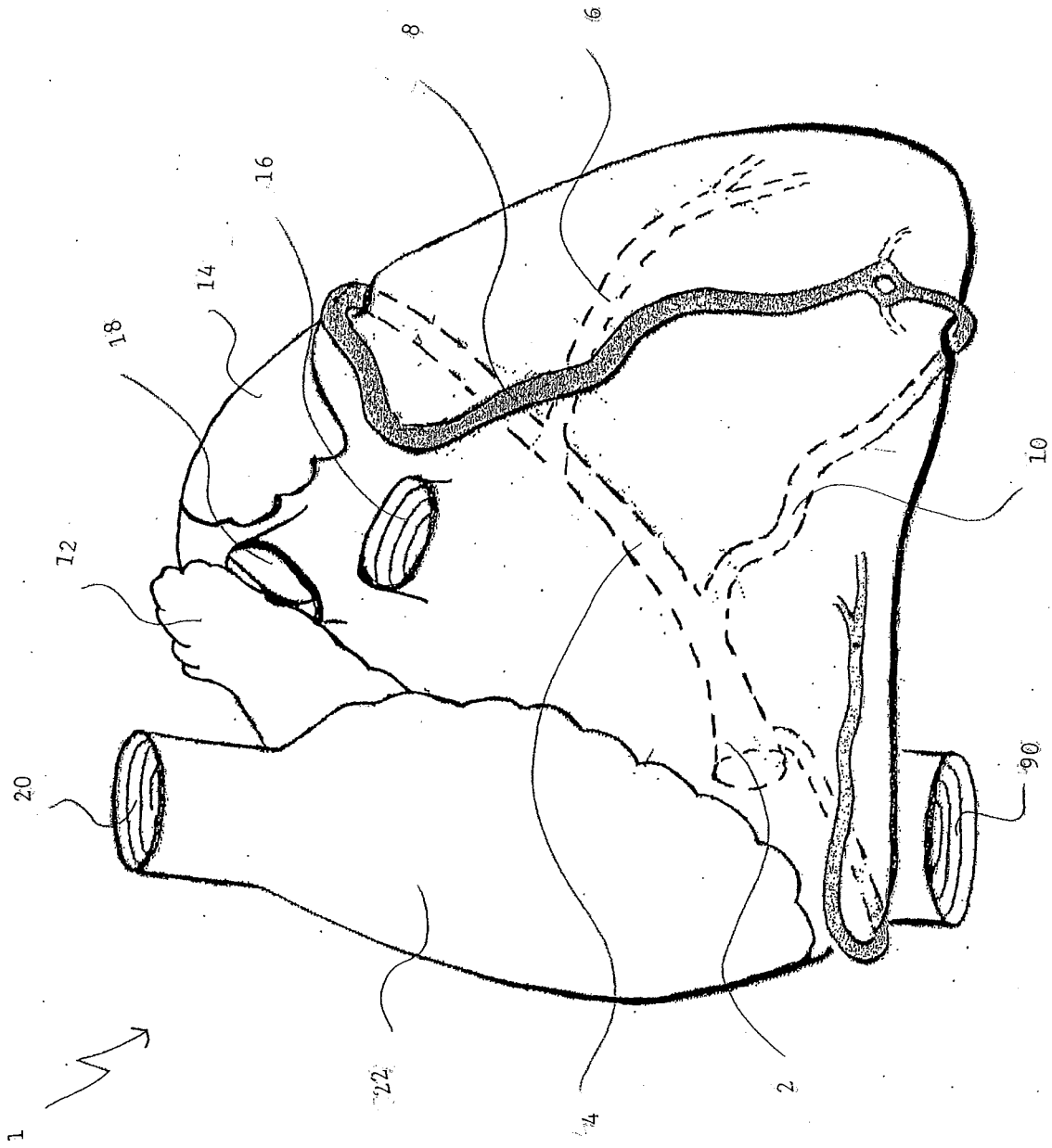


Fig. 1

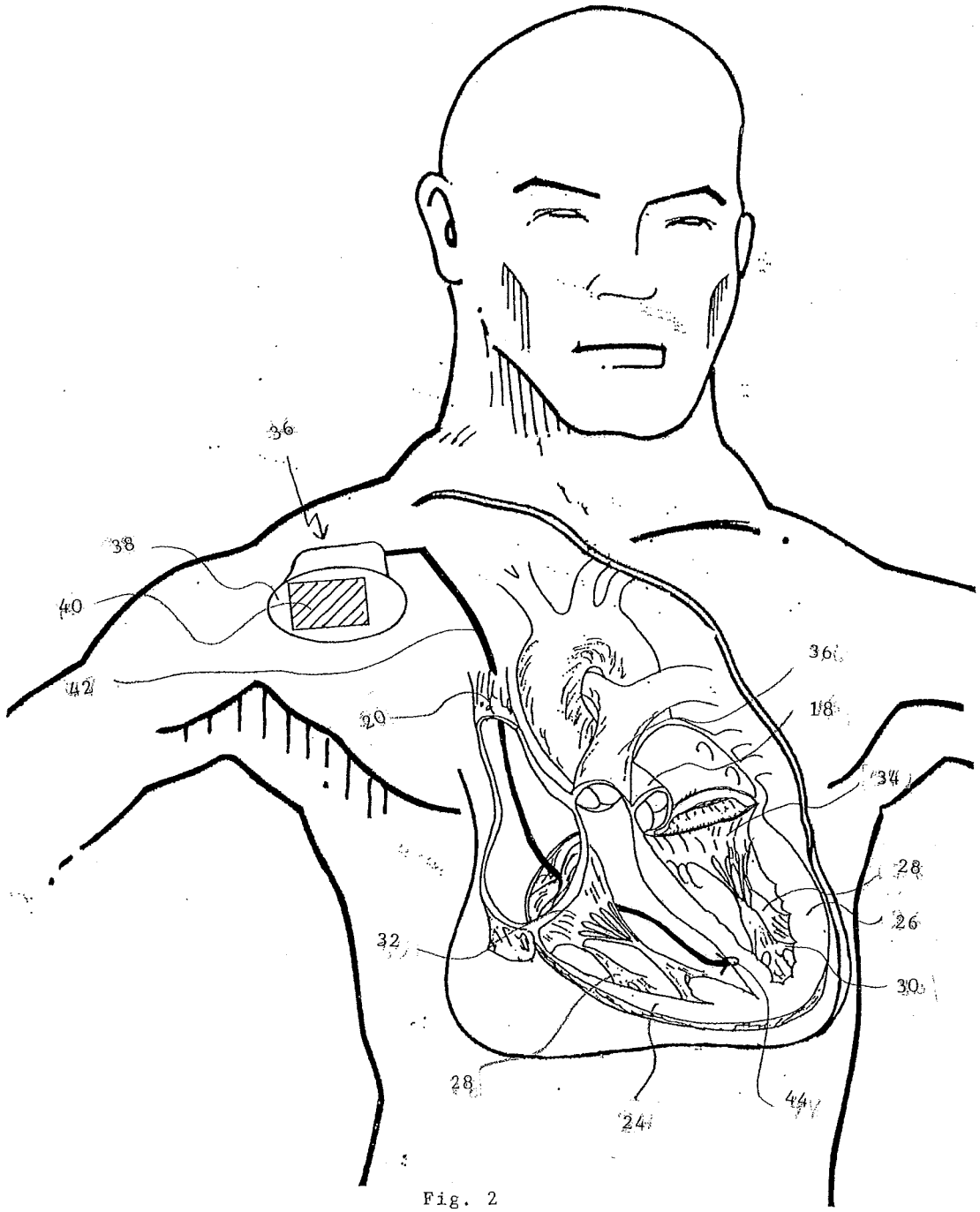


Fig. 2

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00654

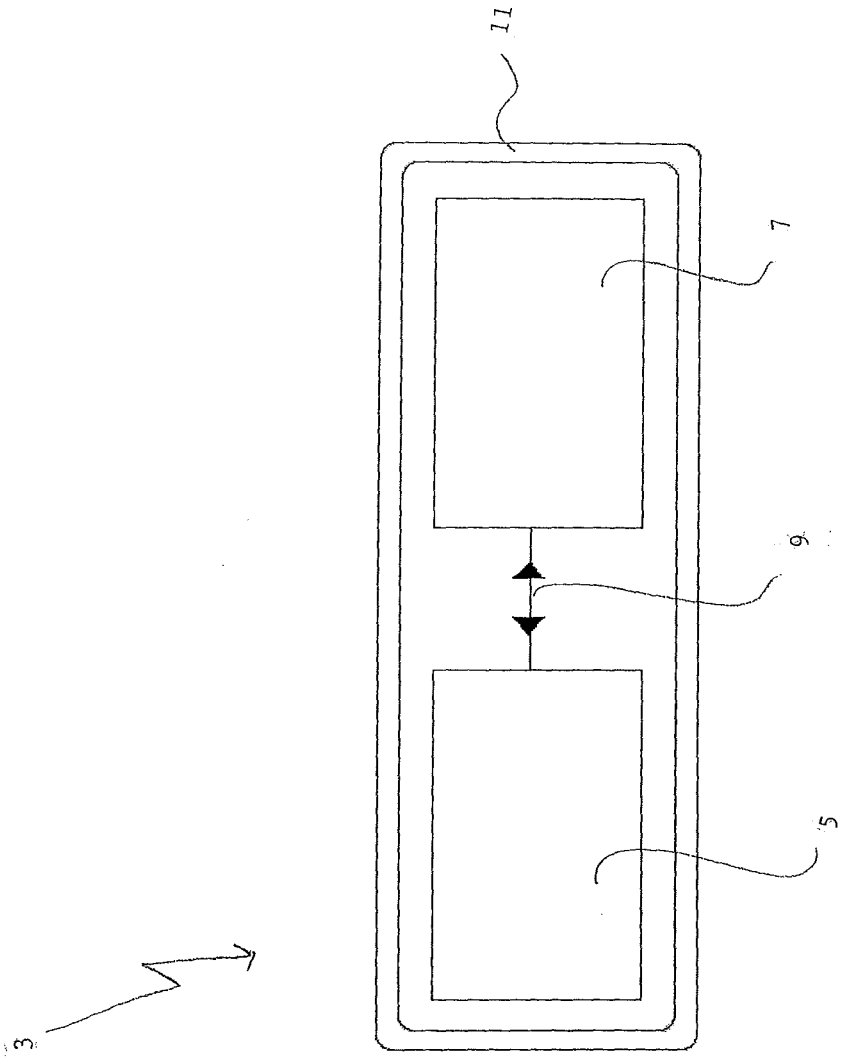


Fig. 3

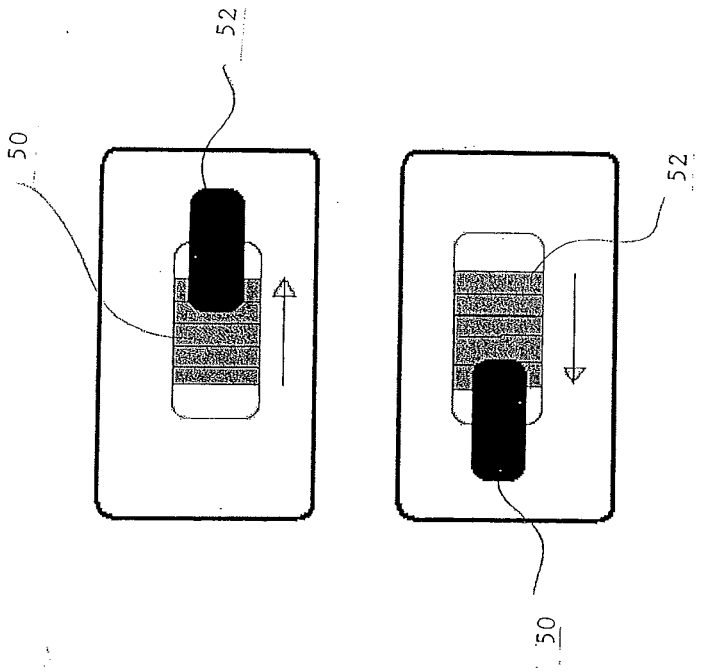


Fig. 4b

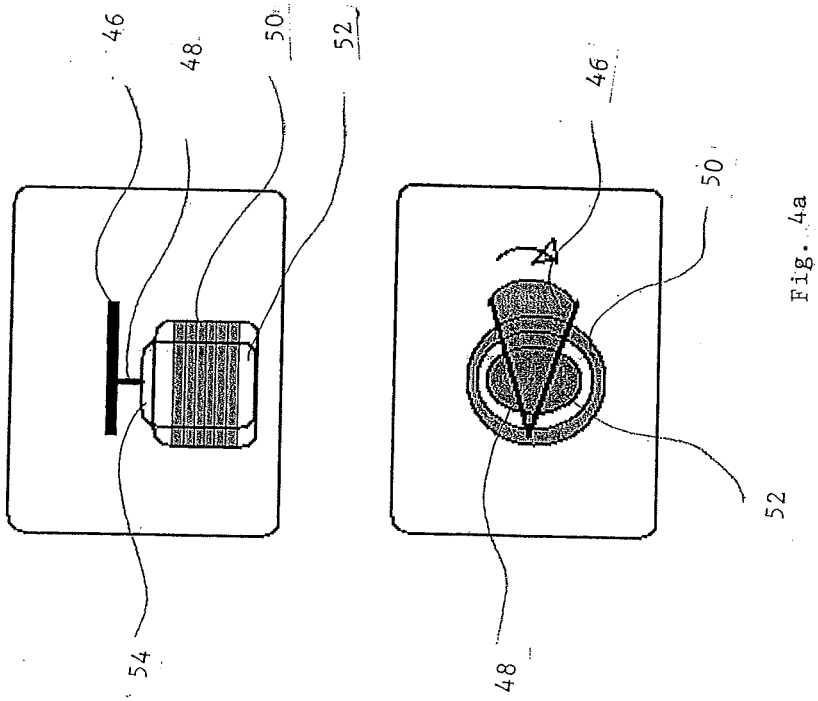


Fig. 4a

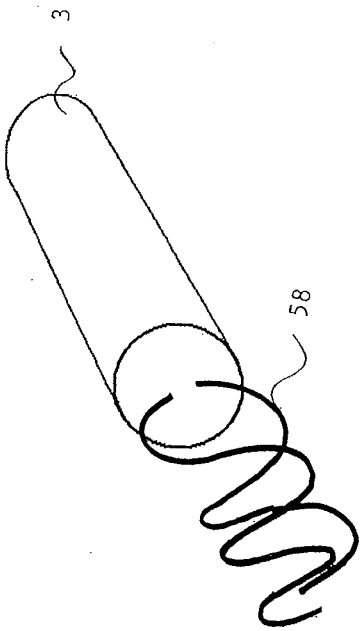


Fig. 5b

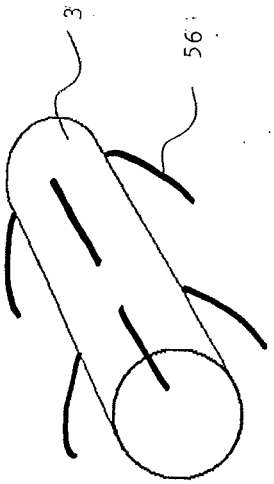


Fig. 5a

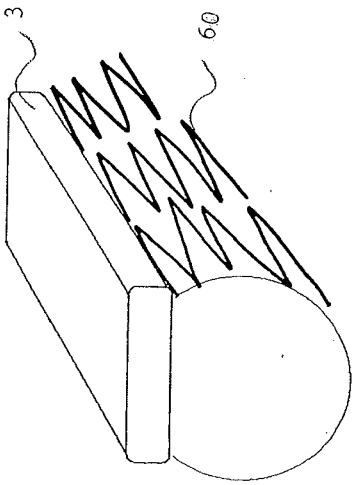


Fig. 5c

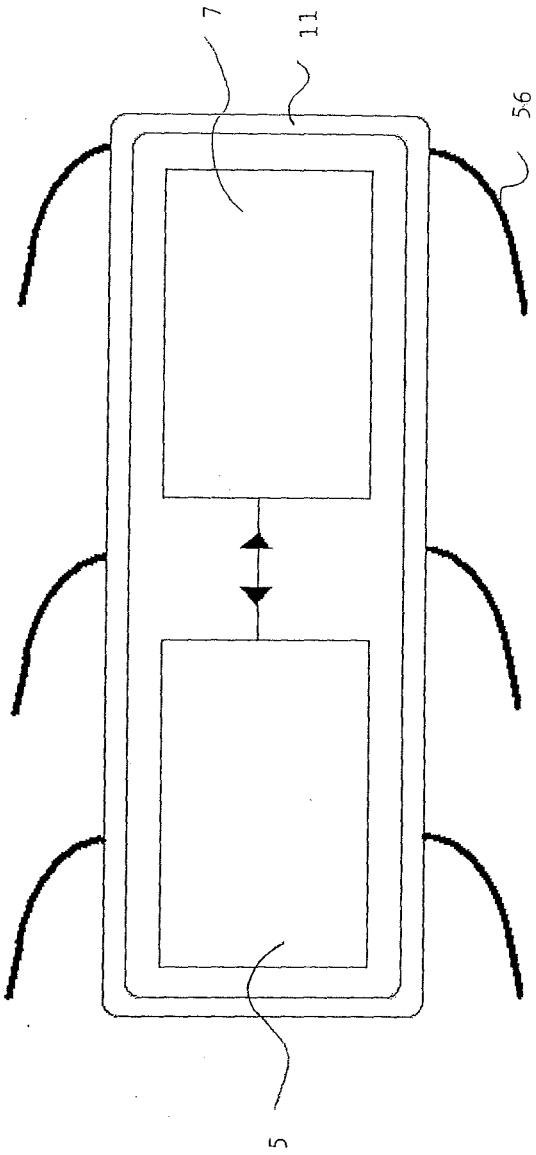


Fig. 6a

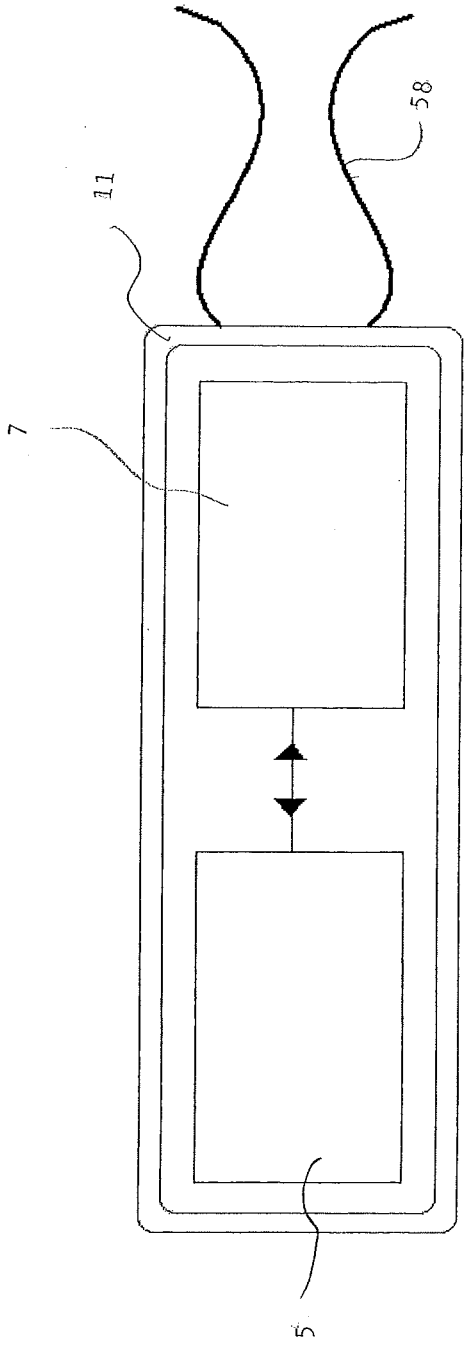


Fig. 6b

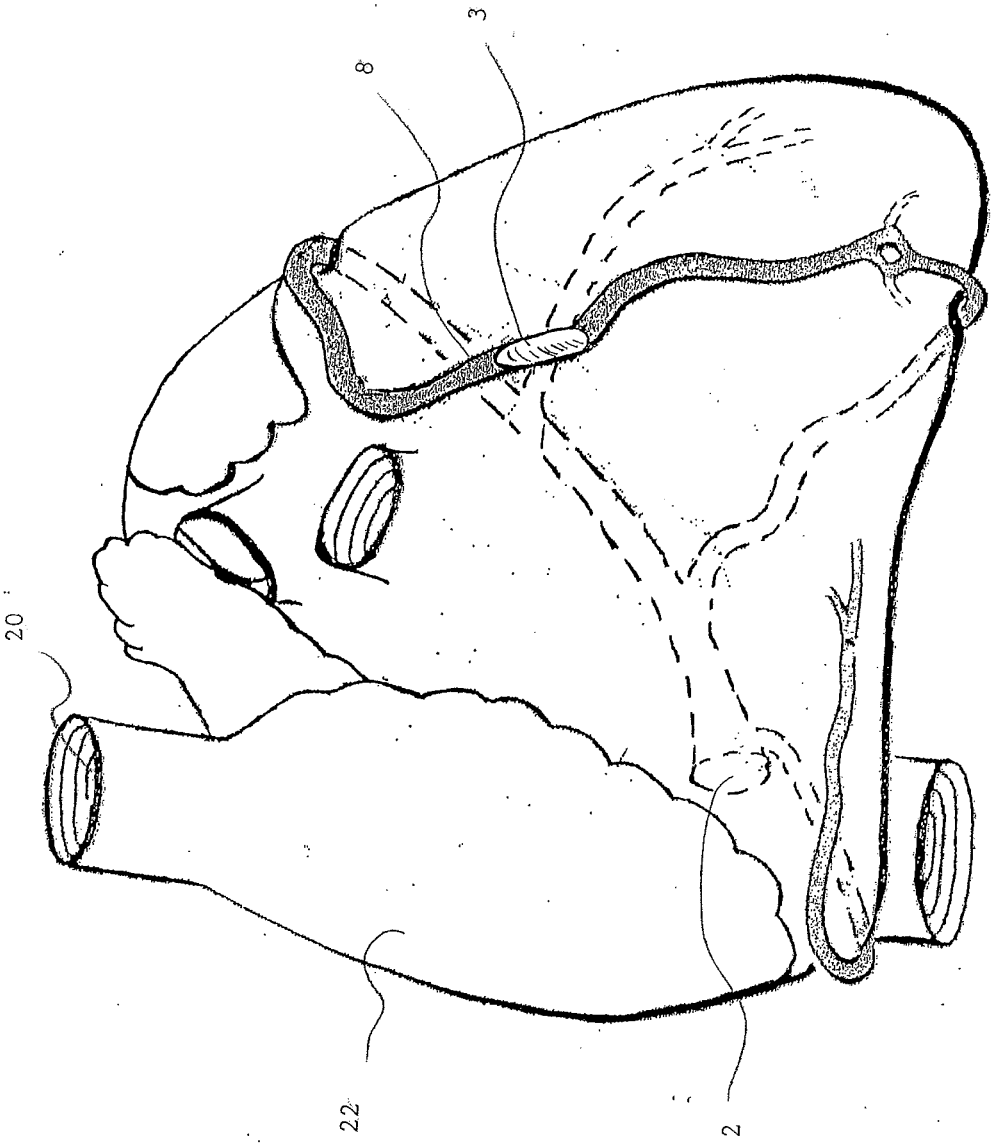


Fig. 7a

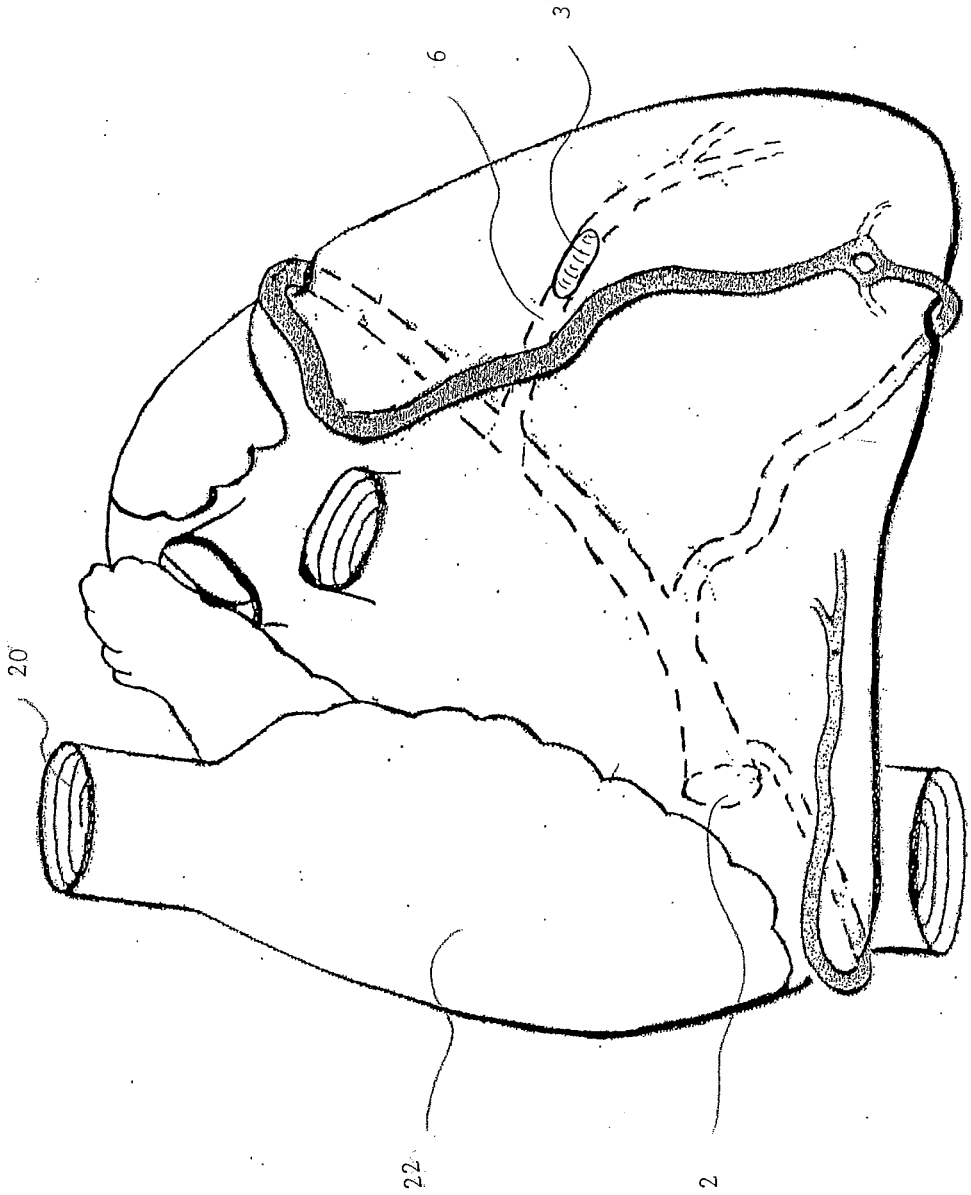


Fig. 7b

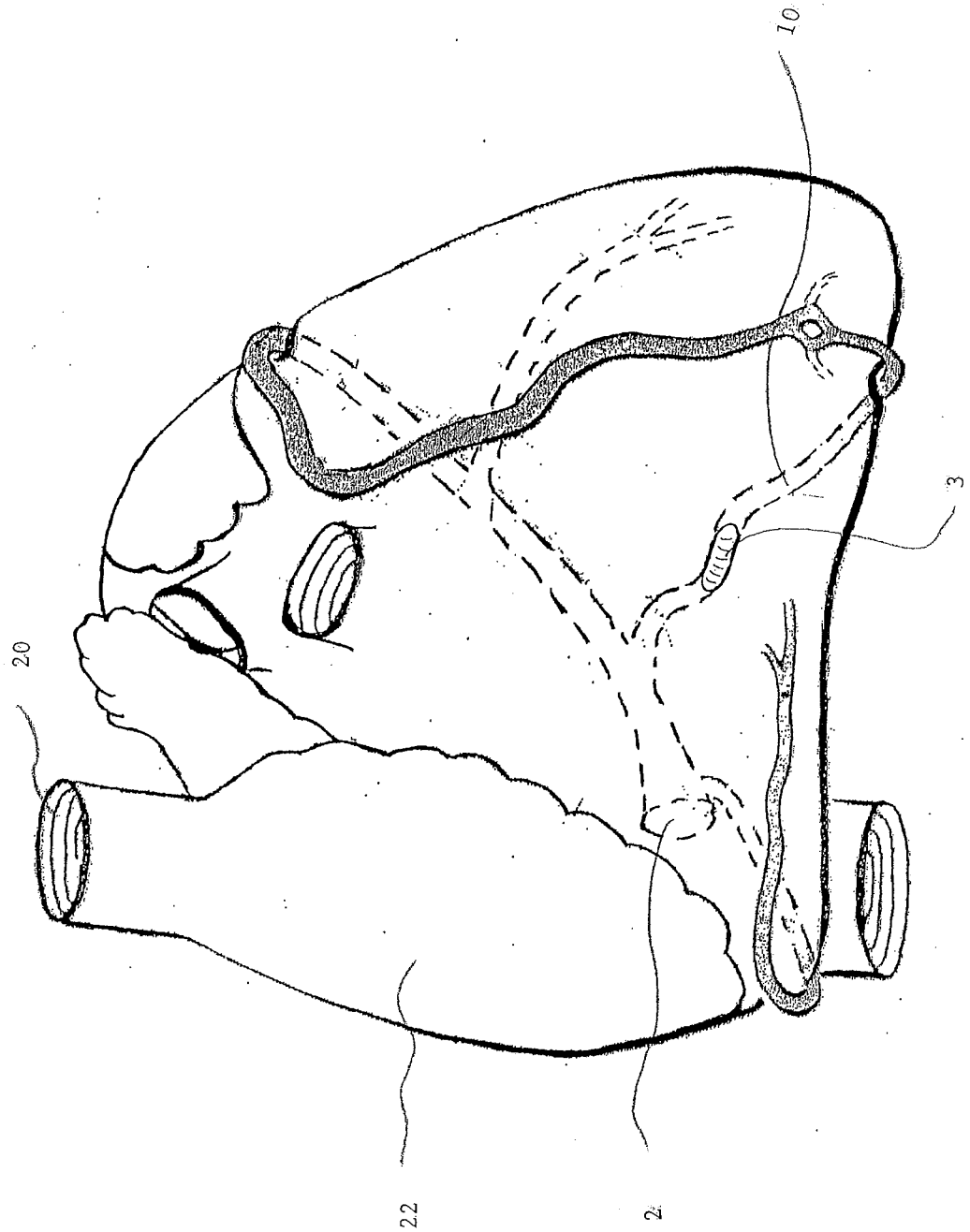


Fig. 7c

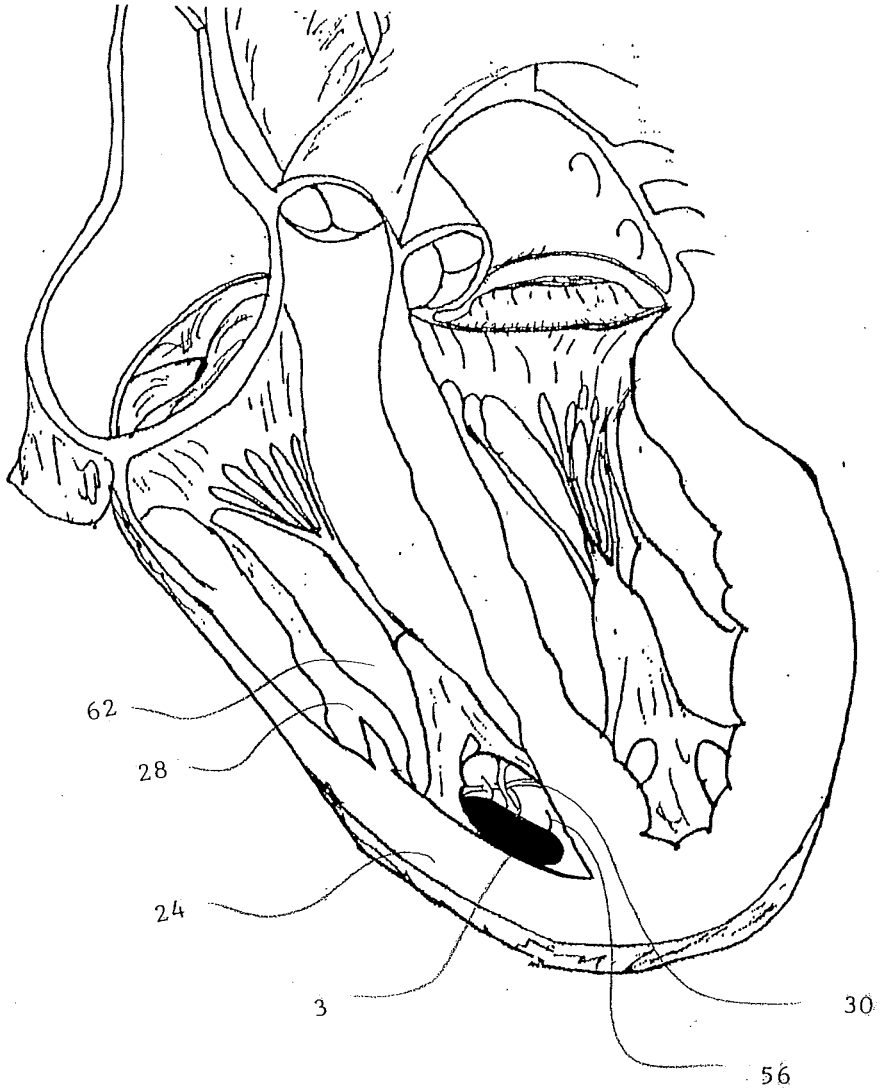


Fig. 7d

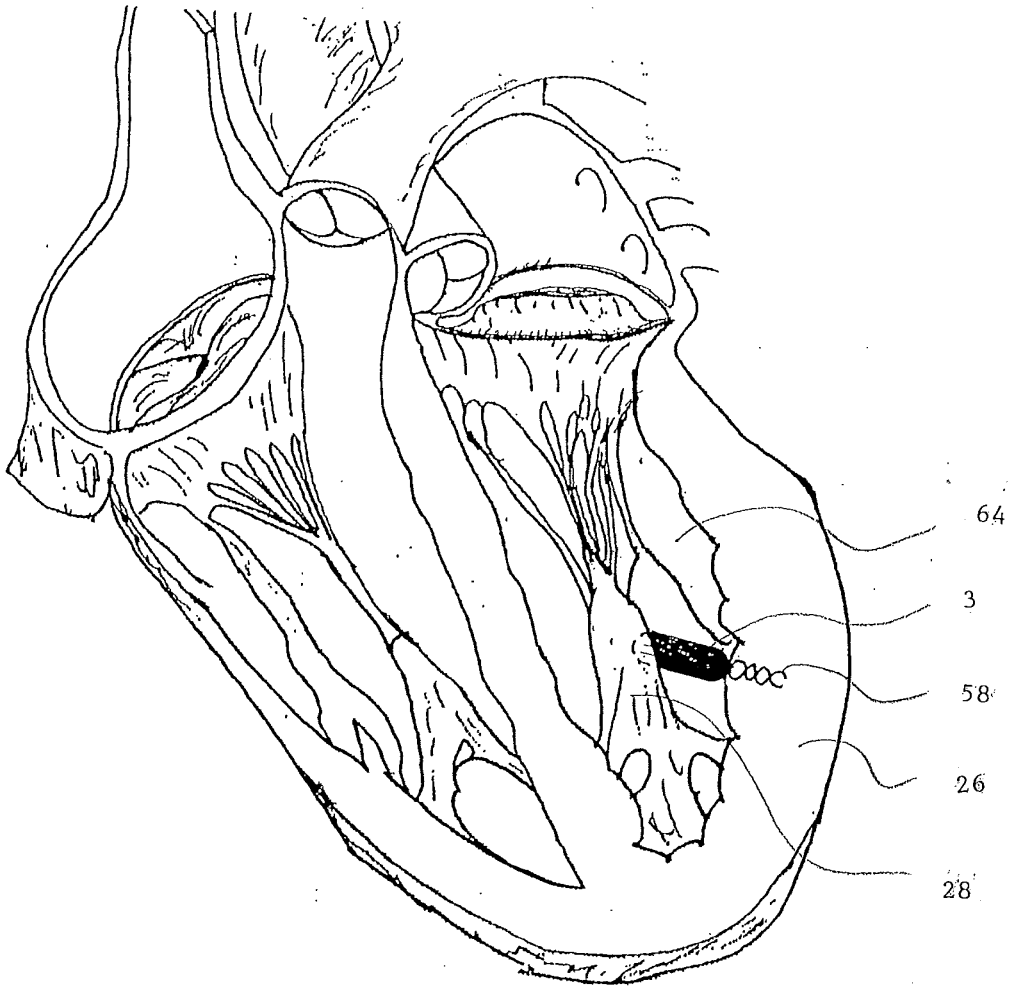


Fig. 7e

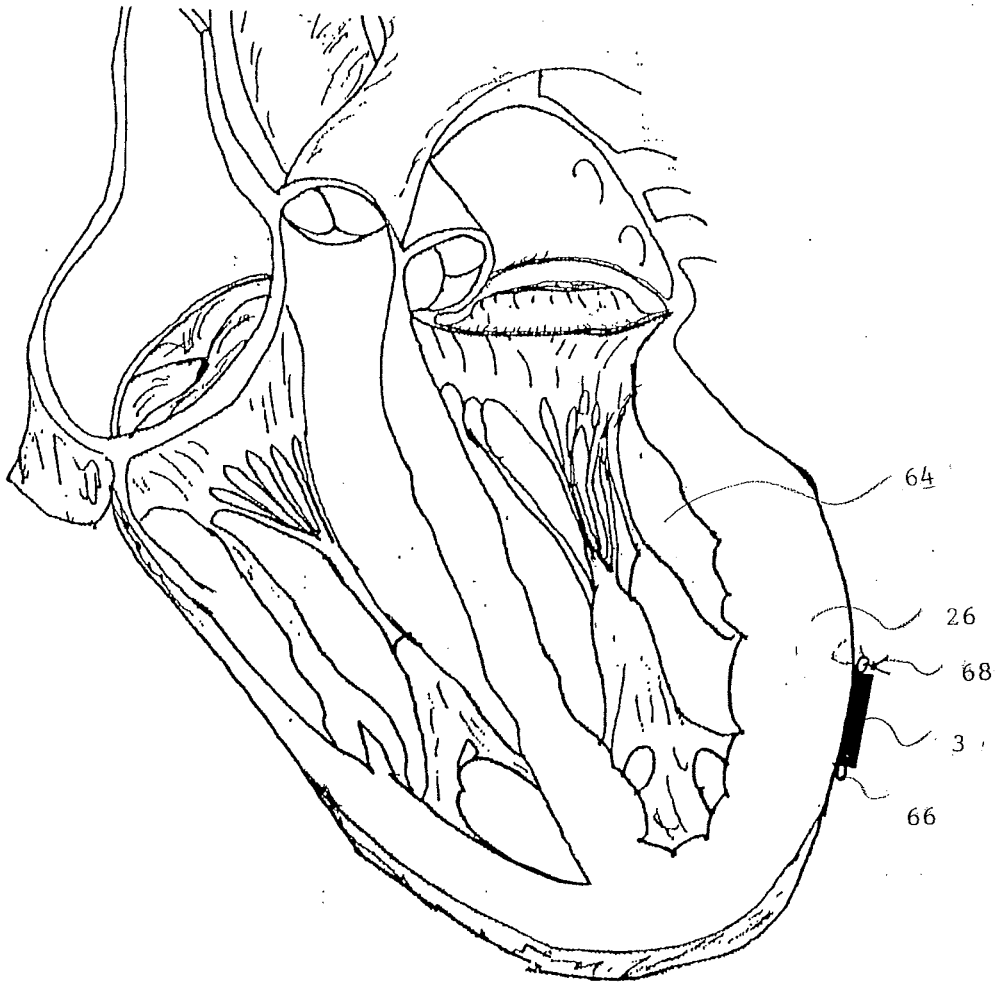


Fig. 7f

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00666

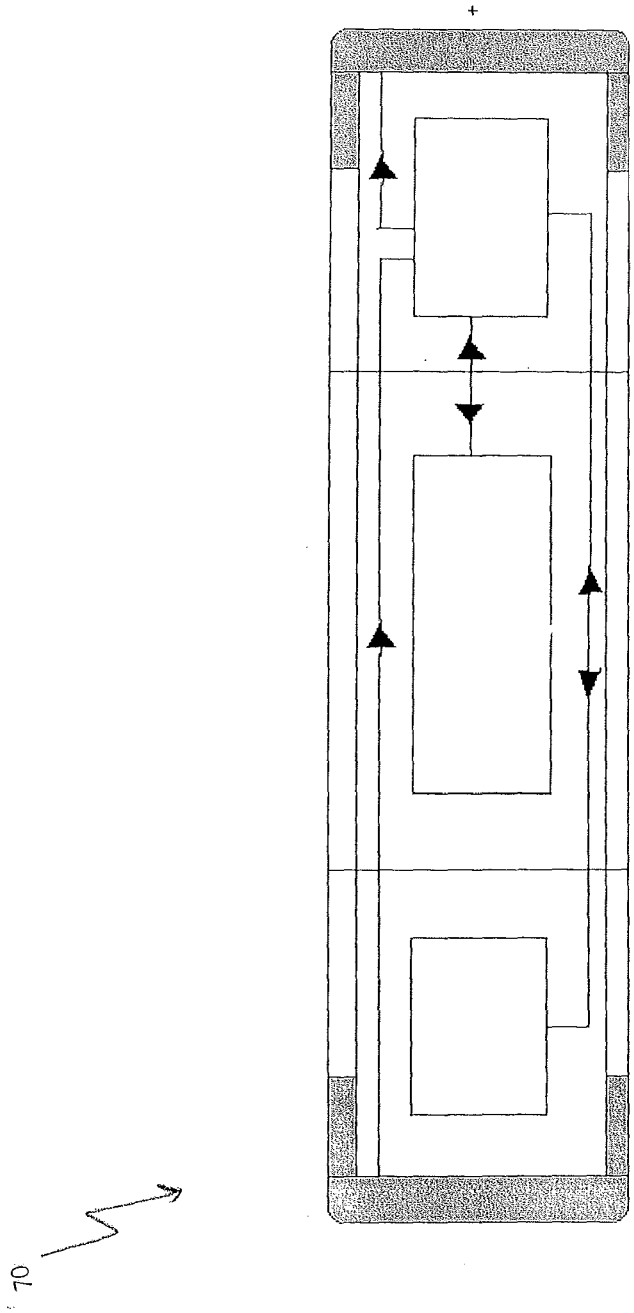


Fig. 8

Fig. 9

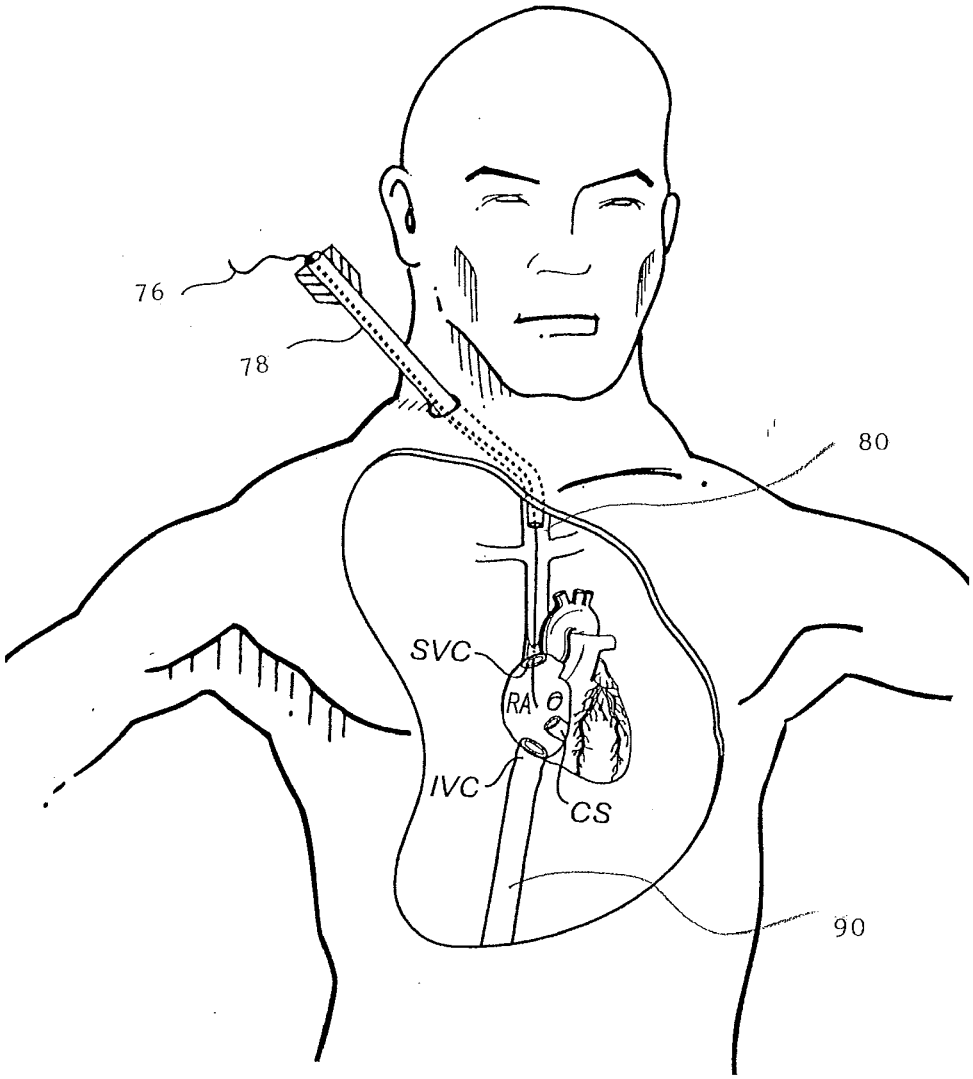


Fig. 10a

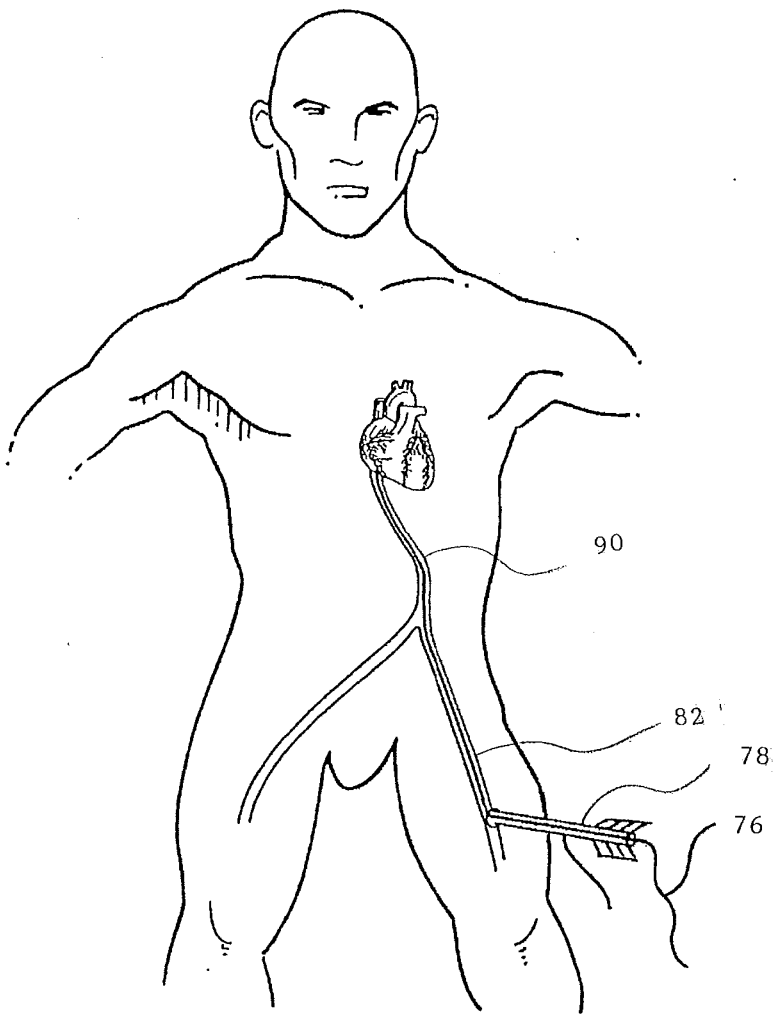


Fig. 10b

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00670

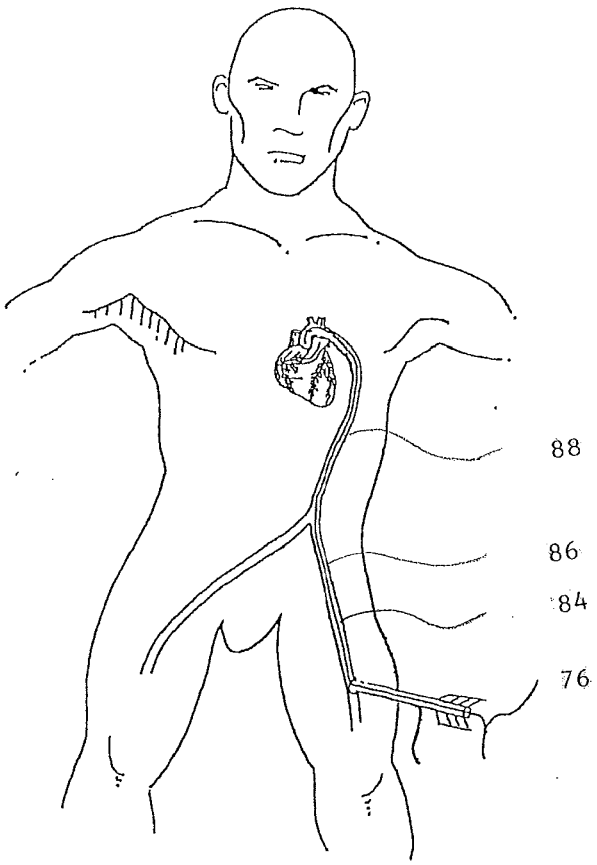


Fig. 10c

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00671

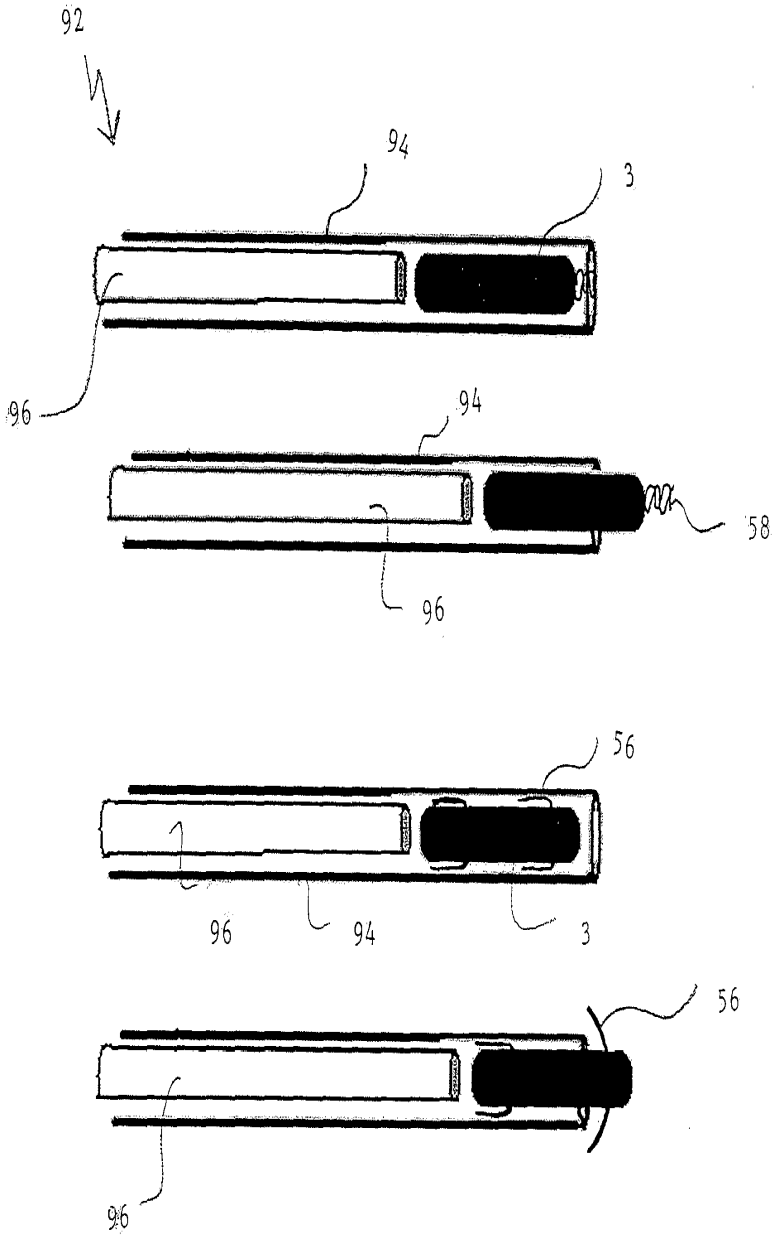


Fig. 11

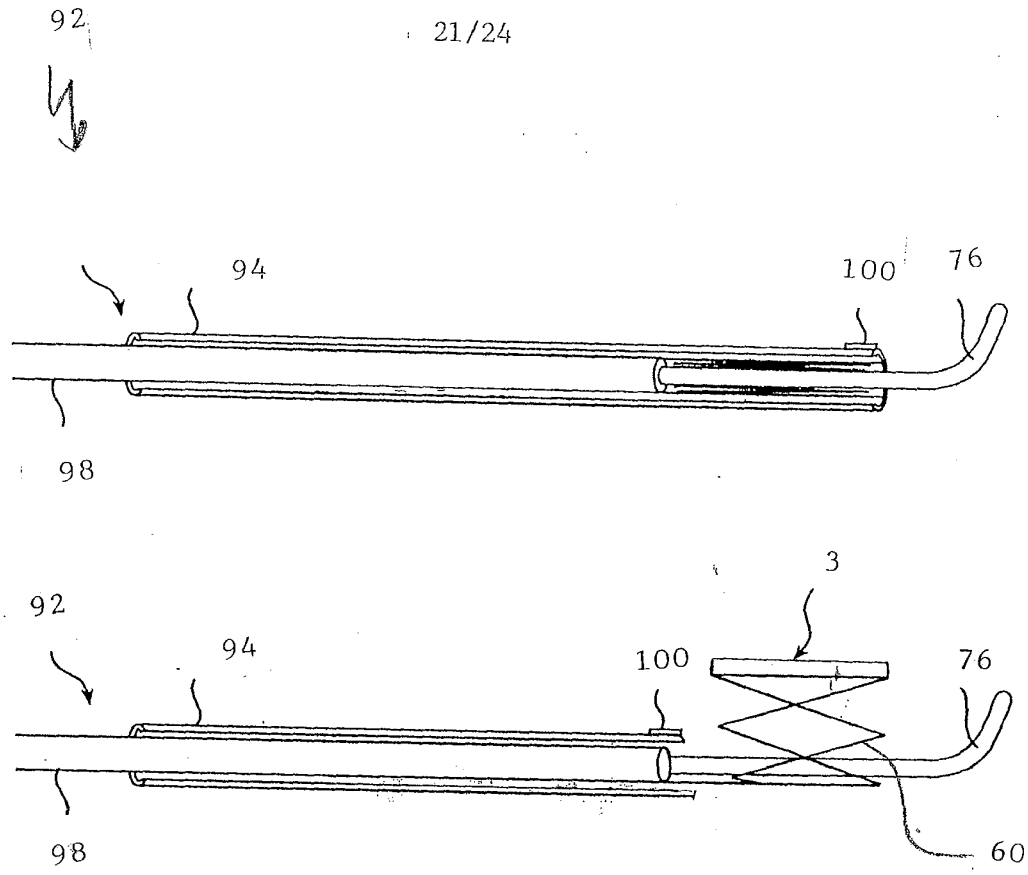


Fig. 12

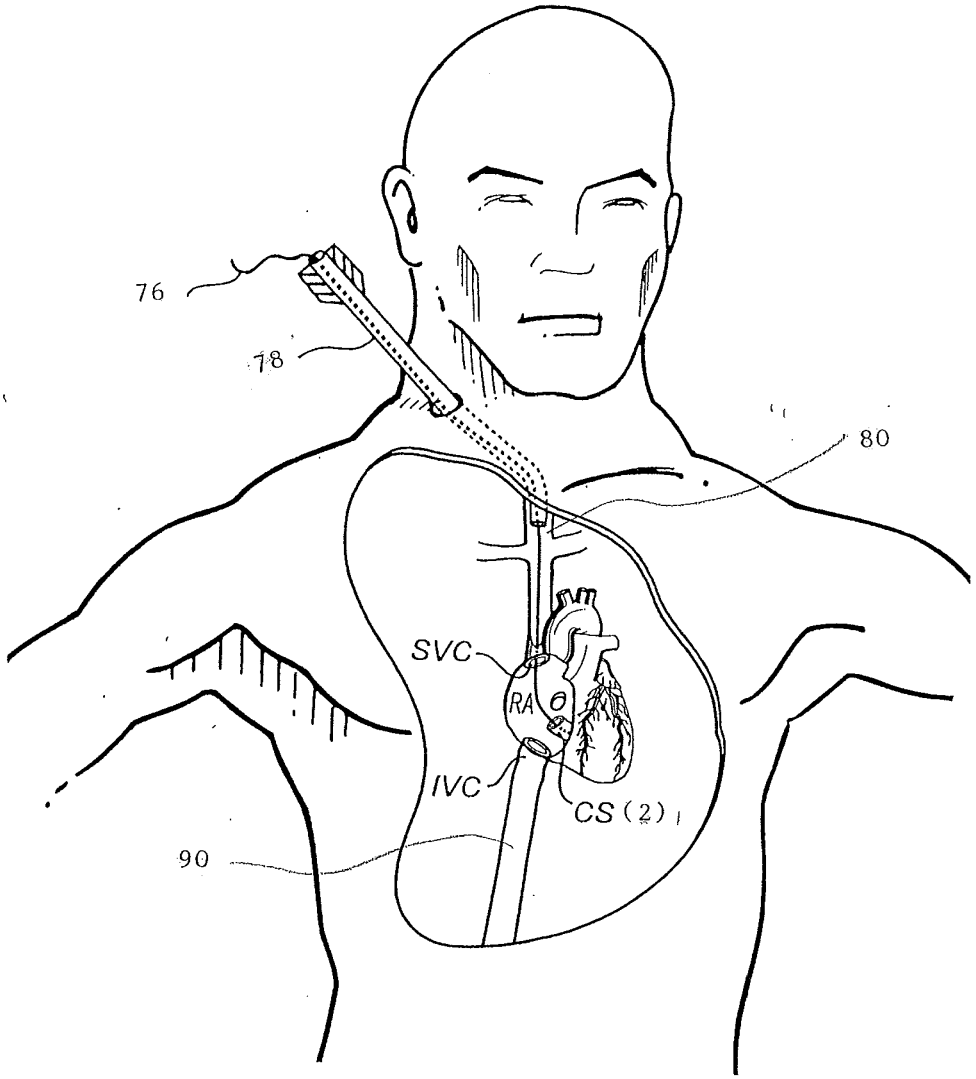


Fig. 13

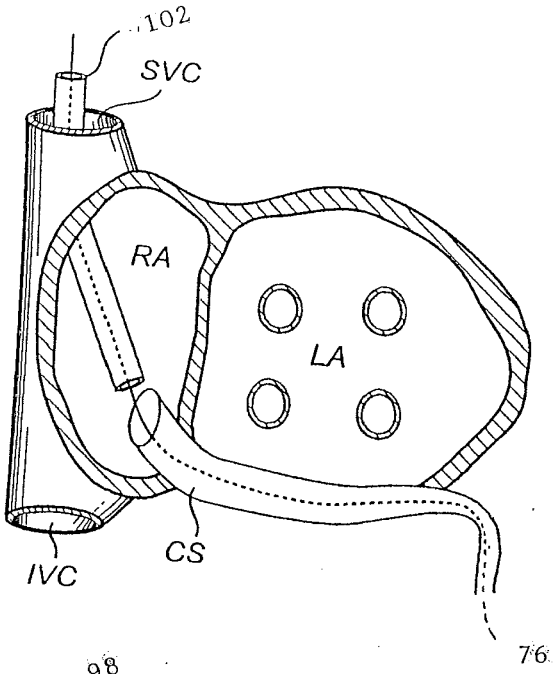


Fig. 14a

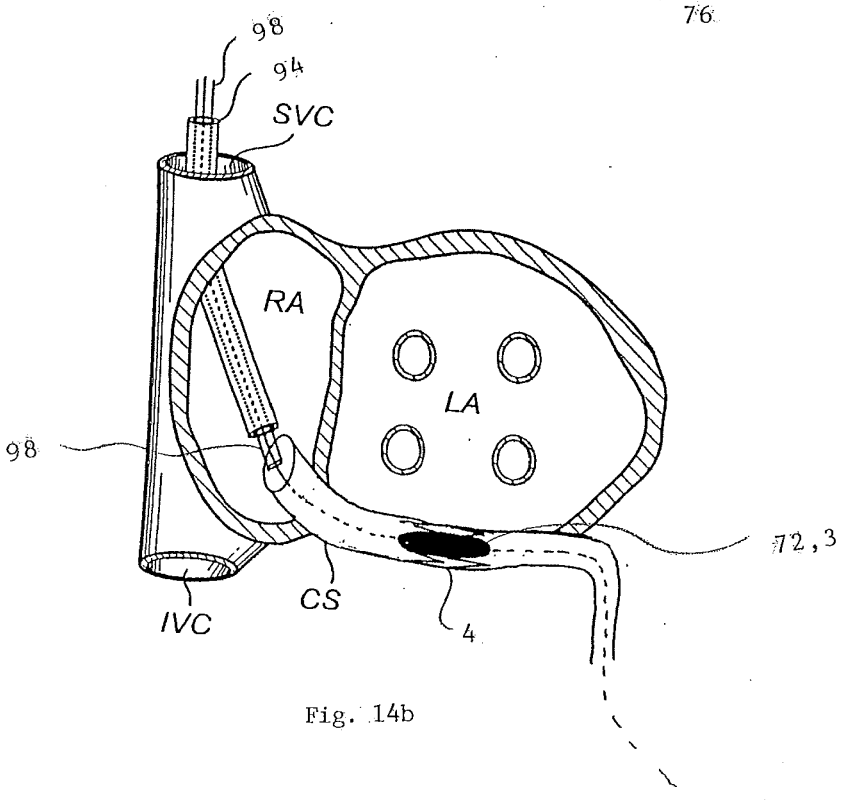


Fig. 14b

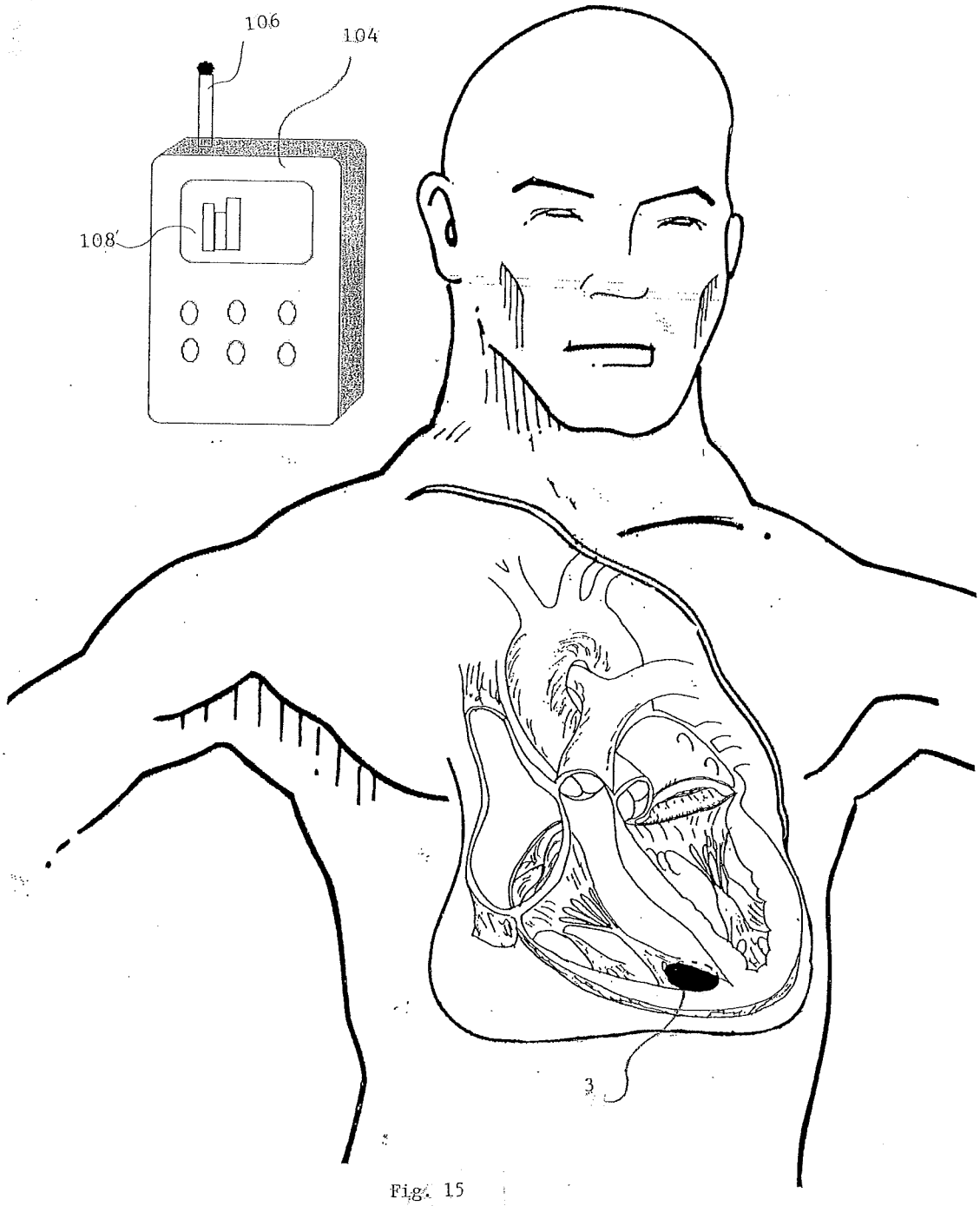


Fig. 15

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/056700

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/365 A61N1/378

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/158584 A1 (CATES ADAM W [US] ET AL) 21 August 2003 (2003-08-21) abstract; figures 1-20 paragraph [0011] - paragraph [0017] paragraph [0045] - paragraph [0152]	1,4,6,7, 9-18, 21-25, 27,28, 30, 32-36,40
Y		8,19,20, 26,29,31

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 September 2006	10/10/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Wetzig, Thomas

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/056700

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/055061 A1 (HOLZER ASHER) 10 March 2005 (2005-03-10) abstract; figures 1-9 paragraph [0010] - paragraph [0043] paragraph [0058] - paragraph [0109]	1,2,5,7, 11-14, 17,18, 21,33
X Y	US 3 835 864 A (RASOR N,US ET AL) 17 September 1974 (1974-09-17) abstract; figures 1,5,10,11 column 1, line 54 - column 3, line 22 column 3, line 55 - column 10, line 43	1-3,33 29
X	US 4 798 206 A (MADDISON ET AL) 17 January 1989 (1989-01-17) abstract; figures 1-16 column 2, line 17 - column 3, line 29 column 4, line 5 - column 8, line 32	1,4,10, 33
X	US 5 431 694 A (SNAPER ET AL) 11 July 1995 (1995-07-11) the whole document	1,4,5,33
Y	US 5 103 837 A (WEIDLICH ET AL) 14 April 1992 (1992-04-14) abstract column 1, line 4 - line 7 column 3, line 46 - line 51	8,19,20
Y	EP 1 541 191 A (JAPAN AS REPRESENTED BY PRESIDENT OF NATIONAL CARDIOVASCULAR CENTER) 15 June 2005 (2005-06-15) abstract; figures 9,10	26,31

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00678

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2005/056700

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 37-39, 41-43
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy (claims 37-39)Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery (claims 41-43)

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00679

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2005/056700

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2003158584 A1	21-08-2003	NONE	
US 2005055061 A1	10-03-2005	NONE	
US 3835864 A	17-09-1974	CA 1003904 A1	18-01-1977
		DE 2147308 A1	23-03-1972
		FR 2107826 A5	12-05-1972
		GB 1371034 A	23-10-1974
		GB 1371033 A	23-10-1974
		IT 942190 B	20-03-1973
		NL 7112915 A	23-03-1972
		SE 7410205 A	09-08-1974
US 4798206 A	17-01-1989	NONE	
US 5431694 A	11-07-1995	NONE	
US 5103837 A	14-04-1992	EP 0388480 A1	26-09-1990
EP 1541191 A	15-06-2005	AU 2002323811 A1	23-02-2004
		AU 2003252379 A1	23-02-2004
		CN 1674958 A	28-09-2005
		WO 2004012810 A1	12-02-2004
		WO 2004012811 A1	12-02-2004

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00680

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 March 2008 (06.03.2008)

PCT

(10) International Publication Number
WO 2008/027297 A3

(51) International Patent Classification:
A61N 1/36 (2006.01)

(21) International Application Number:
PCT/US2007/018697

(22) International Filing Date: 24 August 2007 (24.08.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11/468,603 30 August 2006 (30.08.2006) US

(71) Applicant *(for all designated States except US)*: **CARDIAC PACEMAKERS, INC.** [US/US]; 4100 Hamline Avenue North, St. Paul, MN 55112-5798 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LEE, Kent** [US/US]; 5665 Deer Trail West, Shoreview, MN 55126 (US). **LIBBUS, Imad** [US/US]; 1726 Stanford Avenue, St. Paul, MN 55105 (US). **CAPARSO, Anthony, V.** [US/US]; Apt. 225, 4755 Park Commons Drive, St. Louis Park, MN 55416 (US). **KWOK, Jonathan** [CA/US]; 4854 Churchill Street, Shoreview, MN 55126 (US). **PU, Yachuan** [US/US]; Apt. 7, 1811 Ulysses Street NE, Minneapolis, MN 55418 (US). **HAEFNER, Paul, A.** [US/US]; 252 Cobbler Court, Circle Pines, MN 55014 (US). **JAMES, Kristofer, J.** [US/US]; 1073 Ticonderoga Trail, Eagan, MN 55123 (US).

(74) Agents: **CLISE, Timothy, B.** et al.; Schwegman, Lundberg, Woessner & Kluth, P.A., P.O. Box 2938, Minneapolis, MN 55402 (US).

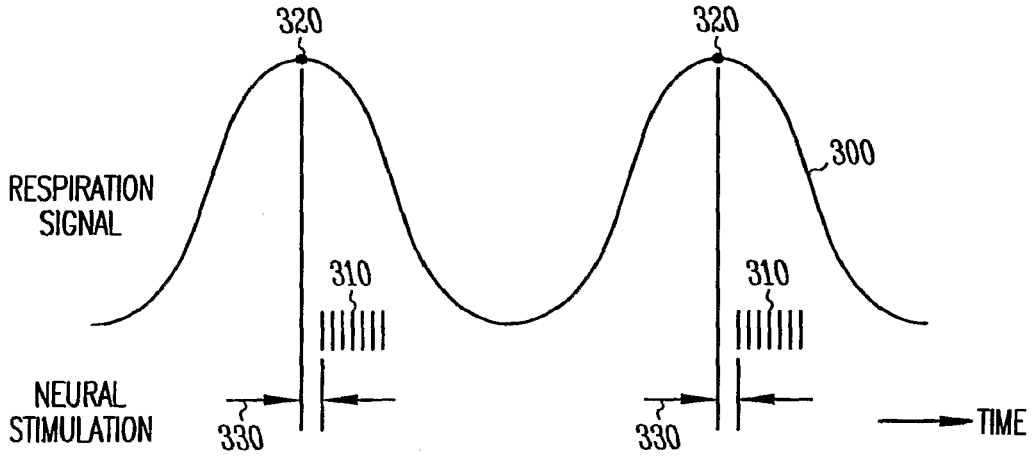
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
5 June 2008

(54) Title: SYSTEM FOR NEURAL STIMULATION DURING DISORDERED BREATHING



(57) Abstract: A neural stimulation system controls the delivery of neural stimulation using a respiratory signal as a therapy feedback input. The respiratory signal is used to increase the effectiveness of the neural stimulation, such as vagal nerve stimulation, while decreasing potentially adverse side effects in respiratory functions. In one embodiment, the neural stimulation system detects apnea and, in response, adjusts the delivery of the neural stimulation pulses and/or delivers a respiratory therapy treating the detected apnea.

WO 2008/027297 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/018697

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/36
ADD. A61B5/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,L, X	US 2006/271108 A1 (LIBBUS IMAD [US] ET AL) 30 November 2006 (2006-11-30) paragraphs [0027], [0028], [0030], [0033], [0037] - [0040]; figures 1,2,4	1-3,7,8
X	US 2004/210261 A1 (KING GARY W [US] ET AL) 21 October 2004 (2004-10-21)	1-10
Y	paragraphs [0005], [0006], [0008], [0009], [0023], [0024], [0032] - [0034], [0038], [0040], [0043]; figures 1-4	11-13

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 March 2008	14/03/2008

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fischer, Olivier

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/018697

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 2005/149127 A1 (LIBBUS IMAD [US]) 7 July 2005 (2005-07-07) paragraphs [0067] - [0071], [0087], [0088], [0097] - [0100]; figures 6,11-14,17,19A,19B	1,2,7,8 3-6,9-13
Y	US 6 251 126 B1 (OTTENHOFF FRANS A M [NL] ET AL) 26 June 2001 (2001-06-26) column 2, lines 36-46 column 4, lines 21-65 figures 1-4	11-13
A	US 2002/107553 A1 (HILL MICHAEL R S [US] ET AL) 8 August 2002 (2002-08-08) paragraphs [0010], [0039] - [0045]; figures 1A-3	1-13
A	US 2004/249416 A1 (YUN ANTHONY JOONKYOO [US] ET AL) 9 December 2004 (2004-12-09) paragraphs [0090], [0093]	1-13

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/018697

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 14-25
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy: claims 14-25 pertain to the delivery of a neural stimulation therapy to the living human body.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00684

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2007/018697

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2006271108 A1	30-11-2006	WO 2006127366 A1	30-11-2006
US 2004210261 A1	21-10-2004	WO 2004093982 A1	04-11-2004
US 2005149127 A1	07-07-2005	NONE	
US 6251126 B1	26-06-2001	US 6269269 B1	31-07-2001
US 2002107553 A1	08-08-2002	CA 2426810 A1	13-06-2002
		EP 1331965 A2	06-08-2003
		JP 2005500863 T	13-01-2005
		WO 0245791 A2	13-06-2002
US 2004249416 A1	09-12-2004	US 2005021092 A1	27-01-2005
		WO 2004110551 A2	23-12-2004

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 April 2008 (24.04.2008)

PCT

(10) International Publication Number
WO 2008/048471 A2

(51) International Patent Classification:
A61M 16/00 (2006.01)

(21) International Application Number:
PCT/US2007/021756

(22) International Filing Date: 12 October 2007 (12.10.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/851,386 13 October 2006 (13.10.2006) US
60/918,257 14 March 2007 (14.03.2007) US

(71) Applicant *(for all designated States except US)*: **APNEX MEDICAL, INC.** [US/US]; 2890 Centre Point Drive, St. Paul, Minnesota 55113 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BOLEA, Stephen, L.** [US/US]; 741 105th Street SE, Watertown, Minnesota 55388 (US). **HOEGH, Thomas, B.** [US/US]; 4407 Grimes Ave. S., Edina, Minnesota 55424 (US). **PERSSON, Bruce, J.** [US/US]; 2107 105th Avenue, Dresser, Wisconsin 54009 (US). **ATKINSON, Robert, E.** [US/US]; 2679 Riviera Drive South, White Bear Lake, Minnesota 55110 (US). **HAUSCHILD, Sidney, F.** [US/US]; 294 Spring St., St. Paul, MN 55102 (US). **KAPLAN, Paula, M.** [US/US]; 2151 Niles Ave., St. Paul, MN 55116 (US). **KUHNLEY, Brian, D.** [US/US]; 15388 76th Ave. N., Maple Grove, MN 55311 (US). **JASPERSON, Keith, E.** [US/US]; 13993 Magnolia St., Andover, MN 55304 (US). **TESFAYESUS, Wondimeneh** [US/US]; 1425 Jessamine Ave. W., #202, St. Paul, MN 55108 (US). **THORP, Christopher, K.** [US/US]; 1050 Lake Susan Dr., Chanhassen, MN 55317 (US).

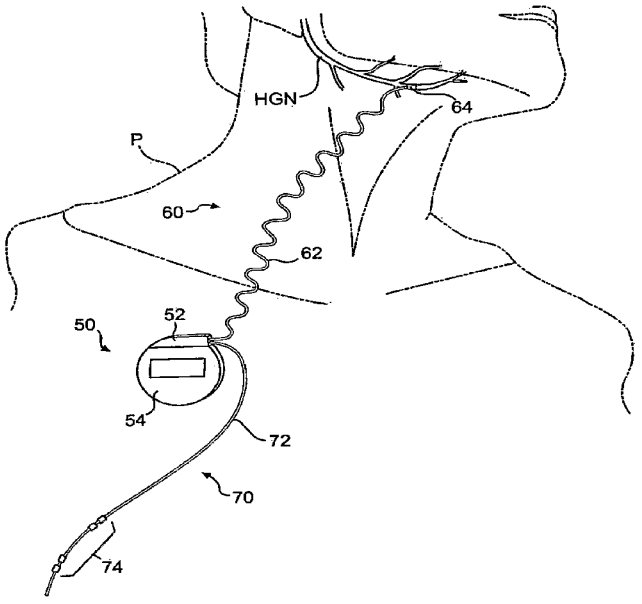
(74) Agent: **GARRETT, Arthur S.**; Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P., 901 New York Avenue, NW, Washington, District Of Columbia, 20001-4413 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

[Continued on next page]

(54) Title: OBSTRUCTIVE SLEEP APNEA TREATMENT DEVICES, SYSTEMS AND METHODS



(57) Abstract: Devices, systems and methods for nerve stimulation for OSA therapy.

WO 2008/048471 A2

ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

OBSTRUCTIVE SLEEP APNEA TREATMENT DEVICES, SYSTEMS AND METHODS

DESCRIPTION OF THE INVENTION

[001] This patent application claims the benefits of priority under 35 U.S.C. §§ 119 and 120 to U.S. Provisional Patent Application Nos. 60/851,386 and 60/918,257, filed on October 13, 2006, and March 14, 2007, respectively. The entire contents of these provisional applications are incorporated herein by reference.

Field of the Invention

[002] The inventions described herein relate to devices, systems and associated methods for treating sleeping disorders. More particularly, the inventions described herein relate to devices, systems and methods for treating obstructive sleep apnea.

Background of the Invention

[003] Obstructive sleep apnea (OSA) is highly prevalent, affecting one in five adults in the United States. One in fifteen adults has moderate to severe OSA requiring treatment. Untreated OSA results in reduced quality of life measures and increased risk of disease including hypertension, stroke, heart disease, etc.

[004] Continuous positive airway pressure (CPAP) is a standard treatment for OSA. While CPAP is non-invasive and highly effective, it is not well tolerated by patients. Patient compliance for CPAP is often reported to be between 40% and 60%.

[005] Surgical treatment options for OSA are available too. However, they tend to be highly invasive (result in structural changes), irreversible, and have poor and/or inconsistent efficacy. Even the more effective surgical procedures are undesirable because they usually require multiple invasive and irreversible operations, they may alter a patient's appearance (e.g., maxillo-mandibulary advancement), and/or they may be socially stigmatic (e.g., tracheostomy).

[006] US Patent No. 4,830,008 to Meer proposes hypoglossal nerve stimulation as an alternative treatment for OSA. An example of an implanted hypoglossal nerve stimulator for OSA treatment is the Inspire™ technology developed by Medtronic, Inc. (Fridely, MN). The Inspire device is not FDA approved and is not for commercial sale. The Inspire device includes an implanted neurostimulator, an implanted nerve cuff electrode connected to the neurostimulator by a lead, and an implanted intra-thoracic pressure sensor

for respiratory feedback and stimulus trigger. The Inspire device was shown to be efficacious (approximately 75% response rate as defined by a 50% or more reduction in RDI and a post RDI of ≤ 20) in an eight patient human clinical study, the results of which were published by Schwartz et al. and Eisele et al. However, both authors reported that only three of eight patients remained free from device malfunction, thus demonstrating the need for improvements.

SUMMARY OF THE INVENTION

[007] To address this and other unmet needs, the present invention provides, in exemplary non-limiting embodiments, devices, systems and methods for nerve stimulation for OSA therapy as described in the following detailed description.

BRIEF DESCRIPTION OF THE DRAWINGS

[008] It is to be understood that both the foregoing summary and the following detailed description are exemplary. Together with the following detailed description, the drawings illustrate exemplary embodiments and serve to explain certain principles. In the drawings:

[009] Figure 1 is a schematic diagram showing a fully implanted neurostimulator system with associated physician programmer and patient controller for treating obstructive sleep apnea;

[010] Figure 2 is a schematic diagram showing the implantable components of Figure 1 implanted in a patient;

[011] Figure 3 is a perspective view of the implantable components shown in Figure 1;

[012] Figure 4 is a detailed perspective view of the implantable neurostimulator (INS) shown in Figure 3;

[013] Figure 5 is a detailed perspective view of the nerve cuff electrode and lead body shown in Figure 3;

[014] Figure 5a is an illustration of exemplary movements a lead body may be configured to withstand;

[015] Figure 6 is a close-up detailed perspective view of the nerve cuff electrode shown in Figure 3;

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[016] Figure 7 is a detailed perspective view of the internal components of the nerve cuff electrode shown in Figure 6;

[017] Figure 8 shows side and end views of an electrode contact of the nerve cuff electrode shown in Figure 7;

[018] Figures 9A and 9B are perspective views of the respiration sensing lead shown in Figure 3;

[019] Figure 10 schematically illustrates surgical access and tunneling sites for implanting the system illustrated in Figure 2;

[020] Figures 11A and 11B schematically illustrate dissection to a hypoglossal nerve;

[021] Figures 12 and 12A-12D schematically illustrate various possible nerve stimulation sites for activating muscles controlling the upper airway;

[022] Figures 13 – 22 and 22A-22D are schematic illustrations of various stimulation lead body and electrode designs for use in a neurostimulator system;

[023] Figures 23 – 24 schematically illustrate alternative implant procedures and associated tools for the stimulation lead;

[024] Figure 25 schematically illustrates an alternative bifurcated lead body design;

[025] Figures 26A – 26B schematically illustrate alternative fixation techniques for the stimulation lead and electrode cuff;

[026] Figure 26C schematically illustrates an alternative embodiment of a stimulation lead having a fixation mechanism;

[027] Figures 27A – 27H schematically illustrate field steering embodiments;

[028] Figures 27I-27Q schematically illustrate alternative embodiments of nerve cuff electrodes with selective fiber stimulation mechanisms;

[029] Figures 28 – 33B schematically illustrate alternative fixation techniques for the respiration sensing lead;

[030] Figure 34 schematically illustrates the distal portion of an exemplary respiration sensing lead

[031] Figures 35A – 35E and 36 schematically illustrate alternative electrode arrangements on the respiration sensing lead;

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[032] Figures 37A-37C schematically illustrate various anatomical positions or bio-Z vectors for the electrodes on the respiration sensing lead;

[033] Figures 38A illustrates an exemplary method of sampling a plurality of vector signals;

[034] Figures 38B – 46 schematically illustrate alternative respiration signal processing techniques;

[035] Figure 47 schematically illustrates an alternative respiration detection technique;

[036] Figures 47A-47D illustrate an exemplary stimulation trigger algorithm;

[037] Figures 48 – 50 schematically illustrate alternative stimulation trigger algorithms;

[038] Figure 50A illustrates an exemplary waveform of a patient's respiratory cycle;

[039] Figure 50B illustrates an exemplary stimulation waveform;

[040] Figures 51A – 51M are schematic illustrations of various external (partially implanted) neurostimulation systems for treating obstructive sleep apnea;

[041] Figures 52A – 52G are schematic illustrations of a specific embodiment of an external (partially implanted) neurostimulation system;

[042] Figures 53 – 56 schematically illustrate alternative screening tools; and

[043] Figures 57A – 58B schematically illustrate alternative intra-operative tools.

DESCRIPTION OF THE EMBODIMENTS

[044] The following detailed description should be read with reference to the drawings in which similar elements in different drawings are numbered the same. The drawings, which are not necessarily to scale, depict illustrative embodiments and are not intended to limit the scope of the invention.

[045] **Description of Fully Implanted Neurostimulator System**

[046] With reference to Figure 1, a neurostimulator system 10 including implanted components 20, physician programmer 30 and patient controller 40 is shown schematically. The implanted components of the system 10 may generally include an implanted neurostimulator (INS) 50 (a.k.a., implanted pulse generator (IPG)), an implanted stimulation

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lead (or leads) 60, and an implanted respiration sensing lead (or leads) 70. The INS 50 generally includes a header 52 for connection of the leads 60/70, and a hermetically sealed housing 54 for the associated electronics and long-life or rechargeable battery (not visible). The stimulation lead 60 generally includes a lead body 62 with a proximal connector and a distal nerve electrode cuff 64. The respiration sensing lead 70 generally includes a lead body 72 with a proximal connector and one or more sensors 74 disposed on or along a distal portion thereof. Suitable designs of the INS 50, stimulation lead 60 and respiration sensing lead 70 are described in more detail hereinafter.

[047] As shown in Figure 2, and by way of example, not limitation, the implanted components 20 (shown faded) of the neurostimulator system 10 are implanted in a patient P with the INS 50 disposed in a subcutaneous pocket, the stimulation lead body 62 disposed in a subcutaneous tunnel, the nerve cuff electrode 64 disposed on a nerve (e.g., hypoglossal nerve (HGN)) innervating a muscle (e.g., genioglossus muscle, not shown) controlling the upper airway, the respiration sensing lead body 72 disposed in a subcutaneous tunnel, and the respiration sensors 74 disposed adjacent lung tissue and/or intercostal muscles outside the pleural space.

[048] Generally, electrical stimulus is delivered by the INS 50 via the stimulation lead 60 to a nerve innervating a muscle controlling upper airway patency to mitigate obstruction thereof. To reduce nerve and muscle fatigue, the stimulus may be delivered for only a portion of the respiratory cycle, such as during inspiration which corresponds to negative pressure in the upper airway. Stimulation may be thus triggered as a function of respiration as detected by respiration sensing lead 70 in a closed-loop feedback system. By way of example, the stimulus may be triggered to turn on at the end of expiration (or at the beginning of inspiration), and triggered to turn off at the beginning of expiration (or at the end of inspiration). Triggering the stimulus as a function of expiration improves capture of the entire inspiratory phase, including a brief pre-inspiratory phase of about 300 milliseconds, thus more closely mimicking normal activation of upper airway dilator muscles. Over-stimulation may cause nerve and/or muscle fatigue, but a 40% to 50% duty cycle may be safely tolerated, thus enabling limited over-stimulation. As an alternative, stimulus may be delivered independent of actual respiration wherein the stimulus duty cycle

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is set for an average inspiratory duration at a frequency approximately equal to an average respiratory cycle.

[049] Stimulus may be delivered to one or more of a variety of nerve sites to activate one muscle or muscle groups controlling patency of the upper airway. For example, stimulation of the genioglossus muscle via the hypoglossal nerve moves or otherwise stiffens the anterior portion of the upper airway, thereby decreasing the critical pressure at which the upper airway collapses during inspiration and reducing the likelihood of an apnea or hypopnea event occurring during sleep. Because the systems described herein work at the level of the tongue, it may be desirable to combine this therapy with a therapy (e.g., UPPP or palatal implant) that work at the level of the soft palate, thus increasing efficacy for a broader range of patients.

[050] With reference back to Figure 1, the physician programmer 30 may comprise a computer 32 configured to control and program the INS 50 via a wireless link to a programming wand 34. The physician programmer 30 may be resident in a sleep lab where the patient undergoes a polysomnographic (PSG) study during which the patient sleeps while the INS 50 is programmed to optimize therapy.

[051] The patient controller 40 may comprise control circuitry and associated user interface to allow the patient to control the system via a wireless telemetry link while at home, for example. The patient controller 40 may include a power switch 42 to turn the system on and slowly ramp up when the patient goes to sleep at night, and turn it off when the patient wakes in the morning. A snooze switch 44 may be used to temporarily put the INS 50 in standby mode during which electrical stimulus is paused for a preprogrammed period of time to allow the patient to temporarily wake, after which the INS 50 turns back on and ramps up to the desired stimulus level. A display 46 may be provided to indicate the status of the INS 50 (e.g., on, off or standby), to indicate satisfactory wireless telemetry link to the INS 50, to indicate remaining battery life of the INS 50, to indicate normal operation of the INS 50, and/or to indicate the need for patient action etc. Display 46 may be configured to be a dash-board-like display, and may be any suitable display available to those of ordinary skill in the art, such as, for example, an LED or LCD display. Furthermore, information may be communicated to the patient controller 40 for display

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purposes by any suitable means known to those of ordinary skill in the art. For example, communication of information may be achieved through inductively coupled or radio frequency telemetry. The patient controller 40 may also have programmability to adjust stimulus parameters (e.g., amplitude) within a pre-set range determined by the physician in order to improve efficacy and/or to reduce sensory perception, for example. Optionally, the patient controller 40 may be configured to function as the programming wand 34 of the physician programmer 30.

[052] Furthermore, the patient controller 40 may be provided with one or more mechanisms for improving patient compliance. For example, patient controller 40 may be provided with a time-keeping mechanism having the capabilities of a conventional alarm clock. In certain embodiments, controller 40 may be programmed by the user and/or the physician to alert the user when action, such as, for example, turning the system 10 on or off, is required by the user. Controller 40 may be configured to alert the user by any suitable means known in the art. For example, controller 40 may emit an audible alarm at programmed time intervals. In other embodiments, the patient controller 40 may be used to monitor a patient. For example, the patient controller 40 may be programmed to periodically send reports of patient actions, patient compliance, system status, etc., to a clinician or caregiver via a telephone or computer network.

[053] With reference to Figure 3, the implanted components 20 are shown schematically with more detail. The implanted components include INS 50, stimulation lead 60, and respiration sensing lead 70. The INS 50 includes header 52 and housing 54. The stimulation lead 60 includes lead body 62 and nerve cuff electrode 64. The respiration sensing lead 70 includes lead body 72 and respiration sensors 74 (e.g., impedance sensing electrodes).

[054] With reference to Figure 4, the INS 50 is shown schematically in more detail. The INS 50 includes header 52 that may be formed using conventional molding or casting techniques and may comprise conventional materials such as epoxy or polyurethane (e.g., Tecothane brand polyurethane). The housing 54 may be formed using conventional stamping or forming techniques and may comprise conventional materials such as titanium or ceramic. The housing 54 may include one or more isolated electrodes, and/or if a

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conductive material is used for the housing 54, the housing 54 may comprise an electrode, which may be used for respiratory sensing, for example. The housing 54 may be hermetically sealed to the header 52 using conventional techniques. The header 52 may include two or more receptacles for receiving the proximal connectors 66/76 of the stimulation lead body 62 and respiration sensing lead body 72. The connectors 66/76 may comprise a conventional design such as IS1 or other in-line designs. The header 52 may also include set screw seals and blocks 56 for receiving set screws (not shown) that establish electrical contact between the INS 50 and the conductors of the leads 60/70 via connectors 66/76, and that establish mechanical fixation thereto. Some electrical contact may be achieved through spring type or cam-locked mechanisms. As shown, two set screw arrangements 56 are shown for the stimulation lead 60 and four set screw arrangements 56 are shown for the respiration sensing lead 70, but the number may be adjusted for the number of conductors in each lead. A hole 58 may be provided in the header 52 for securing the INS 50 to subcutaneous tissue using a suture at the time of implantation.

[055] The INS 50 may comprise a conventional implanted neurostimulator design used in neurostimulation applications, such as those available from Texcel (US), CCC (Uruguay) and NeuroTECH (Belgium), but modified for the present clinical application in terms of stimulation signal parameters, respiratory signal processing, trigger algorithm, patient control, physician programming, etc. The INS may contain a microprocessor and memory for storing and processing data and algorithms. Algorithms may be in the form of software and/or firmware, for example. One of several different embodiments of the neurostimulator may be implemented. For example, the neurostimulator may be an internal/implanted neurostimulator (INS) powered by a long-life primary battery or rechargeable battery, or an external neurostimulator (ENS) wirelessly linked (e.g., inductive) to an implanted receiver unit connected to the leads. The INS (or the receiver unit of the ENS) may be implanted and optionally anchored in a number of different locations including a subcutaneous pocket in the pectoral region, the dorsal neck region, or cranial region behind the ear, for example.

[056] The INS 50 may include any suitable circuitry and programming in accordance with the principles of the present disclosure. In one embodiment, INS 50 may

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include an activity sensor (not shown) for sensing the activity of a patient, including the amount of activity of the patient. The activity sensor may detect motion of a patient by any suitable means available to those of ordinary skill in the art. For example, a patient's motion may be detected by, for example, using an internal accelerometer and/or measuring the impedance of the patient's torso with, for example, the built-in respiration sensor discussed below, and/or measuring a tissue pressure on the surface of the implanted INS 50.

[057] The data corresponding to a patient's detected motion may be stored, evaluated, and utilized in any of a number of various ways. In one embodiment, data corresponding to a patient's motion may be used to determine whether a patient is sleeping or awake. For example, when a patient's activity level falls below a predetermined threshold, it may be assumed that the patient is sleeping. Conversely, when the patient's activity level rises above the pre-determined threshold, it may be assumed that the patient is awake. The activity sensor therefore may be used to facilitate selectively applying treatment when the patient is detected to be sleeping and/or inhibiting treatment when the patient is detected to be awake. Alternatively, data corresponding to a patient's motion may be evaluated over a long period of time, such as, for example, the first few months of treatment, for indications of improvement in a patient's quality of life. It is contemplated that increases in a patient's average level of daily activity will correspond to successful treatment of OSA. This, in turn, may correspond to improvements in the patient's quality of life.

[058] Moreover, the INS 50 may include a long-life battery (not shown) which requires periodic replacement after years of service. Alternatively, the INS may include a rechargeable power source such as a rechargeable battery or super capacitor that is used instead of the long-life battery. To facilitate recharging, the INS may include a receiver coil inductively linked to a transmitter coil that is connected to a recharging unit powered by a larger battery or line power. Because the patient is stationary while sleeping, recharging may be scheduled to occur sometime during sleep to eliminate the need to carry the recharging unit during daily activities. The transmitter coil and the receiver coil may be arranged coaxially in parallel planes to maximize energy transfer efficiency, and may be held in proximity to each other by a patch, garment, or other means as described with

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reference to the external neurostimulator embodiments. Other examples of neurostimulator designs will be described in more detail hereinafter.

[059] With reference to Figure 5, the stimulation lead 60 may comprise a variety of different design embodiments and may be positioned at different anatomical sites. For example, a nerve cuff electrode(s) 64 may be attached to a nerve(s) innervating musculature affecting patency of the upper airway. As an alternative or in addition, the nerve cuff electrode 64 may be replaced with an intramuscular electrode and placed directly in the musculature affecting patency of the upper airway. The nerve electrode 64 may be attached to a specific branch of a nerve innervating the desired muscle(s), or may be attached to a proximal trunk of the nerve in which a specific fascicle innervating the desired muscle(s) is targeted by steering the stimulus with multiple electrodes. One or more electrodes may be used for attachment to one or more portions of nerves on one side (unilateral) of the body, or one or more electrodes may be used for attachment to one or more portions of nerves on both sides (bilateral) of the body. Variations in lead body 62 and electrode 64 design as well as variations in the target stimulation site or sites will be described in more detail hereinafter.

[060] With continued reference to Figure 5, the lead body 62 may be sigmoid shaped, for example, to reduce strain applied to the cuff electrode 64 when the lead body 62 is subject to movement. The sigmoid shape, which may alternatively comprise a variety of other waveform shapes, may have a wavelength of approximately 1.0 to 1.5 cm, and an amplitude of approximately 0.75 to 1.5 cm, for example. The lead body 62 may comprise a tubular jacket with electrical conductors 68 extending therein. The tubular jacket may comprise extruded silicone having an outside diameter of approximately 0.047 inches and an inside diameter of approximately 0.023 inches, for example. The tubular jacket may optionally have a covering of co-extruded polyurethane, for example, to improve durability. The conductors 68, shown in a transparent window in the jacket for purposes of illustration only, may comprise a bifilar coil of insulated (e.g., ETFE) braided stranded wire (BSW) of MP35NLT material. The number of conductors 68 is shown as two, but may be adjusted depending on the desired number of independent electrodes used.

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[061] The various embodiments of stimulation leads, for example, stimulation lead 60, disclosed herein may be fabricated by any suitable means known to those having ordinary skill in the art, and may be made from any suitable material. For example, the discussed sigmoid shape of the tubular jacket of lead body 62 may be formed by first extruding silicone in a semi-cured or semi cross-linked state. Next, the semi cross-linked extruded tubular jacket may be placed in a sigmoid mold and then allowed to become fully cross-linked. In particular, the semi cross-linked extruded tubular jacket may be placed in an oven and heated to convert the semi cross-linked silicone of the extruded tubular jacket to fully cross-linked silicone. Additionally, a lumen within the tubular jacket may be created along a longitudinal axis of the tubular jacket by any suitable means.

[062] Furthermore, in accordance with the principles of the present disclosure, it is contemplated that one or more of the various embodiments of stimulation leads disclosed herein may be implanted in or near highly mobile portions of the body. For example, embodiments of the disclosed stimulation leads may be implanted in the ventral neck, for example, along a path between the clavicle and mandible of a patient. Additionally, although mastication, deglutition, and speech may result in mechanical loading on an implanted stimulation lead, it has been found that gross movement of the head and neck may create high mechanical stresses in the conductors of the lead body, lead jacket, and the junction between the conductor wires and the anchor points, such as, for example, the electrodes. Accordingly, it may be desirable to configure the various embodiments of stimulation leads to withstand certain predetermined amounts of fatigue and/or stresses, which may result from mechanical loading on a lead body due to gross movements of a patient's neck and head.

[063] In particular, research has revealed that approximately 98% of the population may experience a 38.5% elongation or less in the distance between the clavicle and angle of the mandible (e.g., adjacent a contemplated area of implantation for a stimulation lead in accordance with the principles of this disclosure). It has also been found that the angular range of motion of the cervical spine between adjacent vertebrae may be approximately 12 degrees, thereby flexing the lead through this angle with a bend radius assumed to be approximately 1.0 centimeter. *See* Augustus A. White III et al., Clinical Biomechanics of

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the Spine, pp. 84, 356, and 373 (1978). Furthermore, the frequency of gross head movement through the range of motion in the contemplated area of implantation has been estimated to be approximately 300,000 cycles per year, or on the average approximately 50 times per waking hour.

[064] Thus, it may be desirable to design a lead body that is capable of withstanding, among other things, the stresses imparted by the above-noted head and neck movements for an extended amount of time, such as, for example, ten years. In particular, in order to design a lead body that may remain functional for the exemplary ten year implanted life, it may be desirable to configure the lead bodies disclosed herein to withstand at least the above noted elongation and ranges of motion. For example, since implanted lead bodies are likely to be elongated by at least 38.5%, it may be desirable to design lead bodies to withstand being elongated by a predetermined distance Y, such as, for example, approximately 40% (+/- 2%) from an initial unstressed state, for a minimum of 3.0 million cycles without failure, as depicted in Figure 5A. In addition, since it is likely that an implanted lead body may experience an angular range of motion of at least 12 degrees, with a bend radius of approximately 1.0 centimeter, it may be desirable to configure the lead bodies to withstand being flexed around a predetermined radius X, such as, for example, 1.0 centimeter (+/- 0.05 centimeters), for a predetermined amount of rotation W, such as, for example, from approximately 0 degrees to approximately 15 degrees (+/- 3 degrees), such that the 15 degree maximum deflection occurs coincidently with the maximum elongation of the lead body.

[065] With reference to Figure 6, the nerve cuff electrode 64 may comprise a cuff body 80 having a lateral (or superficial) side 82 and a medial (or contralateral, or deep) side 84. The medial side 84 is narrower or shorter in length than the lateral side 82 to facilitate insertion of the medial side 84 around a nerve such that the medial side is on the deep side of the nerve and the lateral side is on the superficial side of the nerve. This configuration reduces the dissection of nerve branches and vascular supply required to get the cuff around a nerve. For the nerve cuff implant sites discussed herein, the medial side 84 may have a length of less than 6 mm, and preferably in the range of approximately 3 to 5 mm, for example. The lateral side 82 may have a length of more than 6 mm, and preferably in the

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range of approximately 7 to 8 mm, for example. The cuff body 80 may be compliant and may be available in different sizes with an inside diameter of approximately 2.5 to 3.0 mm or 3.0 to 3.5 mm, for example. The cuff size may also be adjusted depending on the nominal diameter of the nerve at the site of implantation. The cuff body 80 may have a wall thickness of approximately 1.0 mm and may be formed of molded silicone, for example, and may be reinforced with imbedded fibers or fabrics. An integral tow strap 86 may be used to facilitate wrapping the cuff around a nerve by first inserting the strap 86 under and around the deep side of the nerve and subsequently pulling the strap to bring the medial side 84 in position on the deep side of the nerve and the lateral side 82 on the superficial side of the nerve.

[066] With continued reference to Figure 6, the nerve cuff electrode 64 includes electrode contacts 90A, 90B, and 90C imbedded in the body 80 of the cuff, with their inside surface facing exposed to establish electrical contact with a nerve disposed therein. A transverse guarded tri-polar electrode arrangement is shown by way of example, not limitation, wherein electrode contacts 90A and 90B comprise anodes transversely guarding electrode contact 90C which comprises a cathode.

[067] With this arrangement, the anode electrodes 90A and 90B are connected to a common conductor 68A imbedded in the body 80, and the cathode electrode 90C is connected to an independent conductor 68B extending from the lateral side 82 to the medial side 84 and imbedded in the body 80. By using the conductors 68 to make connections within the body 80 of the cuff 64, fatigue stresses are imposed on the conductors rather than the electrode contacts 90A, 90B and 90C.

[068] With additional reference to Figures 7 and 8, the electrode contacts 90A, 90B and 90C may thus be semi-circular shaped having an arc length of less than 180 degrees, and preferably an arc length of approximately 120 degrees, for example. Each electrode 90 may have two reverse bends (e.g., hooked or curled) portions 92 to provide mechanical fixation to the body 80 when imbedded therein. Each electrode 90 may also have two crimp tabs 94 defining grooves thereunder for crimping to the conductors 68 or for providing a pass-through. As shown in Figure 7, conductor 68A passes through the grooves under the lower crimp tabs 94 of electrodes 90B and 90A, loops 98 around through the grooves under

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the upper crimp tabs 94 of electrodes 90A and 90B, is crimped 96 by the upper tabs 94 of electrodes 90A and 90B to provide mechanical and electrical connection, is looped again back between the crimp tabs 94 on the outside of the electrode contact 90, and is resistance spot welded 95 to provide redundancy in mechanical and electrical connection. Also as shown in Figure 7, conductor 68B passes through the groove under the lower crimp tab 94 of electrode 90C, loops around through the groove under the upper crimp tab 94 of electrode 90C, and is crimped by the upper tab 94 of electrode 90C to provide mechanical and electrical connection. This arrangement avoids off-axis tensile loading at the crimp sites 96 which may otherwise fail due to stress concentration, and the looped portion 98 provides additional strain relief.

[069] Figure 8 provides example dimensions (inches) of an electrode contact 90 for a 2.5 mm inside diameter cuff, wherein the electrode is formed of 90/10 or 80/20 platinum iridium alloy formed by wire EDM, for example. As illustrated, and as exemplary and approximate dimensions, electrode contact 90 may include a surface A having a full radius, a dimension B of 0.079 inches from tangent to tangent, a dimension C of 0.020 inches (3x), a radius of curvature D of 0.049R with a 16 micro-inch RMS, a dimension E of 0.008 inches (2x), a dimension F of 0.0065 inches (+/- 0.001 inches) (2x), a dimension G of 0.006 inches (+ 0.002 inches, - 0.001 inches) (2x), a dimension H of 0.014 inches (2x), a dimension I of 0.010 inches (2x), a dimension J of 0.010 inches (2x), and a dimension K of 0.006 inches (+/- 0.001 inches).

[070] With reference to Figures 9A and 9B, a distal portion of the respiration sensing lead 70 and a distal detail of the sensing lead 70, respectively, are shown schematically. In the illustrated embodiment, the respiration sensing lead 70 and associated sensors 74 are implanted as shown in Figure 2. However, the respiration sensor(s) may comprise a variety of different design embodiments, both implanted and external, and may be positioned at different anatomical sites. Generally, the respiratory sensor(s) may be internal/implanted or external, and may be connected to the neurostimulator via a wired or wireless link. The respiratory sensor(s) may detect respiration directly or a surrogate thereof. The respiratory sensor(s) may measure, for example, respiratory airflow, respiratory effort (e.g., diaphragmatic or thoracic movement), intra-pleural pressure, lung

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impedance, respiratory drive, upper airway EMG, changes in tissue impedance in and around the lung(s) including the lungs, diaphragm and/or liver, acoustic airflow or any of a number other parameters indicative of respiration. Detailed examples of suitable respiration sensing leads and sensors will be described in more detail hereinafter.

[071] With continued reference to Figure 9A and 9B, the respiration sensing lead 70 includes a lead body 72 and a plurality of respiration sensors 74A – 74D comprising ring electrodes for sensing bio-impedance. The lead body 72 of the respiration sensing lead 70 may include a jacket cover comprising an extruded silicone tube optionally including a polyurethane cover (80A durometer), or may comprise an extruded polyurethane tube (55D durometer). The ring electrodes 74A – 74D may comprise 90/10 or 80/20 platinum iridium alloy tubes having an outside diameter of 0.050 inches and a length of 5 mm, and secured to the jacket cover by laser welding and/or adhesive bonding, for example. The lead body 72 may include a plurality of conductors 78 as seen in the transparent window in the jacket cover, which is shown for purposes of illustration only. The conductors 78 may comprise insulated and coiled BSW or solid wire (optionally DFT silver core wire) disposed in the tubular jacket, with one conductor provided for each ring electrode 74A – 74D requiring independent control. Generally, the impedance electrodes 74A – 74D may comprise current emitting electrodes and voltage sensing electrodes for detecting respiration by changes in bio-impedance. The number, spacing, anatomical location and function of the impedance electrodes will be described in more detail hereinafter.

[072] System 10 may also include a plurality of diagnostic mechanisms (e.g., circuitry and/or programming) for monitoring and/or determining the functionality of certain components, such as, for example, stimulation lead 60. In particular, system 10 may include one or more switching circuits (not shown) that facilitate connection of the respiratory/trans-thoracic impedance sensing circuits of the present disclosure (discussed in greater detail below) to stimulation lead 60 for measuring the impedance of lead 60. In some embodiments, the impedance sensing circuit may be connected to each electrode pair. In other embodiments, the impedance sensing circuit may be connected between the case of the implanted INS 50 and each conductor 68 within the lead 60. While those having ordinary skill in the art will readily recognize that any suitable impedance sensing method

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may be utilized to monitor and/or determine the functionality of lead 60, the respiratory/trans-thoracic impedance sensing circuit of the present disclosure may be preferred, since this circuit may be capable of identifying small changes in impedance rather than the large changes detectable by standard methods.

[073] As alluded to above, sensing the impedance of lead 60 may provide for monitoring and/or determining the functionality of lead 60. Specifically, sensing the impedance of lead 60 may facilitate diagnosing and distinguishing between differing types of failures of lead 60. In particular, research has revealed that changes in the impedance of lead 60 may be indicative of certain types of failures, including, but not limited to, corrosion, high contact resistance, breakage, and/or shorting. For example, a broken wire inside the lead could be identified by an excessively high lead impedance value. Corrosion of an electrode with its resultant decrease in effective electrode surface area could be identified by a smaller increase in impedance of that electrode. Similarly, an abnormally low value could correspond with a short between conductors in the lead, or an abrasion of the lead body that exposed a conductor to the tissue. Measuring from the case of the INS to each electrode allows independent identification of the integrity of each wire/electrode in the lead. In addition, sensing the impedance of lead 60 may facilitate periodic, automated adjustment of stimulation pulse amplitude so as to maintain constant current, energy, and/or charge delivery using a simpler voltage mode delivery circuit. Such automated adjustment may facilitate ensuring safety and effectiveness by consistently delivering the prescribed current, energy, or charge in the presence of tissue/electrode impedance variations. By consistently controlling the delivery of only the minimally required energy necessary for stimulation of the nerve, the stimulation amplitude may be programmed closer to the actual stimulation threshold rather than programming a wide margin to ensure continued effectiveness. This enhances safety and reduces power consumption. Moreover, sensing the impedance of lead 60 may allow monitoring of certain system dynamics, such as, for example, doses actually delivered to a patient.

[074] **Description of Implant Procedure**

[075] With reference to Figure 10, surgical access sites are schematically shown for implanting the internal neurostimulator components 20 shown in Figure 1. The internal

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neurostimulator components 20 may be surgically implanted in a patient on the right or left side. The right side may be preferred because it leaves the left side available for implantation of a pacemaker, defibrillator, etc., which are traditionally implanted on the left side. The right side may also be preferred because it lends itself to a clean respiratory signal less susceptible to cardiac artifact and also offers placement of respiratory sensors across the interface between the lung, diaphragm and liver for better detection of impedance changes during respiration.

[076] With continued reference to Figure 10, the INS (not shown) may be implanted in a subcutaneous pocket 102 in the pectoral region, for example. The stimulation lead (not shown) may be implanted in a subcutaneous tunnel 104 along (e.g., over or under) the platysma muscle in the neck region. The respiration sensing lead (not shown) may be implanted in a subcutaneous tunnel 106 extending adjacent the ribcage to an area adjacent lung tissue and/or intercostal muscles outside the pleural space. The nerve cuff electrode (not shown) may be attached to a nerve by surgical dissection at a surgical access site 110 proximate the targeted stimulation site. In the illustrated example, the target nerve is the right hypoglossal nerve and the surgical access site is in the submandibular region.

[077] With reference to Figures 11A and 11B, a surgical dissection 110 to the hypoglossal nerve is shown schematically. A unilateral dissection is shown, but a bilateral approach for bilateral stimulation may also be employed. Conventional surgical dissection techniques may be employed. The branch of the hypoglossal nerve (usually a medial or distal branch) leading to the genioglossus muscle may be identified by stimulating the hypoglossal nerve at different locations and observing the tongue for protrusion. Because elongation and/or flexion may be mistaken for protrusion, it may be desirable to observe the upper airway using a flexible fiber optic scope (e.g., nasopharyngoscope) inserted into the patient's nose, through the nasal passages, past the nasopharynx and velopharynx to view of the oropharynx and hypopharynx and visually confirm an increase in airway caliber by anterior displacement (protrusion) of the tongue base when the nerve branch is stimulated.

[078] The implant procedure may be performed with the patient under general anesthesia in a hospital setting on an out-patient basis. Alternatively, local anesthesia (at

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the surgical access sites and along the subcutaneous tunnels) may be used together with a sedative in a surgical center or physician office setting. As a further alternative, a facial nerve block may be employed. After a post-surgical healing period of about several weeks, the patient may return for a polysomnographic (PSG) test or sleep study at a sleep center for programming the system and titrating the therapy. A trialing period may be employed prior to full implantation wherein the hypoglossal nerve or the genioglossus muscle is stimulated with fine wire electrodes in a sleep study and the efficacy of delivering stimulus to the hypoglossal nerve or directly to the genioglossus muscle is observed and measured by reduction in apnea hypopnea index, for example.

[079] Other nerve target sites are described elsewhere herein and may be accessed by similar surgical access techniques. As an alternative to surgical dissection, less invasive approaches such as percutaneous or laparoscopic access techniques may be utilized, making use of associated tools such as tubular sheaths, trocars, etc.

[080] **Description of Alternative Stimulation Target Sites**

[081] With reference to Figure 12, various possible nerve and/or direct muscle stimulation sites are shown for stimulating muscles controlling patency of the upper airway. In addition to the upper airway which generally includes the pharyngeal space, other nerves and dilator muscles of the nasal passage and nasopharyngeal space may be selectively targeted for stimulation. A general description of the muscles and nerves suitable for stimulation follows, of which the pharyngeal nerves and muscles are shown in detail in Figure 12.

[082] Airway dilator muscles and associated nerves suitable for activation include are described in the following text and associated drawings. The dilator naris muscle functions to widen the anterior nasal aperture (i.e., flares nostrils) and is innervated by the buccal branch of the facial nerve (cranial nerve VII). The tensor veli palatine muscle functions to stiffen the soft palate and is innervated by the medial (or internal) pterygoid branch of the mandibular nerve MN. The genioglossus muscle is an extrinsic pharyngeal muscle connecting the base of the tongue to the chin and functions to protrude the tongue. The genioglossus muscle is typically innervated by a distal or medial branch (or braches) of the right and left hypoglossal nerve. The geniohyoid muscle connects the hyoid bone to the

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chin and the sternohyoid muscle attaches the hyoid bone to the sternum. The geniohyoid muscle functions to pull the hyoid bone anterosuperiorly, the sternohyoid muscle functions to pull hyoid bone inferiorly, and collectively (i.e., co-activation) they function to pull the hyoid bone anteriorly. The geniohyoid muscle is innervated by the hypoglossal nerve, and the sternohyoid muscle is innervated by the ansa cervicalis nerve.

[083] By way of example, a nerve electrode may be attached to a specific branch of the hypoglossal nerve innervating the genioglossus muscle (tongue protruder), or may be attached to a more proximal portion (e.g., trunk) of the hypoglossal nerve in which a specific fascicle innervating the genioglossus muscle is targeted by steering the stimulus using an electrode array. Activating the genioglossus muscle causes the tongue to protrude thus increasing the size of anterior aspect of the upper airway or otherwise resisting collapse during inspiration.

[084] As an alternative to activation of any or a combination of the airway dilator muscles, co-activation of airway dilator and airway restrictor or retruder muscles may be used to stiffen the airway and maintain patency. By way of example, a nerve electrode may be attached to specific branches of the hypoglossal nerve innervating the genioglossus muscle (tongue protruder), in addition to the hyoglossus and styloglossus muscles (tongue retruders), or may be attached to a more proximal portion (e.g., trunk) of the hypoglossal nerve in which specific fascicles innervating the genioglossus, hyoglossus and styloglossus muscles are targeted by steering the stimulus using an electrode array. Activating the hyoglossus and styloglossus muscles causes the tongue to retract, and when co-activated with the genioglossus, causes the tongue to stiffen thus supporting the anterior aspect of the upper airway and resisting collapse during inspiration. Because the tongue retruder muscles may overbear the tongue protruder muscle under equal co-activation, unbalanced co-activation may be desired. Thus, a greater stimulus (e.g., longer stimulation period, larger stimulation amplitude, higher stimulation frequency, etc.) or an earlier initiated stimulus may be delivered to the portion(s) of the hypoglossal nerve innervating the genioglossus muscle than to the portion(s) of the hypoglossal nerve innervating the hyoglossus and styloglossus muscles.

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[085] With continued reference to Figure 12, examples of suitable nerve stimulation sites include B; A + C; A + C + D; B + D; C + D; and E. Sites B and E may benefit from selective activation by field steering using an electrode array. As mentioned before, nerve electrodes may be placed at these target nerve(s) and/or intramuscular electrodes may be placed directly in the muscle(s) innervated by the target nerve(s).

[086] Site A is a distal or medial branch of the hypoglossal nerve proximal of a branch innervating the genioglossus muscle and distal of a branch innervating the geniohyoid muscle. Site B is a more proximal portion of the hypoglossal nerve proximal of the branches innervating the genioglossus muscle and the geniohyoid muscle, and distal of the branches innervating the hyoglossus muscle and the styloglossus muscle. Site C is a medial branch of the hypoglossal nerve proximal of a branch innervating the geniohyoid muscle and distal of branches innervating the hyoglossus muscle and the styloglossus muscle. Site D is a branch of the ansa cervicalis nerve distal of the nerve root and innervating the sternohyoid. Site E is a very proximal portion (trunk) of the hypoglossal nerve proximal of the branches innervating the genioglossus, hyoglossus and styloglossus muscles.

[087] Activating site B involves implanting an electrode on a hypoglossal nerve proximal of the branches innervating the genioglossus muscle and the geniohyoid muscle, and distal of the branches innervating the hyoglossus muscle and the styloglossus muscle.

[088] Co-activating sites A+C involves implanting a first electrode on a hypoglossal nerve proximal of a branch innervating the genioglossus muscle and distal of a branch innervating the geniohyoid muscle, and implanting a second electrode on the hypoglossal nerve proximal of a branch innervating the geniohyoid muscle and distal of branches innervating the hyoglossus muscle and the styloglossus muscle.

[089] Co-activating sites A+C+D involves implanting a first electrode on a hypoglossal nerve proximal of a branch innervating the genioglossus muscle and distal of a branch innervating the geniohyoid muscle; implanting a second electrode on the hypoglossal nerve proximal of a branch innervating the geniohyoid muscle and distal of branches innervating the hyoglossus muscle and the styloglossus muscle; and implanting a

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third electrode on a branch of an ansa cervicalis nerve distal of the nerve root and innervating the sternohyoid.

[090] Co-activating sites B+D involves implanting a first electrode on a hypoglossal nerve proximal of branches innervating the genioglossus muscle and the geniohyoid muscle, and distal of branches innervating the hyoglossus muscle and the styloglossus muscle; and implanting a second electrode on a branch of an ansa cervicalis nerve distal of the nerve root and innervating the sternohyoid.

[091] Co-activating sites C+D involves implanting a first electrode on a hypoglossal nerve proximal of a branch innervating the geniohyoid muscle, and distal of branches innervating the hyoglossus muscle and the styloglossus muscle and implanting a second electrode on a branch of an ansa cervicalis nerve distal of the nerve root and innervating the sternohyoid.

[092] Activating site E involves implanting an electrode on a hypoglossal nerve proximal of the branches innervating the genioglossus, hyoglossus and styloglossus muscles; and selectively activating (e.g., by field steering) the genioglossus muscle before or more than the hyoglossus and styloglossus muscles.

[093] With reference now to Figures 12A-12D, additional possible nerve stimulation sites are shown for effecting muscles controlling patency of the upper airway. For example, the cranial root of the accessory nerve AN (cranial nerve XI) innervates the levator veli palatini muscle of the soft palate, which elevates the soft palate. The cranial root of the accessory nerve AN also innervates the palatoglossal muscle, which functions to pull the soft palate inferiorly when the genioglossus is co-activated via the hypoglossal nerve (HGN). Moreover, because the cranial root of the accessory nerve AN also innervates various other muscles including, but not limited to, the palatopharyngeus, specific fibers in the accessory nerve AN may be selectively stimulated with one or more of the fiber selective stimulation means described in greater detail below, in order to only activate desired fibers of the nerve. The glossopharyngeal nerve GN (cranial nerve IX) innervates the stylopharyngeus, which functions to dilate the lateral walls of the pharynx. However, since the glossopharyngeal nerve GN is a multi-function nerve with both afferent and efferent fibers, one or more of the fiber selective stimulation means described in greater

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detail below may be used to facilitate targeting the fibers that innervate only the stylopharyngeus. The cranial root of the accessory nerve AN and the glossopharyngeal nerve GN may be singularly activated, or these nerves may be co-activated with other nerve sites, such as, for example, the hypoglossal nerve, for increased efficacy.

[094] Another possible nerve stimulation site may include the superior laryngeal nerve SLN. The superior laryngeal nerve SLN descends posterior and medial from the internal carotid artery and divides into the internal laryngeal nerve ILN and external laryngeal nerve ELN. While the external laryngeal nerve ELN descends behind the sternohyoid with the superior thyroid artery, the internal laryngeal nerve ILN descends near the superior laryngeal artery. The internal laryngeal nerve ILN contains sensory (afferent) fibers that are connected to receptors in the larynx. Some of these receptors include, but are not limited to, mechanoreceptors which detect pressure changes in a patient's upper airway associated with its collapse and institute a physiological response to re-open the patient's upper airway. Therefore, stimulation of specific afferent fibers inside the ILN nerve may result in triggering a reflex response that causes upper airway dilation by activating several muscles groups.

[095] As discussed below, the superior laryngeal nerve SLN, in addition to being a sensory nerve, is also a motor nerve. Therefore, it is contemplated that one or more of the fiber selective stimulation means described in greater detail below may be utilized to facilitate only stimulating the sensory or afferent fibers of the nerve.

[096] **Description of Alternative Nerve Electrodes**

[097] Any of the alternative nerve electrode designs described hereinafter may be employed in the systems described herein, with modifications to position, orientation, arrangement, integration, etc. made as dictated by the particular embodiment employed. Examples of other nerve electrode designs are described in U.S. Patent No. 5,531,778, to Maschino et al., U.S. Patent No. 4,979,511 to Terry, Jr., and U.S. Patent No. 4,573,481 to Bullara, the entire disclosures of which are incorporated herein by reference.

[098] With reference to the following figures, various alternative electrode designs for use in the systems described above are schematically illustrated. In each of the embodiments, by way of example, not limitation, the lead body and electrode cuff may

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comprise the same or similar materials formed in the same or similar manner as described previously. For example, the lead body may comprise a polymeric jacket formed of silicone, polyurethane, or a co-extrusion thereof. The jacket may contain insulated wire conductors made from BSW or solid wire comprising MP35N, MP35N with Ag core, stainless steel or Tantalum, among others. The lead body may be sigmoid shaped to accommodate neck and mandibular movement. Also, a guarded cathode tri-polar electrode arrangement (e.g., anode-cathode-anode) may be used, with the electrodes made of 90/10 or 80/20 PtIr alloy with silicone or polyurethane backing.

[099] With specific reference to Figures 13A and 13B, a self-sizing and expandable design is shown to accommodate nerve swelling and/or over-tightening. Figure 13A shows a perspective view of a nerve electrode cuff 130 on a nerve such as a hypoglossal nerve, and Figure 13B shows a cross-sectional view of the nerve cuff electrode 130 on the nerve. In this embodiment, the implantable nerve cuff electrode 130 comprises a compliant sheet wrap 132 configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet by sutures 138, for example. The sheet 132 includes a plurality of radially and longitudinally distributed fenestrations 134 to allow expansion of the sheet 132 to accommodate nerve swelling and/or over tightening. Electrode contacts 136 comprising a coil, foil strip, conductive elastomer or individual solid conductors may be carried by the sheet 132 with an exposed inside surface to establish electrical contact with the nerve.

[0100] With specific reference to Figures 14A – 14C, another self-sizing and expandable design is shown to accommodate nerve swelling and/or over-tightening. Figure 14A shows a perspective view of a nerve electrode cuff 140 on a nerve such as a hypoglossal nerve, and Figure 14B shows a cross-sectional view of the nerve cuff electrode 140 on the nerve. In this embodiment, the implantable nerve cuff electrode 140 comprises a compliant sheet wrap 142 configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet by sutures 148A, or by a buckle 148B as shown in Figure 14C, for example. The opposite portions of the sheet 142 comprise one or more narrow strips 144 integral with the sheet 142 to allow expansion and to accommodate nerve swelling and/or over tightening. Electrode contacts 146 comprising a coil, foil strip,

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conductive elastomer or individual solid conductors may be carried by the sheet 142 with an exposed inside surface to establish electrical contact with the nerve.

[0101] With specific reference to Figures 15A – 15C, another self-sizing and expandable design is shown to accommodate nerve swelling and/or over-tightening. Figure 15A shows a perspective view of a nerve electrode cuff 150 on a nerve such as a hypoglossal nerve, and Figure 15B shows a cross-sectional view of the nerve cuff electrode 150 on the nerve. In this embodiment, the implantable nerve cuff electrode 150 comprises a compliant sheet wrap 152 configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet 152 by sutures 158, for example. The opposite portions of the sheet 152 are offset from the nerve and a thickened portion of the sheet 152 fills the offset space. The offset distance reduces the amount of compressive force that the electrode cuff can exert on the nerve. To further reduce the pressure on the nerve, the sheet 152 includes a plurality of radially distributed slits 154 extending partly through the thickness of the sheet 152 to allow expansion and to accommodate nerve swelling and/or over tightening.

[0102] With specific reference to Figures 16A and 16B, another self-sizing and expandable design is shown to accommodate nerve swelling and/or over-tightening. Figure 16A shows a perspective view of a nerve electrode cuff 160 on a nerve such as a hypoglossal nerve, and Figure 16B shows a cross-sectional view of the nerve cuff electrode 160 on the nerve. In this embodiment, the implantable nerve cuff electrode 160 comprises a compliant sheet wrap 162 configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet 162 by sutures 168, for example. The sheet 162 includes a plurality of radially distributed and longitudinally extending convolutions 164 that may comprise alternative thick 164A and thin 164B portions in the sheet 162 and/or overlapping portions 164C of the sheet 162 to allow expansion and to accommodate nerve swelling and/or over tightening. Electrode contacts 166 comprising a coil, foil strip, conductive elastomer or individual solid conductors may be carried by the sheet 162 with an exposed inside surface to establish electrical contact with the nerve. Nerve cuff electrode 160 may accommodate one or two lead bodies 62A, 62B for connection to the electrode contacts 166 on the same or opposite sides of the nerve.

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[0103] Turning now to Figures 16C-16D, additional self-sizing and expandable designs are shown to accommodate nerve swelling and/or over-tightening. With specific reference to Figure 16C, there is depicted a nerve cuff electrode 1600 having a cuff body with a relatively wide semi-cylindrical lateral side 1601 and a plurality of opposing arms 1602 extending thereform for placement on the deep (contralateral) side of the nerve. Although the embodiment depicted in Figure 16C includes two such opposing arms 1602, nerve cuff electrode 1600 may include any suitable number of opposing arms 1602. Lateral side 1601 may include an array of electrode contacts 1603. For example, in the depicted embodiment, lateral side may include three electrode contacts 1603. The three electrode contacts 1603 may include one cathode electrode contact 1603 disposed between two anode electrode contacts 1603, as shown.

[0104] Arms 1602 may be secured around a nerve (not shown) by any suitable means. For example, it is contemplated that arms 1602 may be elastic in nature, so as to gently grasp the nerve on its deep (contralateral) side. Alternatively, arms 1602 may be actively secured about a nerve by, for example, suturing an end portion of arms 1602 to, e.g., a portion of lateral side 1601. In embodiments where arms 1602 may be actively secured about a nerve, arms 1602 may be provided with a safety mechanism (not shown) that permits nerve cuff electrode 1600 to become disengaged from a nerve it is secured about upon the application of a predetermined amount of force. This predetermined force will be established at a level that is below that which can cause damage to the nerve.

[0105] As shown in Figure 16D, opposing arms 1602 may be configured to expand and/or deform as necessary, in order to accommodate nerve swelling caused by, for example, localized trauma inflicted upon the nerve during cuff implantation. For example, each of opposing arms 1602 may have an unattached terminal end 1602a. In order to facilitate expansion, opposing arms 1602 may be also made from any suitable material known to those having ordinary skill in the art. For example, arms 1602 may be made from an elastomer, such as, for example, silicone or polyurethane. Additionally, one or both of arms 1602 may be provided with one or more limiting mechanisms (not shown) to limit the amount of expansion arms 1602 may undergo as a result of, for example, nerve swelling.

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Such limiting mechanisms may include any suitable mechanism, including, but not limited to, flanges, barbs, and/or sutures.

[0106] With reference to Figure 16E, there is depicted another design of a self-sizing and expandable nerve cuff electrode 1610. For the purposes of this disclosure, nerve cuff electrode 1610 may be substantially similar to nerve cuff electrode 1600 depicted in Figures 16C-16D. Nerve cuff electrode 1610, however, may differ from nerve cuff electrode 1600 in at least two significant ways. First, for example, lateral side 1611 of nerve cuff electrode 1610 may carry two anode electrode contacts 1613 and the medial side 1612 may carry one cathode electrode contact 1613 in an arrangement that may be referred to as transverse guarded tri-polar. Second, for example, nerve cuff electrode 1610 may include three arms 1614-1616 extending from lateral side 1611. In the depicted embodiment, arms 1614 and 1616 may be configured to extend substantially in the same direction from the same edge 1611a of lateral side 1611, while arm 1615 may be configured to extend in substantially the opposing direction from an opposing edge 1611b of lateral side 1611. In the depicted embodiment, arm 1615 may be disposed between arms 1614 and 1616, and may be configured to carry the cathode electrode contact 1613, as mentioned above. However, any suitable arrangement of arms 1614-1616 and/or electrode contacts 1613 may be utilized within the principles of this disclosure.

[0107] As shown in Figure 16F, certain embodiments of nerve curve electrode 1600 and/or nerve cuff electrode 1610 may include one or more elongated arms 1617. Arms 1617 may include any suitable length, so as to allow arms 1617 to wrap around a body portion of the cuff electrode one or more times in a spiral-like fashion, when the cuff electrode is mounted about an un-swollen nerve. However, arms 1617 may allow the cuff electrode to remain mounted on the nerve as it accommodates large amounts of nerve swelling by unraveling and/or unwrapping as the nerve swells. For example, each of the arms 1617 may overlap lateral side 1601 or 1611 to accommodate larger amounts of nerve swelling without allowing the cuff to become detached from the nerve. The elongated arms 1617 may extend around the body of the cuff electrode to form a spiral when the nerve is in a substantially un-swollen state, as shown.

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[0108] With reference to Figure 17, a modular nerve electrode cuff 170 is shown that includes a semi-cylindrical body portion 172 with an array of electrode contacts 176 with separate insulative strips 174 for placement on the deep (contralateral side) of the nerve, which typically has more nerve branches and connecting blood vessels. In this embodiment, independent placement of the electrode body 172 on the superficial (lateral) side of the nerve and placement of the insulative strips 174 on the deep (contralateral) side of the nerve minimizes dissection. The strips 174 may be connected to the electrode body 172 by sutures or buckles as described previously. This embodiment is also self-sizing to accommodate nerve swelling and/or over-tightening.

[0109] With reference to Figure 18, a nerve cuff electrode 180 is shown that has a cuff body with a relatively wide semi-cylindrical lateral side 182 and a relatively narrow semi-cylindrical medial side 184 that may extend through a small fenestration around the deep (contralateral) side of a nerve to securely and gently grasp the nerve while minimizing dissection. In the illustrated example, the lateral side 182 carries two anode electrode contacts 186 and the medial side 184 carries one cathode electrode contact 186 in an arrangement that may be referred to as transverse guarded tri-polar. A tow strap 188 is provided for inserting the medial side 184 around the deep side of the nerve. The tow strap 188 may be integrally formed with the medial side 184 of the cuff body, and may include a reinforced tip 188A with a serrated or marked cut line 188B.

[0110] With reference to Figures 19A and 19B, a nerve cuff electrode 190 is shown that has a cuff body with a relatively wide semi-cylindrical lateral side 192 and a relatively narrow semi-cylindrical medial side 194 that may extend through a small fenestration around the deep (contralateral) side of a nerve to securely and gently grasp the nerve while minimizing dissection. In the illustrated example, the lateral side 192 carries one cathode electrode contact 196C and two guarding anode electrode contacts 196B and 196D, and the medial side 194 carries one anode electrode contact 196A in an arrangement that may be referred to as transverse and longitudinal guarded quad-polar. The provision of guarding electrode contacts 196B and 196C reduces extrinsic stimulation due to the lack of insulative material on the medial side 194. The embodiments of Figures 18, 19A and 19B illustrate

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two different electrode contact arrangements, but the number and arrangement may be modified to suit the particular application.

[0111] With reference to Figure 20, a nerve cuff electrode array 200 is shown that utilizes a series of relatively narrow independent cuffs 200A, 200B and 200C with corresponding independent lead bodies 62. Providing a series of relatively narrow independent cuffs 200A, 200B and 200C minimizes the required dissection around the nerve for implantation thereof. Also, the series of independent cuffs 200A, 200B and 200C allows more selectivity in electrode placement to adjust for anatomical variation or multiple target stimulation sites, for example. Providing multiple independent lead bodies 62 allows for more options in routing and placement of the individual lead bodies 62 (e.g., alternate placement of lead body 62A) and also prevents tissue encapsulation around the lead bodies 62 from collectively affecting encapsulation of the nerve cuffs 200. Each of the cuffs 200A, 200B and 200C may include a cuff body 202 with one or more imbedded electrode contacts (not shown) and a tow strap 204 as described before. Also, each of the cuffs 200A, 200B and 200C may include suture 208 or a buckle 206 to lock onto the tow strap 204 for connecting opposite ends of the body 202 around the nerve.

[0112] With reference to Figures 21A and 21B, a nerve cuff electrode 210 is shown with multiple electrode contacts 216 radially spaced around the inside surface of a compliant split cuff body 212 to establish multiple electrical contact points around the circumference of the nerve. Each of the electrode contacts 216 may be connected to independent conductors in the lead body 62 via axially extending wires 217. This arrangement allows for field steering as discussed herein. The compliant split cuff body 212 together with axially extending wires 217 allows for self-sizing to accommodate nerve swelling and/or over-tightening. One or more pairs of tabs 214 extending from opposite end portions of the cuff body 212 may be connected by a suture (not shown) as described herein. As shown in Figure 21B, the proximal and distal ends of the cuff body 212 may have tapered thickness extensions 218 to provide strain relief and reduce mechanical irritation of the nerve due to contact with the edge of the cuff.

[0113] With reference to Figure 22, a nerve cuff electrode 220 is shown with a separable lead 62 in what may be referred to as a modular design. In this embodiment, the

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nerve cuff electrode 220 includes a semi-circular flexible cuff body (or housing) 222 with a receptacle 224 configured to accommodate a distal end of a lead body 62 therein. The receptacle 224 may provide a releasable mechanical lock to the lead body 52 as by a press fit, mating detents, etc. The distal end of the lead body 62 carries an array of ring electrodes 65, with windows 226 provided in the cuff body 222 configured to align with the ring electrodes 65 and permit exposure of the ring electrodes 65 to the nerve to establish electrical connection therebetween. The cuff body 222 may be attached to the nerve or simply placed adjacent the nerve. Any of the cuff designs described herein may be provided with a receptacle to accommodate a removable lead body. This embodiment allows postoperative removal of the lead body 62 without removal of the cuff 220, which may be beneficial in revision operations, for example.

[0114] Turning now to Figure 22A, there is depicted another design for a nerve cuff electrode 2000 where a substantially cylindrical distal portion 62' of lead body 62 carries an array of electrodes 2001. Electrodes 2001 may include ring electrodes that extend completely around the circumference of lead body 62, or, alternatively, may include generally semi-circular electrodes that extend partially around the circumference of lead body 62. The electrode may be selectively insulated on any portion of its surface to allow directional stimulation. Nerve cuff electrode 2000 may further include a nerve securing mechanism for securing lead body 62 to a nerve, such as, for example, a hypoglossal nerve. The nerve securing mechanism may include, for example, a compliant sheet wrap 2002 that is attached on one end to a distal portion of lead body 62, and unattached on the other opposing end. Compliant sheet wrap 2002 may be attached to lead body 62 by any suitable means.

[0115] As shown in Figure 22B, compliant sheet wrap 2002 may be configured to be wrapped around a nerve and secured thereto by, for example, connecting opposite portions of the sheet wrap 2002 together. Sheet wrap 2002 may be provided with one or more features to facilitate such connections. For example, it is contemplated that a portion 2002b of sheet wrap 2002 that is closest to lead body 62 may be provided with a projection 2002c that is configured for insertion into a corresponding opening 2002e provided on a portion 2002d of sheet wrap 2002 that is opposite portion 2002b. Opening 2002e may be

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configured to retain projection 2002c despite the forces exerted on sheet wrap 2002 during normal nerve swelling. However, opening 2002e may be configured to release projection 2002c when forces greater than a predetermined threshold are exerted on sheet wrap 2002, so as to prevent injury to the nerve. As shown in Figure 22C, in some embodiments, opening 2002e may be provided as a slot, which, in addition to securing projection 2002c, may allow projection 2002c to slide within the opening 2002e, thereby allowing expansion of the sheet wrap 2002 to accommodate nerve swelling and/or over tightening of the sheet wrap 2002. Additionally, both portions 2002b and 2002d may be provided with suitable openings to facilitate the insertion of sutures (not shown) or other suitable fastening mechanisms. Sheet wrap 2002 may have any desired width. For example, sheet wrap 2002 may have a substantially tapered width, in order to securely wrap the nerve while minimizing dissection.

[0116] Compliant sheet wrap 2002 may be provided with any of a number of means that allow sheet wrap 2002 to expand, in order to accommodate nerve swelling and/or over tightening. For example, in one embodiment, sheet wrap 2002 may be provided with a plurality of radially and/or longitudinally distributed fenestrations (not shown). In other embodiments, sheet wrap 2002 may be provided with a plurality of undulations 2002a, such as, for example, sigmoid undulations, which may allow for expansion of sheet wrap 2002.

[0117] With reference now to Figure 22D, there is depicted another design for a nerve cuff electrode 2200 where a distal portion 62'' of lead body 62 carries an array of electrodes 2201. For the purposes of this disclosure, nerve cuff electrode 2200 may include substantially the same features as nerve cuff electrode 2000 depicted in Figures 22A-22C. Nerve cuff electrode 2200, however, may differ from nerve cuff electrode 2000 in that distal portion 62'' may be substantially flat or paddle-shaped. Furthermore, electrode contacts 2201, rather than being circular or semi-circular in configuration, may be substantially flat in configuration. In certain procedures, it is contemplated that the paddle-shaped distal portion 62'', along with the substantially flat electrode contacts 2201, may promote greater contact between electrode contacts 2201 and the nerve they are mounted upon.

[0118] **Description of Alternative Implant Procedure for the Stimulation Lead**

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[0119] With reference to Figures 23A – 23C, an insertable paddle-shaped lead 230 design is shown. The insertable lead 230 may have a paddle-shape (rectangular) cross-section with a tubular jacket 232 and one or more conductors 234 extending therethrough to one or more distally placed electrode contact(s) 236. The electrode contact(s) 236 may be imbedded in a molded distal end of the jacket 232 such that the electrode contact 236 has an exposed surface to face the nerve when implanted as shown in Figure 23B. The space between the nerve and electrode is shown for purposes of illustration only, as the electrodes may be placed in direct contact with the nerve. Soft tines 238 may be integrally formed at the distal end of the tubular jacket 232 for purposes of mild fixation to tissue when implanted. The insertable lead 230 is configured to be placed adjacent to the nerve (thereby negating the need for a cuff) by inserting the lead 230 at the surgical access site 110 and following the nerve distally until the electrode contacts 236 are placed adjacent the target stimulation site. The insertable lead 232 may be used alone or in conjunction with another lead as shown in Figures 23B and 23C. In the illustrated example, a first lead 230A is inserted along a superficial side of the nerve and a second lead 230B is inserted along a deep side of the nerve.

[0120] A method of implanting lead 230 may generally comprise accessing a proximal extent of the nerve by minimal surgical dissection and retraction of the mylohyoid muscle as shown in Figure 23C. Special tools may alternatively be employed for percutaneous or laparoscopic access as shown and described with reference to Figures 24A – 24C. Subsequently, two paddle-shaped leads 230 with distal electrode contacts 236 may be inserted into the surgical access site and advanced beyond the access site along a distal aspect of the nerve to the desired stimulation site on either side of the nerve. These techniques minimize trauma and facilitate rapid recovery.

[0121] A less invasive method of implanting a paddle-shaped lead 230 is shown in Figures 24A – 24C. In this embodiment, a rectangular tubular trocar 240 with a sharpened curved tip is placed through a percutaneous access site 111 until a distal end thereof is adjacent the superficial side of the nerve. A paddle-shaped lead 230 is inserted through the lumen of the trocar 240 and advanced distally beyond the distal end of the trocar 240 along the nerve, until the electrode contacts 236 are positioned at the target stimulation site. As

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shown in Figure 24B, which is a view taken along line A-A in Figure 24A, the insertable lead 230 includes multiple electrode contacts 236 in an anode-cathode-anode arrangement, for example, on one side thereof to face the nerve when implanted. In this embodiment, tines are omitted to facilitate smooth passage of the lead 230 through the trocar. To establish fixation around the nerve and to provide electrical insulation, a backer strap 242 of insulative material may be placed around the deep side of the nerve. To facilitate percutaneous insertion of the backer 242, a curved tip needle 244 may be inserted through a percutaneous access site until the tip is adjacent the nerve near the target stimulation site. A guide wire 246 with a J-shaped tip may then be inserted through the needle 244 and around the nerve. The backer 242 may then be towed around using the guide wire 246 as a leader, and secured in place by a buckle (not shown), for example.

[0122] With reference to Figure 25, a bifurcated lead 250 is shown to facilitate separate attachment of electrode cuffs 64 to different branches of the same nerve or different nerves for purposes described previously. Any of the nerve cuff electrode or intramuscular electrode designs described herein may be used with the bifurcated lead 250 as shown. In the illustrated example, a first lead furcation 252 and a second lead furcation 254 are shown merging into a common lead body 62. Each furcation 252 and 254 may be the same or similar construction as the lead body 62, with modification in the number of conductors. More than two electrode cuffs 64 may be utilized with corresponding number of lead furcations.

[0123] **Description of Stimulation Lead Anchoring Alternatives**

[0124] With reference to Figures 26A and 26B, an elastic tether 264 with a limited length is utilized to prevent high levels of traction on the electrode cuff 64 around the hypoglossal nerve (or other nerve in the area) resulting from gross head movement. In other words, tether 264 relieves stress applied to the electrode cuff 64 by the lead body 62. Figures 26A and 26B are detailed views of the area around the dissection to the hypoglossal nerve, showing alternative embodiments of attachment of the tether 264. The proximal end of the tether 264 may be attached to the lead body 62 as shown in Figure 26A or attached to the electrode cuff 64 as shown in Figure 26B. The distal end of the tether 264 may be

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attached to the fibrous loop carrying the digastrics tendon as shown in Figure 26A or attached to adjacent musculature as shown in Figure 26B.

[0125] By way of example, not limitation, and as shown in Figure 26A, a tubular collar 262 is disposed on the lead body 62 to provide connection of the tether 264 to the lead body 62 such that the lead body 62 is effectively attached via suture 266 and tether 264 to the fibrous loop surrounding the digastrics tendon. The tether 264 allows movement of the attachment point to the lead body 62 (i.e., at collar 262) until the tether 264 is straight. At this point, any significant tensile load in the caudal direction will be borne on the fibrous loop and not on the electrode cuff 64 or nerve. This is especially advantageous during healing before a fibrous sheath has formed around the lead body 62 and electrode cuff 64, thus ensuring that the cuff 64 will not be pulled off of the nerve. It should be noted that the length of the tether 262 may be less than the length of the lead body 62 between the attachment point (i.e., at collar 262) and the cuff 64 when the tensile load builds significantly due to elongation of this section of lead body 62.

[0126] The tether 264 may be formed from a sigmoid length of braided permanent suture coated with an elastomer (such as silicone or polyurethane) to maintain the sigmoid shape when in the unloaded state. The tether 264 may also be made from a monofilament suture thermoformed or molded into a sigmoid shape. The distal end of the tether 264 may be attached to the fibrous loop using a suture 266 or staple or other secure means. Note that the tether 264 may be made from a biodegradable suture that will remain in place only during healing.

[0127] Also by way of example, not limitation, an alternative is shown in Figure 26B wherein the tether 264 is attached to the electrode cuff 64. The distal end of the tether 264 may be attached to the adjacent musculature by suture 266 such the musculature innervated by branches of the hypoglossal nerve or other musculature in the area where the electrode cuff 64 is attached to the nerve. The tether 264 ensures that the electrode cuff 64 and the hypoglossal nerve are free to move relative to the adjacent musculature (e.g., hyoglossal). As significant tensile load is applied to the lead body 62 due to gross head movement, the tether 264 will straighten, transmitting load to the muscle rather then to the nerve or electrode cuff 64.

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[0128] As alluded to above, stimulation lead 60 may comprise a number of differing design embodiments. One such embodiment has been discussed above with respect to Figure 5. Another such embodiment is depicted in Figure 26C, which illustrates a stimulation lead 2600. Stimulation lead 2600 may be substantially similar to and/or may include one or more of the features described in connection with stimulation lead 60. As shown in Figure 26C, stimulation lead 2600 may include a lead body 2662 having a first, proximal lead body portion 2663. First lead body portion 2663 may be substantially similar to lead body 62. For example, first lead body portion 2663 may include a similar flexibility as lead body 62. Lead body 2662 may further include a second, distal lead body portion 2664 leading to the distal end of lead body 2662 at the nerve cuff electrode. Second lead body portion 2664 may include a material property that is different than lead body portion 2663, such as, for example, a greater flexibility, in order to accommodate stresses imparted upon lead body 2662 by a nerve cuff electrode and movement of the patient's head, neck, and other neighboring body portions. The highly flexible distal portion 2664 reduces the stress (torque and tension) imparted by lead body 2662 on the electrode cuff, thereby reducing the likelihood that the cuff will be detached from the nerve or damage the nerve.

[0129] Lead body portion 2664 may be made more flexible than lead body portion 2663 by any of a variety of ways. For example, lead body portion 2664 may be made from a material having differing flexibility. Alternatively, the diameters of the braided stranded wires (BSW) and/or wire insulation that make up the lead body portion 2664 may be reduced when possible.

[0130] With continuing reference to Figure 26C, stimulation lead 2600 may further include an anchor 2665 operably connected to lead body 2662. Although anchor 2665 in the illustrated embodiment is depicted as being disposed in between lead body portions 2663 and 2664, anchor 2665 may be disposed at any suitable location along the length of lead body 2662. Furthermore, anchor 2665 may be fixedly or movably connected to lead body 2662.

[0131] Anchor 2665 may include any suitable configuration known in the art. For example, anchor 2665 may include a substantially flat body portion 2666. Body portion 2666 may be configured to be secured to tissue, such as, for example, tissue proximate a

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treatment site, by any suitable means available in the art. For example, body portion 2666 may be provided with openings 2667 to facilitate, for example, suturing anchor 2665 to nearby tissue. Anchor 2665 can thereby isolate stress (tension) to one portion of lead body 2662, and particularly portion 2663, caused by gross head and neck movement.

[0132] **Description of Field Steering Alternatives**

[0133] With reference to Figures 27A – 27G, a field steering nerve cuff electrode 64 is shown schematically. As seen in Figure 27A, the nerve cuff electrode 64 may include four electrode contacts 90A – 90D to enable field steering, and various arrangements of the electrode contacts 90A – 90D are shown in Figures 27B – 27G. Each of Figures 27B – 27G includes a top view of the cuff 64 to schematically illustrate the electrical field (activating function) and an end view of the cuff 64 to schematically illustrate the area of the nerve effectively stimulated. With this approach, electrical field steering may be used to stimulate a select area or fascicle(s) within a nerve or nerve bundle to activate select muscle groups as described herein.

[0134] With specific reference to Figure 27A, the nerve cuff electrode 64 may comprise a cuff body having a lateral (or superficial) side 82 and a medial (or contralateral, or deep) side 84. The medial side 84 is narrower or shorter in length than the lateral side 82 to facilitate insertion of the medial side 84 around a nerve such that the medial side is on the deep side of the nerve and the lateral side is on the superficial side of the nerve. An integral tow strap 86 may be used to facilitate wrapping the cuff around a nerve. The nerve cuff electrode 64 includes electrode contacts 90A, 90B, 90C and 90D imbedded in the body of the cuff, with their inside surface facing exposed to establish electrical contact with a nerve disposed therein. Electrode contacts 90A and 90B are longitudinally and radially spaced from each other. Electrode contacts 90C and 90D are radially spaced from each other and positioned longitudinally between electrode contacts 90A and 90B. Each of the four electrode contacts may be operated independently via four separate conductors (four filar) in the lead body 62.

[0135] With specific reference to Figures 27B – 27G, each includes a top view (left side) to schematically illustrate the electrical field or activating function (labeled E), and an end view (right side) to schematically illustrate the area of the nerve effectively stimulated

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(labeled S) and the area of the nerve effectively not stimulated (labeled NS). Electrodes 90A – 90D are labeled A – D for sake of simplicity only. The polarity of the electrodes is also indicated, with each of the cathodes designated with a negative sign (-) and each of the anodes designated with a positive sign (+).

[0136] With reference to Figure 27B, a tripolar transverse guarded cathode arrangement is shown with electrodes C and D comprising cathodes and electrodes A and B comprising anodes, thus stimulating the entire cross-section of the nerve.

[0137] With reference to Figure 27C, a bipolar diagonal arrangement is shown with electrode C comprising a cathode and electrode A comprising an anode, wherein the fascicles that are stimulated may comprise superior fascicles of the hypoglossal nerve, and the fascicles that are not stimulated may comprise inferior fascicles of the hypoglossal nerve (e.g., fascicles that innervate the intrinsic muscles of the tongue).

[0138] With reference to Figure 27D, another bipolar diagonal arrangement is shown with electrode D comprising a cathode and electrode B comprising an anode, wherein the fascicles that are stimulated may comprise inferior fascicles of the hypoglossal nerve.

[0139] With reference to Figure 27E, a bipolar axial arrangement is shown with electrode A comprising a cathode and electrode B comprising an anode, wherein the fascicles that are stimulated may comprise lateral fascicles of the hypoglossal nerve.

[0140] With reference to Figure 27F, a bipolar transverse arrangement is shown with electrode C comprising a cathode and electrode D comprising an anode, wherein the fascicles that are stimulated may comprise medial fascicles of the hypoglossal nerve.

[0141] With reference to Figure 27G, a modified tripolar transverse guarded cathode arrangement is shown with electrode C comprising a cathode and electrodes A and B comprising anodes, thus stimulating the entire cross-section of the nerve with the exception of the inferior medial fascicles.

[0142] Nerves like the hypoglossal nerve or superior laryngeal nerve typically include a plurality of fibers having relatively larger diameters and a plurality of fibers having relatively smaller diameters. In the case of single function nerves, such as, for example, the hypoglossal nerve HGN, all of the nerve fibers may either be sensory or motor

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in function. However, in the case of multi-function nerves, such as, for example, the superior laryngeal nerve SLN, the fibers having relatively larger diameters are typically motor (efferent) fibers, and the fibers having relatively smaller diameters are typically sensory (afferent) fibers. Accordingly, there may be a need to selectively stimulate the differing diameter fibers in a nerve.

[0143] Turning now to Figure 27H, there is depicted an embodiment of a uni-directional stimulation electrode 2700 having a distal end 2700a and a proximal end 2700b. Electrode 2700 may include a substantially cylindrical nerve cuff 2701 in accordance with the principles of the present disclosure. As illustrated, nerve cuff 2701 may include an outer surface 2701a and an inner surface 2701b. Electrode 2700 may further include a plurality of electrode contacts 2702-2704. Electrode contacts 2702-2704 may be used as any suitable electrode contact known to those of ordinary skill in the art. For example, electrode contact 2702 may be used as an anode, electrode contact 2703 may be used as a cathode, and electrode contact 2704 may be used as a second anode. Electrode contacts 2702-2704 may also include any suitable shape and/or configuration known in the art. For example, electrode contacts 2702-2704 may include a substantially semi-circular configuration.

[0144] Electrode contacts 2702-2704 may be disposed on nerve cuff 2701 in any suitable configuration to achieve the desired effect. For example, electrode contacts 2702-2704 may be disposed on inner surface 2701b. As depicted in Figure 27H, cathode electrode contact 2703 may be disposed approximately equidistant from distal end 2700a and proximal end 2700b, and anode electrode contacts 2702 may be differentially spaced around cathode electrode contact 2703, so as to control the direction of stimulation of electrode 2700. For example, anode electrode contact 2702 may be spaced from cathode electrode contact 2703 by any suitable distance χ, while second anode electrode contact 2704 may be spaced from cathode electrode contact 2703 by a distance that is approximately two or three times greater than distance χ. In this exemplary configuration, the direction of stimulation may be in the direction of arrow 2705.

[0145] In use, electrode 2700 may be implanted upon a nerve in accordance with the principles of this disclosure. Electrode 2700 may be oriented on the nerve it is implanted on in any suitable manner, such as, for example, according to the direction of intended

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stimulation. Thus, in circumstances where it may be desired to stimulate efferent (motor) fibers of a nerve, such as, for example, the superior laryngeal nerve SLN, while avoiding stimulation to afferent (sensory) fibers of the nerve, the electrode 2700 may be oriented on the nerve in a manner such that anode electrode contact 2702 is located distally of cathode electrode contact 2703, with distal and proximal designations based on the relative location of the electrode contact on the nerve. Alternatively, in circumstances where it may be desired to stimulate afferent fibers of a nerve while avoiding stimulation of efferent fibers of the nerve, the electrode 2700 may be oriented on the nerve in a manner such that anode electrode contact 2702 is located proximally of cathode electrode contact 2703.

[0146] With reference now to Figure 27I, there is depicted an embodiment of a stimulation electrode 2750 for, among other things, selectively stimulating differing diameter fibers of a nerve, such as, for example, the hypoglossal nerve or superior laryngeal nerve. Electrode 2750 may include a body 2751, and may include any suitable configuration in accordance with the principles of the present disclosure. Additionally, electrode 2750 may include an array 2752 of suitable electrode contacts known to those skilled in the art. Although the depicted embodiment of electrode 2750 includes five electrode contacts 2753a-2753e, array 2752 may include a greater or lesser number of electrode contacts. Electrode contacts 2753a-2753e may be disposed on body 2751 in any suitable configuration to produce the desired effect. For example, as depicted in Figure 27I, electrode contacts 2753a-2753e may be disposed serially, with approximately a one (1) millimeter spacing in between each electrode contact 2753a-2753e. Electrode contacts 2753a-2753e may be configured to function as either anode electrode contacts or cathode electrode contacts, as desired.

[0147] Electrode contacts 2753 may be connected to an implanted neurostimulator (INS), such as, for example, INS 50, in accordance with the present disclosure. The INS may be programmed to select any of electrode contacts 2753a-2753e for nerve stimulation. For example, in circumstances where it may be desired to stimulate the smaller diameter fibers of a nerve, it is contemplated that all electrode contacts 2753a-2753e may be selected for nerve stimulation, since closely spaced electrode contacts typically affect smaller diameter fibers (e.g., afferent or sensory fibers). In these circumstances, electrode contacts

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2753a, 2753c, and 2753e may function as anode electrode contacts and electrode contacts 2753b and 2753d may function as cathode electrode contacts. In circumstances where it may be desired to stimulate the larger diameter fibers of a nerve, it is contemplated that only electrode contacts 2753a, 2753c, and 2753e may be selected for nerve stimulation, since loosely spaced electrode contacts typically affect larger diameter fibers (e.g., efferent or motor fibers). In these circumstances, electrode contacts 2753a and 2753e may function as anode electrode contacts, and 2753c may function as a cathode electrode contact.

[0148] Alternatively, electrode 2750 may be utilized to reduce muscle fatigue when implanted on single function nerves, such as, for example, the hypoglossal nerve. In such circumstances, muscle fatigue may be reduced by alternatively switching between using loosely spaced electrode contacts 2753a, 2753c, and 2753e, to stimulate large diameter fibers, and closely spaced electrode contacts 2753a-2753e, to stimulate small diameter fibers.

[0149] Turning to Figs. 27J-27K, in accordance with the present disclosure, there is depicted another embodiment of a nerve cuff electrode 2760 for facilitating reduction in muscle fatigue. Nerve cuff electrode 2760 may include a body 2761 having a plurality of electrode contacts 2762, 2763, and 2764. Electrode contacts 2762-2764 may include any suitable electrode contacts in accordance with the present disclosure. Although the depicted embodiment of nerve cuff electrode 2760 includes three electrode contacts 2762-2764, nerve cuff electrode 2760 may include a greater or lesser number of electrode contacts. Furthermore, electrode contacts may be disposed on body 2761 in any suitable configuration to achieve the desired effect, such as, for example, serially, as depicted. In the depicted embodiment, electrode contacts 2762 and 2764 may function as anode electrode contacts, while electrode contact 2763 may function as a cathode electrode contact. Electrode contact 2763 may include two distinct, substantially triangularly shaped portions 2763a and 2763b. However, portions 2763a and 2763b may include any suitable shape. In addition, portions 2763a and 2763b may be configured to be of differing conductive properties, so that, for the same stimulation pulse (e.g., a slow rising, small amplitude pulse having a relatively long duration of approximately 0.2 to 0.35 milliseconds) applied to each of the portions 2763a and 2763b, the resultant charge densities at the surface

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of each of the portions 2763a and 2763b may be different. For example, portions 2763a and 2763b may be made of electrically differing materials. For discussion purposes only, it is assumed that portion 2763a is configured to deliver a charge density lower than that of portion 2763b. However, portion 2763a may be configured to deliver a charge density that is higher than the charge density of portion 2763b.

[0150] Since the small diameter fibers of a nerve are typically stimulated by low charge densities and large diameter fibers of the nerve are typically stimulated by high charge densities, portions 2763a and 2763b may be sequentially utilized to alternate between stimulating the small and large diameter fibers of a nerve. In other words, in use, a stimulation pulse may be first delivered to portion 2763a to stimulate the small diameter fibers of a nerve. A subsequent stimulation pulse may be then delivered to portion 2763b to stimulate the large diameter fibers of a nerve. It is contemplated that alternating between stimulating the small and large diameter fibers of a nerve may facilitate reducing muscle fatigue while also ensuring sufficient muscle mass is stimulated to maintain the necessary contraction and force generation to successfully treat OSA.

[0151] Turning now to Figure 27L, there is illustrated yet another embodiment of a nerve cuff electrode 2780 for facilitating reduction in muscle fatigue. For the purposes of this disclosure, nerve cuff electrode 2780 may be substantially similar to nerve cuff electrode 2760. Nerve cuff electrode 2780, however, may differ from nerve cuff electrode 2760 in at least one significant way. For example, rather than having two substantially triangular portions, cathode electrode contact 2783 may comprise two substantially different portions 2783a and 2783b. Portions 2783a and 2783b may be spaced apart from one another and may include differing surface areas. For example, as illustrated, portion 2783a may include a smaller surface area than portion 2783b. Furthermore, portions 2783a and 2783b may include any suitable shape known in the art. Although portions 2783a and 2783b in the illustrated embodiment together define a substantially triangular shaped electrode contact 2783, portions 2783a and 2783b together may or may not define any suitable shape known in the art.

[0152] Each of portions 2783a and 2783b may be configured to be substantially similar in conductance despite their differing surface areas. For example, portion 2783a

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may be made of a first material having a relatively lower conductance, while portion 2783b may be made of a second material having a relatively higher conductance. Thus, when subjected to the same stimulation pulse (e.g., a slow rising, small amplitude pulse having a relatively long duration of approximately 0.2 to 0.35 milliseconds), portion 2783a may have a higher charge density than portion 2783b because of its relatively smaller surface area than portion 2783b. Similarly, when subjected to the same stimulation pulse, portion 2783b may have a lower charge density than portion 2783a because of its relatively larger surface area than portion 2783a. Accordingly, because of the differing charge densities, portion 2783a may be adapted to stimulate large diameter fibers of a nerve, and portion 2783b may be adapted to stimulate small diameter fibers of the nerve.

[0153] In use, a stimulation pulse may be first delivered to portion 2783a to stimulate the large diameter fibers of a nerve. A subsequent stimulation pulse may be then delivered to portion 2783b to stimulate the small diameter fibers of the nerve. It is contemplated that alternating between stimulating the small and large diameter fibers of a nerve may facilitate muscle fatigue while also ensuring that sufficient muscle mass is stimulated to maintain the necessary contraction and force generation to successfully treat OSA.

[0154] In certain embodiments, such as when nerve cuff electrodes 2760 and 2780 are implanted on a multi-function nerve (e.g., the superior laryngeal nerve SLN), it is contemplated that portions 2763a/2763b and portions 2783a/2783b may be utilized to selectively stimulate either the afferent or efferent fibers of the nerve.

[0155] With reference now to Figures 27M-27Q, there is depicted yet another embodiment of a nerve cuff electrode 2790 for minimizing muscle fatigue. Nerve cuff electrode 2790 may include a cuff body 2791 for mounting about a nerve 2792 in accordance with the present disclosure. Cuff body 2791 may include a plurality of electrode contacts 2793-2796 also in accordance with the present disclosure. Although the depicted embodiment of nerve cuff electrode 2790 includes four electrode contacts 2793-2796, nerve cuff electrode 2790 may include a greater or lesser number of electrode contacts.

[0156] Nerve cuff electrode 2790 may be configured to selectively stimulate both small diameter fibers contained in fascicle 2777a and large diameter fibers contained in

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fascicle 2777b of nerve 2792. For example, as shown in Figure 27P, by applying an exemplary slow rising, long pulse width waveform to electrode contacts 2796 and 2793, nerve cuff electrode 2790 may stimulate the small diameter fibers contained in fascicle 2777a of nerve 2792. Similarly, as shown in Figure 27Q, by applying an exemplary fast rising, short pulse width waveform to electrode contacts 2794 and 2795, nerve cuff electrode 2790 may stimulate the large diameter fibers contained in fascicle 2777b of nerve 2792. Fascicles 2777a and 2777b may be stimulated simultaneously or separately. In embodiments, where it is desirable to stimulate fibers contained in fascicles 2777a and 2777b, the pulse generator (e.g., INS 50) may be provided with dual output ports.

[0157] **Description of Respiration Sensing Lead Anchoring Alternatives**

[0158] With reference to the following figures, various additional or alternative anchoring features for the respiration sensing lead 70 are schematically illustrated. Anchoring the respiration sensing lead 70 reduces motion artifact in the respiration signal and stabilizes the bio-impedance vector relative to the anatomy.

[0159] In each of the embodiments, by way of example, not limitation, the respiration sensing lead 70 includes a lead body 70 with a proximal connector and a plurality of distal respiration sensors 74 comprising ring electrodes for sensing bio-impedance. The lead body 72 of the respiration sensing lead 70 may include a jacket cover containing a plurality of conductors 78, one for each ring electrode 74 requiring independent control. Generally, the impedance electrodes 74 may comprise current emitting electrodes and voltage sensing electrodes for detecting respiration by changes in bio-impedance.

[0160] With reference to Figures 28 – 33, various fixation devices and methods are shown to acutely and/or chronically stabilize the respiratory sensing lead 70. With specific reference to Figure 28, the INS 50 is shown in a subcutaneous pocket and the stimulation lead 60 is shown in a subcutaneous tunnel extending superiorly from the pocket. The respiration sensing lead 70 is shown in a subcutaneous tunnel superficial to muscle fascia around the rib cage. A suture tab or ring 270 may be formed with or otherwise connected to the distal end of the lead body 72. Near the distal end of the lead 70, a small surgical incision may be formed to provide access to the suture tab 270 and the muscle fascia under

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the lead 70. The suture tab 270 allows the distal end of the lead 70 to be secured to the underlying muscle fascia by suture or staple 272, for example, which may be dissolvable or permanent. Both dissolvable and permanent sutures/staples provide for acute stability and fixation until the lead body 72 is encapsulated. Permanent sutures/staples provide for chronic stability and fixation beyond what tissue encapsulation otherwise provides.

[0161] With reference to Figures 29A – 29C, a fabric tab 280 may be used in place of or in addition to suture tab 270. As seen in Figure 29A, the fabric tab 280 may be placed over a distal portion of the lead body 72, such as between two distal electrodes 74. A small surgical incision may be formed proximate the distal end of the lead 70 and the fabric tab 280 may be placed over the over the lead body 72 and secured to the underlying muscle fascia by suture or staple 282, for example, which may be dissolvable or permanent, to provide acute and/or chronic stability and fixation. With reference to Figures 29B and 29C (cross-sectional view taken along line A-A), the fabric tab 280 may comprise a fabric layer (e.g., polyester) 284 to promote chronic tissue in-growth to the muscle fascia and a smooth flexible outer layer (silicone or polyurethane) 286 for acute connection by suture or staple 282.

[0162] With reference to Figure 30, lead 70 includes a split ring 290 that may be formed with or otherwise connected to the distal end of the lead body 72. The split ring 290 allows the distal end of the lead 70 to be secured to the underlying muscle fascia by suture or staple 292, for example, which may be dissolvable or permanent. The ring 290 may be formed of compliant material (e.g., silicone or polyurethane) and may include a slit 294 (normally closed) that allows the lead 70 to be explanted by pulling the lead 70 and allowing the suture 292 to slip through the slit 294, or if used without a suture, to allow the ring to deform and slide through the tissue encapsulation. To further facilitate explantation, a dissolvable fabric tab 282 may be used to acutely stabilize the lead 70 but allow chronic removal.

[0163] With reference to Figures 31A – 31C, deployable anchor tines 300 may be used to facilitate fixation of the lead 70. As seen in Figure 31A, the self-expanding tines 300 may be molded integrally with the lead body 72 or connected thereto by over-molding, for example. The tines 300 may comprise relatively resilient soft material such as silicone

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or polyurethane. The resilient tines 300 allow the lead 70 to be delivered via a tubular sheath or trocar 304 tunneled to the target sensing site, wherein the tines 300 assume a first collapsed delivery configuration and a second expanded deployed configuration. As seen in Figure 31B and 31B', the tubular sheath or trocar 304 may be initially tunneled to the target site using an obtruator 306 with a blunt dissection tip 308. After the distal end of the tubular sheath 304 has been tunneled into position by blunt dissection using the obtruator 306, the obtruator 306 may be removed proximally from the sheath 304 and the lead 70 with collapsible tines 300 may be inserted therein. As seen in Figure 31C, when the distal end of the lead 70 is in the desired position, the sheath 304 may be proximally retracted to deploy the tines 300 to engage the muscle fascia and adjacent subcutaneous tissue, thus anchoring the lead 70 in place.

[0164] With reference to Figures 32A and 32B, an alternative deployable fixation embodiment is shown schematically. In this embodiment, self-expanding tines 310 are held in a collapsed configuration by retention wire 312 disposed in the lumen of the lead body 72 as shown in Figure 32A. Each of the tines 310 includes a hole 314 through which the retention wire 312 passes to hold the tines 310 in a first collapsed delivery configuration as shown In Figure 32A, and proximal withdrawal of the retention wire 314 releases the resilient tines 310 to a second expanded deployed configuration as shown in Figure 32B. The lead 70 may be tunneled to the desired target site with the tines 310 in the collapsed configuration. Once in position, the wire 312 may be pulled proximally to release the tines 310 and secure the lead 70 to the underlying muscle fascia and adjacent subcutaneous tissue to establish fixation thereof.

[0165] With reference to Figures 33A and 33B, another alternative deployable fixation embodiment is shown schematically. In this embodiment, self-expanding structures such as one or more resilient protrusions 320 and/or a resilient mesh 325 may be incorporated (either alone or in combination) into the distal end of the lead 70. By way of example, not limitation, resilient protrusions 320 may comprise silicone or polyurethane loops and resilient mesh 325 may comprise a polyester fabric connected to or formed integrally with the lead body 72. Both the resilient protrusions 320 and the resilient mesh 325 may be delivered in a collapsed delivery configuration inside tubular sheath 304 as

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shown in Figure 33A, and deployed at the desired target site by proximal retraction of the sheath 304 to release the self-expanding structures 320/325 to an expanded deployed configuration as shown in Figure 33B. Both the resilient protrusions 320 and the resilient mesh 325 engage the underlying muscle fascia through tissue encapsulation and adjacent subcutaneous tissues to provide fixation of the lead 70 thereto.

[0166] Other fixation embodiments may be used as well. For example, the fixation element may engage the muscle fascia and adjacent subcutaneous tissues or may be embedded therein. To this end, the electrodes may alternatively comprise intramuscular electrodes such as barbs or helical screws.

[0167] **Description of Respiration Sensing Electrode Alternatives**

[0168] A description of the various alternatives in number, spacing, anatomical location and function of the impedance electrodes follows. Generally, in each of the following embodiments, the respiration sensing lead includes a lead body and a plurality of respiration sensors comprising ring electrodes for sensing bio-impedance. The lead body may include a plurality of insulated conductors disposed therein, with one conductor provided for each ring electrode requiring independent connection and/or control. The impedance electrodes may comprise current emitting electrodes and voltage sensing electrodes for detecting respiration by changes in bio-impedance.

[0169] With reference to Figure 34, the distal portion of a respiration sensing lead 70 is shown by way of example, not limitation. The respiration sensing lead 70 includes a lead body 72 with a proximal connector and a plurality of distal impedance electrodes 74. In this example, the lead body 72 and electrodes 74 are cylindrical with a diameter of 0.050 inches. The distal current-carrying electrode 74A may be 5 mm long and may be separated from the voltage-sensing electrode 74B by 15mm. The distal voltage sensing electrode may be 5 mm long and may be separated from the proximal combination current-carrying voltage-sensing electrode 74C by 100 mm. The proximal electrode 74C may be 10 mm long. The proximal portion of the lead 70 is not shown, but would be connected to the INS (not shown) as described previously. The lead body incorporates a plurality of insulated electrical conductors (not shown), each of which correspond to an electrode 74A – 74C. The electrodes and conductors may be made of an alloy of platinum-iridium. The lead body

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72 may comprise a tubular extrusion of polyurethane, silicone, or a co-extrusion of polyurethane over silicone. The conductors may be formed of multi-filar wire coiled to provide extensibility for comfort and durability under high-cycle fatigue.

[0170] With reference to Figures 35A – 35E, the position of the electrodes 74 may be characterized in terms of bio-impedance or bio-Z vectors. The bio-Z vector may be defined by the locations of the voltage-sensing electrodes (labeled V_1 & V_2). The voltage-sensing electrodes may be located on either side of the current-carrying electrodes (labeled I_1 & I_2). For example, it is possible to locate either one or both of the voltage-sensing electrodes between the current-carrying electrodes as shown in Figure 35A (4-wire configuration ($I_1 - V_1 - V_2 - I_2$)), and it is possible to locate either one or both of the current-carrying electrodes between the voltage-sensing electrodes as shown in Figure 35B (inverted 4-wire configuration ($V_1 - I_1 - I_2 - V_2$)). While at least two separate electrodes (I_1 & I_2) are required to carry current and at least two separate electrodes (V_1 & V_2) are required to measure voltage, it is possible to combine the current carrying and voltage sensing functions in a common electrode. Examples of combining voltage sensing and current carrying electrodes are shown in Figures 35C – 35E. Figure 35C (2-wire configuration ($I_1V_1 - I_2V_2$)) shows combination electrode I_1V_1 and I_2V_2 where each of these electrodes is used to carry current and sense voltage. Figures 35D (3-wire configuration ($I_1 - V_1 - I_2V_2$)) and 35E (inverted 3-wire configuration ($V_1 - I_1 - I_2V_2$)) show combination electrode I_2V_2 which is used to carry current and sense voltage.

[0171] With reference to Figure 36, insulative material such as strips 73 may cover one side of one or more electrodes 74A – 74D to provide directional current-carrying and/or voltage-sensing. The insulative strips may comprise a polymeric coating (e.g., adhesive) and may be arranged to face outward (toward the dermis) such that the exposed conductive side of each electrode 74 faces inward (toward the muscle fascia and thoracic cavity). Other examples of directional electrodes would be substantially two-dimensional electrodes such as discs or paddles which are conductive on only one side. Another example of a directional electrode would be a substantially cylindrical electrode which is held in a particular orientation by sutures or sutured wings. Another example of a directional electrode would be an electrode on the face or header of the implanted pulse generator. It

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would likely be desirable for the pulse generator to have a non-conductive surface surrounding the location of the electrode.

[0172] In addition to the cylindrical electrodes shown, other electrode configurations are possible as well. For example, the electrodes may be bi-directional with one planar electrode surface separated from another planar electrode surface by insulative material. Alternatively or in combination, circular hoop electrodes may be placed concentrically on a planar insulative surface. To mitigate edge effects, each electrode may comprise a center primary electrode with two secondary side electrodes separated by resistive elements and arranged in series. An alternative is to have each primary current-carrying electrode connected by a resistive element to a single secondary side electrode. The conductive housing of the INS 50 may serve as an current-carrying electrode or voltage-sensing electrode. Alternatively or in addition, an electrode may be mounted to the housing of the INS 50.

[0173] Because bio-impedance has both a real and imaginary component, it is possible to measure the bio-Z phase as well as magnitude. It may be preferable to extract both magnitude and phase information from the bio-Z measurement because the movement of the lung-diaphragm-liver interface causes a significant change in the phase angle of the measured impedance. This may be valuable because motion artifacts of other tissue have less impact on the bio-Z phase angle than they do on the bio-Z magnitude. This means the bio-Z phase angle is a relatively robust measure of diaphragm movement even during motion artifacts.

[0174] An example of a bio-Z signal source is a modulated constant-current pulse train. The modulation may be such that it does not interfere with the stimulation signal. For example, if the stimulation signal is 30Hz, the bio-Z signal source signal may be modulated at 30Hz or a sub-multiple of 30Hz such that bio-Z and stimulation do not occur simultaneously. The pulses in the pulse train may have a pulse width between 1uS to 1mS, such as 100uS. The pulses may be separated by a period of time roughly equal to the pulse width (i.e., on-time of the pulses). The number of pulses in a train may be determined by a trade-off between signal-to-noise and power consumption. For example, no more than 10

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pulses may be necessary in any given pulse train. The magnitude of current delivered during the pulse on-time may be between 10uA and 500uA, such as 50uA.

[0175] Other wave forms of bio-Z source signal may be used, including, without limitation, pulse, pulse train, bi-phasic pulse, bi-phasic pulse train, sinusoidal, sinusoidal w/ ramping, square wave, and square w/ ramping. The bio-Z source signal may be constant current or non-constant current, such as a voltage source, for example. If a non-constant current source is used, the delivered current may be monitored to calculate the impedance value. The current-carrying electrodes may have a single current source, a split-current source (one current source split between two or more current-carrying electrodes), or a current mirror source (one current source that maintains set current levels to two or more current-carrying electrodes). Different characteristics of the sensed signal may be measured including, without limitation, magnitude, phase shift of sensed voltage relative to the current source signal, and multi-frequency magnitude and/or phase shift of the sensed signal. Multi-frequency information may be obtained by applying multiple signal sources at different frequencies or a single signal source which contains two or more frequency components. One example of a single multi-frequency source signal is a square wave current pulse. The resultant voltage waveform would contain the same frequency components as the square wave current pulse which would allow extraction of Bio-Z data for more than a single frequency.

[0176] With reference to Figure 37, the bio-Z vector may be oriented with regard to the anatomy in a number of different ways. For example, using the electrode arrangement illustrated in Figure 34 and the anatomical illustration in Figure 37, the bio-Z vector may be arranged such that the proximal combination electrode is located just to the right of and above the xiphoid below the pectoral muscle between the 5th and 6th ribs and the distal current-carrying electrode is located mid-lateral between the 7th and 8th ribs, with the distal voltage-sensing electrode positioned between the 6th and 7th ribs 10mm proximal of the distal current-carrying electrode. This arrangement places the electrodes along the interface between the right lung, diaphragm and liver on the right side of the thoracic cavity. The lung-diaphragm-liver interface moves relative to the bio-Z vector with every respiratory cycle. Because the lung has relatively high impedance when inflated and the liver has

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relatively low impedance due to the conductivity of blood therein, this bio-Z vector arrangement across the lung-diaphragm-liver interface provides for a strong respiratory signal that is indicative of changes between inspiration and expiration. In addition, because the heart is situated more on the left side, positioning the bio-Z vector on the right side reduces cardiac artifact. The net result is a bio-Z vector that provides an excellent signal-to-noise ratio.

[0177] A variety of different bio-Z vector orientations relative to the anatomy may be employed. Generally, bio-Z vectors for monitoring respiration may be located on the thorax. However, bio-Z electrodes located in the head and neck may also be used to define respiratory bio-Z vectors. By way of example, not limitation, the bio-Z vector may be arranged transthoracically (e.g., bilaterally across the thorax), anteriorly on the thorax (e.g., bilaterally across the thoracic midline), across the lung-diaphragm-liver interface, perpendicular to intercostal muscles, between adjacent ribs, etc. A single bio-Z vector may be used, or multiple independent vectors may be used, potentially necessitating multiple sensing leads. One or more bio-Z sub-vectors within a given bio-Z vector may be used as well.

[0178] With reference to Figures 37A – 37C, thoracic locations defining examples of bio-Z vectors are shown schematically. Figure 37A is a frontal view of the thorax, Figure 37B is a right-side view of the thorax, and Figure 37C is a left-side view of the thorax. In each of Figures 37A – 37C, the outline of the lungs and upper profile of the diaphragm are shown. As mentioned previously, a bio-Z vector may be defined by the locations of the voltage-sensing electrodes. Thus, Figures 37A – 37C show locations for voltage sensing electrodes which would define the bio-Z vector.

[0179] There are several short bio-Z vectors which provide excellent signals correlated to diaphragmatic movement. In general, these vectors have at least one end at or near the lower edge of the ribcage. The short diaphragmatic bio-Z vectors have been successfully used in canines in vector lengths ranging from approximately less than ½ inch to a few inches in length. Figure 37A shows a variety of locations which are representative of the locations which define such vectors. Locations shown just below the ribcage on the person's right side are designated as A, B, C, and D. Locations shown just below the

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ribcage on the person's left side are E, F, G, and H. Locations shown just above the lower edge of the ribcage on the person's right side are I, J, K, and L. Locations shown just above the lower edge of the ribcage on the person's left side are M, N, P, and Q. The locations just above the lower edge of the ribcage would fall within a few inches of the lower edge. Short diaphragmatic monitoring vectors would be comprised of location pairs which are relatively closely spaced. For example, vectors D-E, D-C, D-L, and D-K all provide good diaphragmatic signal. The possible vectors fall into three groups. Exemplary vectors which measure primarily diaphragmatic muscle contraction are A-B, B-C, C-D, D-E, E-F, F-G, and G-H. Exemplary vectors which measure a combination of diaphragmatic muscle contraction combined with movement of the lung into the pleural pocket as the diaphragm contracts are I-J, P-R, A-I, A-J, B-I, B-J, G-P, H-R, H-P, and G-R. Exemplary vectors which measure diaphragmatic muscle contraction combined with movement of the diaphragm away from the thoracic wall as that portion of the lung expands are J-K, K-L, M-N, and N-P. It is known that the signal from any given location may be affected by body position and free vs. obstructed respiration. The respiratory signal from short vectors at or near the lower edge of the ribcage may be more robust (e.g., may be not be substantially affected) to body position and obstructed respiration. A further means of obtaining a signal which may be also more robust to body position would be to measure the respiratory impedance from complimentary vectors and sum the resulting bio-Z measurements. Complimentary vectors would be mirror-images or nearly mirror images of one another. Examples of vectors and their mirror images may be C-D and E-F, B-C and G-F, C-K and F-N.

[0180] By way of example, not limitation, the following bio-Z vectors may be effective for monitoring respiration and/or for measuring artifacts for subsequent removal of the artifact from the respiration signal. Vector C-G is across the upper left and upper right lobes of the lungs, and provides a good signal of ribcage expansion with moderate cardiac artifact. Vector D-F is a short-path version of C-G that provides a good respiratory signature largely correlated with ribcage expansion, with less cardiac artifact than C-G, but may be sensitive to movement of arms due to location on pectoral muscles. Vector C-D is a short-path ipsilateral vector of the upper right lung that may be sensitive to arm movement

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but has less cardiac artifact. Vector B-H is a transverse vector of the thoracic cavity that captures the bulk of the lungs and diaphragm movement. Vector B-H, however, may be relatively less susceptible to changes in body position, and may still provide a generally good signal when the patient changes positions. In certain circumstances, the signal produced by vector B-H may have a less than desired signal to noise ratio. However, it is contemplated that generally available methods of signal processing in accordance with the present disclosure may be utilized the improve signal to noise ratio of the signal produced by Vector B-H. Vector A-E is an ipsilateral vector across the lung-diaphragm-liver interface. Because the liver is higher in conductivity and has a different impedance phase angle than the lung, vector A-E1 yields a good signal on both bio-Z magnitude and phase with limited cardiac artifact. Vector B-K is an ipsilateral vector across the lung-diaphragm-liver interface that is substantially between a common set of ribs with a current path that is mostly perpendicular to the intercostal muscles. Because resistivity of muscle is much higher perpendicular to the muscle direction than parallel, vector B-K reduces current-shunting through the muscle which otherwise detracts from the signal of the lung-diaphragm-liver interface. Vector A-K is an ipsilateral vector across the lung-diaphragm-liver interface similar to vector A-E1 but is more sensitive to movement of the lung-diaphragm-liver interface than to changes in resistivity of the lung-diaphragm-liver interface due to inspired air volume and is thus a good indicator of diaphragm movement. Vector B-E1 is a vector across the middle and lower right lung and is good for detecting diaphragm movement with little cardiac artifact. Vector C-E1 is a vector across the upper and middle right lung and is also good for detecting diaphragm movement with little cardiac artifact. Vector D-E1 is a vector across the upper right lung with little cardiac artifact. Vector A-D is an ipsilateral across a substantial portion of the right lung and diaphragm with little cardiac artifact, but may be susceptible to motion artifact due to arm movement. Vector E1-E2 is a vector across the heart and provides a good cardiac signal that may be used for removing cardiac artifact from a respiratory signal. Vector E2-J is a vector across the lung-diaphragm-stomach interface that provides a good measure of diaphragm movement using bio-Z phase vs. magnitude because the stomach has almost no capacitive component and generally low conductivity. Vector L-M is a trans-diaphragm vector that is generally

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across the lung-diaphragm-liver interface with little cardiac artifact. Vector L-M may be relatively less susceptible to body position and movement and may yield a good signal even if the patient is laying on the side of the sensing lead. In embodiments where the signal produced by vector L-M has a less than desired signal to noise ratio, it is contemplated that generally available methods of signal processing may be utilized to improve the signal to noise ratio of the signal produced by vector L-M.

[0181] Electrodes placed at any of the above-noted locations may include, but are not limited to, combination electrodes, such as, for example, electrodes capable of both providing a current charge and sensing a voltage.

[0182] With reference to Figures 37A and 38D, an exemplary vector selection method 3800 for detecting and utilizing a signal from the vector that produces the most desirable signal of all vectors is dicussed. The disclosed vector selection method 3800 may be performed continuously, periodically, singularly, and/or may be repeated as desired. For example, method 3800 may be performed once in a 24 hour period. In addition, one or more steps associated with method 3800 may be selectively omitted and/or the steps associated with method 3800 may be performed in any order. The steps associated with method 3800 are described in a particular sequence for exemplary purposes only.

[0183] With specific reference to Figure 38D, method 3800 may include a plurality of steps 3801-3803 for detecting and utilizing the signal with the best characteristics of all signals produced by a plurality of vectors. Specifically, method 3800 may include sampling short distance vectors first to determine if any of these vectors are producing a desirable signal, step 3801. Method 3800 may also include sampling intermediate distance vectors if the short distance vectors are not producing a desirable signal, step 3802. Method 3800 may further include sampling long distance vectors if the intermediate distance vectors are not producing a desirable signal, step 3803.

[0184] Turning to Figure 37A, there is depicted an exemplary embodiment of a neurostimulator in accordance with the principles of the present disclosure. The exemplary neurostimulator may include an implanted INS 50 and implanted electrode contacts AA-DD. While the depicted embodiment includes electrode contacts AA-DD disposed between a patient's 5th and lowest ribs, electrode contacts AA-DD may be disposed at any suitable

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location. Furthermore, electrode contacts AA-DD may include, but are not limited to, the combination electrodes discussed above. In the depicted embodiment, exemplary short distance vectors may include the vectors between, for example, adjacent electrode contacts AA, BB, CC, and DD; exemplary intermediate distance vectors may include the vectors AA-CC, AA-DD, and BB-DD, and exemplary long distance vectors may include the vectors between the INS 50 and each of electrode contacts AA-DD.

[0185] With reference to Figures 37A and Figure 38A, step 3801 may include, for example, sampling short distance vectors AA-BB, BB-CC, and CC-DD first to determine whether any of these vectors may be producing a sufficient signal in accordance with the principles of this disclosure, since these vectors generally produce signals with desirable signal to noise ratios. Next, step 3802 of method 3800 may include sampling the intermediate distance vectors AA-CC, AA-DD, and BB-DD if the short distance vectors are producing a less than desirable signal. Lastly, step 3803 of method 3800 may include sampling the long distance vectors INS-AA, INS-BB, INS-CC, and INS-DD if the intermediate distance vectors are producing a less than desirable signal.

[0186] In some embodiments, it is contemplated that several short, intermediate, and long distance vectors may be continually sampled, even if a desirable signal is being received from a short distance vector, in order to identify secondary vector signals that may be utilized if the currently utilized vector signal fails for any reason. However, fully processing the data from signals generated by all of the vectors may require complex sensing circuitry and processing of detection algorithms that may utilize undesirable amounts of battery power. Therefore, it may be desirable to only monitor selected characteristics of the secondary vector signals. With specific reference to Figure 38B, there is depicted an embodiment of a method 3850 for utilizing multiple sensing channels to optimize respiratory sensing with minimal additional hardware and power consumption. It uses a single sensing circuit which is time multiplexed (interleaved) to sample each of the vectors. Since, as noted above, fully processing the data from all vector signals may require higher computational power, method 3850 may be used to identify the best vector signal for respiration detection, while simultaneously monitoring the remaining vectors signals for only relevant fiducial points. These fiducial points may include, but are not limited to,

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significant "landmarks" within a signal, such as, for example, peak amplitude and time, point of highest slew rate, and zero crossing. The detected fiducial points for the secondary vector signals may be then stored in a circular buffer memory 3854 for analysis if the primary signal fails for any reason, thereby, allowing immediate switching to an alternate vector signal and eliminating the need for a long signal acquisition period after a need to switch vector signals has been determined.

[0187] In particular, method 3850 may include feeding the signals from all available vectors into a plurality of channel selection switches 3851. The signals may be then analyzed for relevant fiducials by the respiratory impedance sensing circuit 3853. Once relevant fiducials have been discriminated, it may be possible to identify the best vector signal for respiration signal analysis. The fiducials of the remaining vectors may be then stored in circular buffer memory 3854 (as noted above) to facilitate switching to a secondary vector signal if the primary signal is no longer suitable for respiration detection.

[0188] The periodic monitoring (or interleaving) of secondary vector signals may facilitate faster switching to those vector signals when necessary. In particular, it is contemplated that when a decision to switch to a secondary vector signal is made (i.e., when the primary signals degrades to a point where it is no loner desirable for detecting respiration), the saved data (e.g., relevant fiducials) may be used to "seed" a signal analysis algorithm with recently collected data, so as to promote faster vector switching by eliminating the need to wait for collection of sufficient data for the secondary vector signal. In other words, because select information of a secondary signal is available before the signal is actually used for respiration detection, analysis of the secondary signal for, among other things, respiration detection may begin slightly faster than it would have if no data was available.

[0189] Furthermore, in certain embodiments, additional impedance sensors may be used as backup sensors to the sensor generating the primary vector signal. In these embodiments, data from the secondary sensors may be also analyzed to identify and save relevant fiducials in the memory. This stored information may be used to provide supplemental or alternate information to facilitate identifying appropriate respiratory timing, when switching vector signals becomes necessary as a result of primary signal degradation.

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[0190] The respiratory bio-Z signal is partly due to the resistivity change which occurs when air infuses lung tissue, partly due to the relative movement of electrodes as the rib cage expands, and partly due to the displacement of other body fluids, tissue and organs as the lungs move along with the ribcage and diaphragm. As described above, each vector measures certain of these changes to different extents. It may be desirable, therefore, to combine vectors which have complementary information or even redundant information to improve the respiratory information of the bio-Z signal. To this end, multiple vectors may be used. For example, one vector may be used to sense changes in the lung-diaphragm-liver interface and a second vector may be used to detect changes (e.g., expansion, contraction) of the lung(s). Examples of the former include A-K, B-K, A-E1, B-E1, and A-B. Examples of the later include D-F, B-D, C-G, D-E1, and C-E1. Note that some vector combinations which share a common vector endpoint such as A-E1, D-E1 and B-E1, B-D may use a common electrode which would simplify the respiratory sensing lead or leads.

[0191] An advantage of using the lung-diaphragm-liver interface vector is that it provides a robust signal indicative of the movement of the diaphragm throughout the respiratory cycle. The liver is almost two times more electrically conductive than lung tissue so a relatively large bio-Z signal can be obtained by monitoring the movement of the lung-diaphragm-liver interface. Because the liver functions to filter all the blood in the body, the liver is nearly completely infused with blood. This helps to dampen out the cardiac artifact associated with the pulsatile flow of the circulatory system. Another advantage of this location is that vectors can be selected which avoid significant current path through the heart or major arteries which will help reduce cardiac artifact.

[0192] It is worth noting that diaphragm movement is not necessarily synchronous with inspiration or expiration. Diaphragm movement typically causes and therefore precedes inspiration and expiration. Respiratory mechanics do allow for paradoxical motion of the ribcage and diaphragm, so diaphragm movement is not necessarily coincident with inspiration. During REM sleep, the diaphragm is the dominant respiratory driver and paradoxical motion of the ribs and diaphragm can be problematic, especially if movement of the ribcage is being relied upon as an inspiratory indicator. Monitoring the diaphragm for pre-inspiratory movement becomes especially valuable under these circumstances. Bio-

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Z monitoring of the diaphragm can be used as a more sophisticated indicator of impending inspiration rather than the antiquated approach of desperately trying to identify and respond to inspiration in pseudo-real time based on sensors which are responding to characteristics of inspiration.

[0193] For purposes of monitoring respiration, it is desirable to minimize shunting of the electrical current through tissues which are not of interest. Shunting may result in at least two problems: reduced signal from the lungs; and increased chance of artifacts from the shunted current path. Skeletal muscle has non-isotropic conductivity. The muscle's transverse resistivity (1600 ohm-cm) is more than 5 times its longitudinal resistivity (300 ohm-cm). In order to minimize the adverse effect of shunting current, it is desirable to select bio-Z sensing vectors which are perpendicular to muscle structure if possible. One such example is to locate two or more electrodes of a bio-Z sensing array substantially aligned with the ribs because the intercostal muscles are substantially perpendicular to the ribs.

[0194] **Description of Respiration Signal Processing**

[0195] With reference to Figure 39, the neurostimulation system described herein may operate in a closed-loop process 400 wherein stimulation of the targeted nerve may be delivered as a function of a sensed feedback parameter (e.g., respiration). For example, stimulation of the hypoglossal nerve may be triggered to occur during the inspiratory phase of respiration. Alternatively, the neurostimulation system described herein may operate in an open-loop process wherein stimulation is delivered as a function of preset conditions (e.g., historical average of sleeping respiratory rate).

[0196] With continued reference to Figure 39, the closed-loop process 400 may involve a number of generalized steps to condition the sensed feedback parameter (e.g., bio-Z) into a useable trigger signal for stimulation. For example, the closed-loop process 400 may include the initial step of sensing respiration 350 using bio-Z, for example, and optionally sensing other parameters 360 indicative of respiration or other physiologic process. The sensed signal indicative of respiration (or other parameter) may be signal processed 370 to derive a usable signal and desired fiducials. A trigger algorithm 380,

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which will be discussed in greater detail below, may then be applied to the processed signal to control delivery of the stimulation signal 390.

[0197] As noted above, the present disclosure contemplates conditioning sensed bio-impedance into a useable trigger signal for stimulation. However, one exemplary limitation to using sensed bio-impedance may be the body's nominal impedance. In practice, a sensed bio-impedance signal may be obtained by applying a suitable, known current through one portion of a tissue of interest and measuring the voltage potential across the same tissue. This measurement technique is illustrated in Figure 38C and may be referred to herein as the "direct measurement" technique. The applied current and measured voltage potentials may be used to calculate the impedance of the tissue. It is this measured impedance that may constitute the sensed bio-impedance signal. However, sense bio-impedance signals of the present disclosure have been found to typically include two components, a relatively large nominal body impedance component and a relatively small respiratory impedance component. Thus, since the body's impedance constitutes a large portion of the sensed signal, it may be difficult to detect that relatively small impedance changes associated with respiration on top of a body's nominal impedance. Therefore, in accordance with the principles of the present disclosure, it may be desirable to "filter" the sensed impedance signal in a manner so as to remove most or all of the body's nominal impedance, in order to improve resolution of the respiratory signal. In some embodiments, this may be achieved with the aid of a conventional Wheatstone bridge at or near the front-end of an impedance measuring circuit. In particular, the Wheatstone bridge may facilitate precise measurements of the relatively small impedance changes associated with respiration by removing most, if not all, of the body's nominal impedance.

[0198] Turning now to Figure 39A, there is depicted an exemplary Wheatstone bridge 3900. The Wheatstone bridge 3900 may include an electrical current source 3901. Wheatstone bridge 3900 may also include a first resistor R_1 having an impedance Z_1 connected in series to a second resistor R_2 having an impedance Z_2. Resistors R_1 and R_2 may be connected in parallel to resistor R_3 having an impedance Z_3, which may be connected serially to the patient's body having an impedance Z_{body}. As discussed below, impedances Z_2 and Z_3 may be substantially similar to each other. Wheatstone bridge 3900

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may further include any suitable voltage measuring device, such as, for example, those used in conjunction the direct measurement technique described above.

[0199] In use, the impedance Z_1 of exemplary bridge 3900 may be closely matched to the expected impedance of a patient's body Z_{body}, the impedance Z_2 matched to impedance Z_3, and the voltage potential across voltage measuring device 3902 may be measured. It is contemplated that if impedances Z_1-Z_3 are closely matched to Z_{body}, the measured voltage potential across voltage measuring device 3902 will be predominantly due to respiratory impedance changes and the voltage signal due to the body's nominal impedance will be largely removed. Further, it is contemplated that the voltage changes measured at 3902 due to respiratory impedance changes will have an amplitude that is approximately ½ of the amplitude of the voltage changes, measured with the above-noted direct-measurement technique, assuming the same currently flow through the body. The removal of the voltage signal due to the body's nominal impedance while retaining ½ of the voltage signal amplitude due to changes in respiratory impedance, may facilitate detecting the small impedance changes associated with respiration by improving the resolution of those changes.

[0200] In other embodiments, the body's nominal impedance may be removed or reduced from a sensed signal by, for example, introducing a nominal offset removal module 3921 into an impedance measuring circuit 3920 of the present disclosure, as depicted in Figure 39B. An exemplary impedance-measuring circuit may generally include feeding a sensed respiratory signal into a demodulator. The signal exiting the demodulator may be then fed into an integrator, and the integrated signal exiting the integrator may then be digitized for analysis. It is therefore contemplated that introducing nominal offset removal module 3921 to act upon the upon the signal exiting the demodulator may achieve the desired effect of removing or reducing the body's nominal impedance from a sensed impedance signal.

[0201] Turning now to Figure 39C, module 3921 may include a switch S, a resistor R, a capacitor C, and a non-inverting amplifier A. The switch S, resistor R, and capacitor C create a sample and hold reference voltage to the difference amplifier A. The amplifier subtracts this reference voltage from the input signal. The result is to remove or reduce the

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nominal body impedance component of the signal leaving mainly the respiratory component of the measured impedance. The Resistor-Capacitor (R-C) combination is selected such that it will track with changes in nominal impedance levels but does not significantly distort the respiratory signal. Respiratory signal frequency components of interest are typically between 0.05Hz and 3Hz. There are several options for how the Nominal Offset Removal may be operated. An implanted bio-impedance circuit would typically use a modulated excitation signal for measuring impedance. In that case, the switch, S may be open when there is no signal present and may be closed whenever a signal is present. For example, if a Demodulator Signal is present for 1ms every 100ms, switch S would be closed during all or a part of the time that Signal In is present. Switch S may also be operated such that it does not close on every instance when Demodulator Signal is present. The switch S, may be closed on every 10th or 100th instance when Demodulator Signal is present. A third possibility is to close switch S only when Signal Out causes the Integrator to reach an unacceptable threshold. The integrator reaching an unacceptable threshold may be indicative that the reference voltage provided by the R-C combination is no longer providing a sufficiently good estimate of the nominal signal component and so needs to be updated with new information.

[0202] Turning now to Figure 39D, there is depicted an alternative embodiment of nominal offset removal module. A further improvement on the Nominal Offset Removal module is shown in Fig. 39D. If it is desired to measure two or more different impedance signals it will be necessary to have a different nominal offset reference voltage provided to amplifier A for each signal. It is also desirable to keep the component count as low as possible. In the diagram below, S0 and S1 may be closed and S2 may be open to provide an offset reference for a first signal with the appropriate combination of R-C1. S0 and S2 may be closed and S1 may be open to provide an offset reference for a second signal with the appropriate combination of R-C2. This strategy allows rapid sequential measurement of two or more impedance signals.

[0203] With reference to Figure 40, the signal processing step 370 may include general signal amplification and noise filtering 372. The step of amplification and filtering 372 may include band pass filtering to remove DC offset, for example. The respiratory

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waveform may then be processed to remove specific noise artifacts 374 such as cardiac noise, motion noise, etc. A clean respiratory waveform may then be extracted 376 along with other waveforms indicative of specific events such as obstructive sleep apnea (OSA), central sleep apnea (CSA), hypopnea, sleep stage, etc. Specific fiducial points may then be extracted and identified (e.g., type, time, and value).

[0204] The step of removing specific noise artifacts 374 may be performed in a number of different ways. However, before signal processing 374, both cardiac and motion noise artifact may be mitigated. For example, both cardiac and motion noise artifact may be mitigated prior to signal processing 374 by selection of bio-Z vectors that are less susceptible to noise (motion and/or cardiac) as described previously. In addition, motion artifact may be mitigated before signal processing 374 by minimizing movement of the sensing lead and electrodes relative to the body using anchoring techniques described elsewhere herein. Furthermore, motion artifact may be mitigated prior to signal processing 374 by minimizing relative movement between the current-carrying electrodes and the voltage-sensing electrodes, such as by using combined current-carrying and voltage-sensing electrodes.

[0205] After cardiac and motion artifact has been mitigated using the pre-signal processing techniques described above, both cardiac and motion artifact may be removed by signal processing 374.

[0206] For example, the signal processing step 374 may involve the use of a low pass filter (e.g., less than 1 Hz) to remove cardiac frequency noise components which typically occur at 0.5 to 2.0 Hz, whereas resting respiration frequency typically occurs below 1.0 Hz.

[0207] Alternatively, the signal processing step 374 may involve the use of a band pass or high pass filter (e.g., greater than 1Hz) to obtain a cardiac sync signal to enable removal of the cardiac noise from the bio-Z signal in real time using an adaptive filter, for example. Adaptive filters enable removal of noise from a signal in real time, and an example of an adaptive filter is illustrated in Figure 41. To remove cardiac artifact from the bio-Z signal which contains both cardiac noise n(k) and respiratory information s(k), a signal n'(k) that represents cardiac noise is input to the adaptive filter and the adaptive filter

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adjusts its coefficients to reduce the value of the difference between y(k) and d(k), removing the noise and resulting in a clean signal in e(k). Notice that in this application, the error signal actually converges to the input data signal, rather than converging to zero.

[0208] Another signal processing technique to remove cardiac noise is to combine signals from two or more bio-Z vectors wherein respiration is the predominate signal with some cardiac noise. This may also be used to reduce motion artifact and other asynchronous noise. Each of the two or more signals from different bio-Z vectors may be weighted prior to combining them into a resultant signal Vw(i). If it is assumed that (a) the respiratory bio-impedance is the largest component in each measured vector, (b) the non-respiratory signal components in one vector are substantially independent of the non-respiratory components in the other vector, and (c) the ratio of the non-respiratory component to the respiratory components in one vector is substantially equal to the same ratio in the other vector, then a simple weighting scheme may be used wherein each signal is divided by it's historic peak-to-peak magnitude and the results are added. For example, if M_A = historical average peak-to-peak magnitude of signal from vector A, M_B = historical average peak-to-peak magnitude of signal from vector B, $V_A(i)$ = data point (i) from vector A, $V_B(i)$ = data point (i) from vector B, then the resultant signal $V_W(i)$ (i.e., weighted average of A & B for data point (i)) may be expressed as $V_W(i) = V_A(i)/M_A + V_B(i)/M_B$.

[0209] Yet another signal processing technique for removing cardiac noise is to subtract a first signal that is predominantly respiration from a second signal that is predominantly cardiac. For example, the first signal may be from a predominantly respiratory bio-Z vector (e.g., vector B-H) with some cardiac noise, and the second signal may be from a predominantly cardiac bio-Z vector (e.g., vector E1-E2) with some respiration signal. Each of the two signals from the different bio-Z vectors may be weighted prior to subtracting them. The appropriate weighting may be determined, for example, by calculating the power density spectra in the range of 2-4Hz for a range of weighted differences across at least several respiratory cycles. A minimum will occur in the power density spectra for the weighted averages which are sufficiently optimal.

[0210] Motion artifact may be removed by signal processing 374 as well. Motion artifact may be identified and rejected using signal processing techniques such as

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monitoring voltage magnitude, testing the correlation of magnitude and phase, and/or testing correlation at two or more frequencies. Motion artifacts may cause a large change in measured bio-impedance. A typical feature of motion artifacts is that the voltage swings are much larger than respiration. Another feature is that the voltage changes are highly erratic. Using these characteristics, which will be described in more detail below, motion artifact may be removed from the respiration signal.

[0211] The step of extracting waveforms indicative of respiration and other events 374 may be better explained with reference to Figures 42 – 46 which schematically illustrate various representative unfiltered bio-Z signals. Figure 42 schematically illustrates a bio-Z signal 420 with representative signatures indicative normal respiration (i.e., event free) during an awake period 422 and a sleeping period 424. Figure 43 schematically illustrates a bio-Z signal 430 with representative signatures indicative of normal respiration during sleeping periods 424 interrupted by a period of motion 432 (i.e., motion artifact). Figure 44 schematically illustrates a bio-Z signal 440 with representative signatures indicative of normal respiration during a sleeping period 424 followed by periods of hypopnea (HYP) 442 and recovery 444. Figure 45 schematically illustrates a bio-Z signal 450 with representative signatures indicative of normal respiration during a sleeping period 424 followed by periods of obstructive sleep apnea (OSA) 452 and recovery 454 (which typically includes an initial gasp 456). Figure 46 schematically illustrates a bio-Z signal 460 with representative signatures indicative of normal respiration during a sleeping period 424 followed by periods of central sleep apnea (CSA) 462 (which typically includes a cessation in breathing 468) and recovery 464.

[0212] The step of extracting 374 waveform data indicative of an awake period 422 vs. a sleep period 424 from a bio-Z signal 420 may be explained in more detail with reference to Figure 42. In addition, the step of filtering 372 waveform data indicative of motion 432 from a bio-Z signal 430 may be explained in more detail with reference to Figure 43. One way to determine if a person is awake or moving is to monitor the coefficient of variation (CV) of sequential peak-to-peak (PP) magnitudes over a given period of time. CV is calculated by taking the standard deviation (or a similar measure of variation) of the difference between sequential PP magnitudes and dividing it by the average

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(or a similar statistic) of the PP magnitudes. N is the number of respiratory cycles which occur in the selected period of time.

[0213] The CV may be calculated as follows:

[0214] $$CV = \frac{sd(dPP)}{\overline{PP}}$$

[0215] Where:

[0216] $$sd(dPP) = \sqrt{\frac{\sum_{i=1}^{N}\left(dPP_i - \overline{dPP}\right)}{(N-1)}}$$

[0217] $$\overline{dPP} = \frac{\sum_{i=1}^{N}(dPP_i)}{(N)}$$

[0218] $$dPP_i = PP_{i+1} - PP_i$$

[0219] $$\overline{PP} = \frac{\sum_{i=1}^{N}(PP_i)}{(N)}$$

[0220] Generally, if the CV is greater than 0.20 over a one minute period then person is awake. Also generally, if the CV is less than 0.20 over a one-minute period then person is asleep. These events may be flagged for the step of fiducial extraction 378 wherein data (e.g., event duration, CV, PP range, PPmin, PPmax, etc.) may be time stamped and stored with an event identifier. If CV is greater than 1.00 over a 20 second period then body movement is affecting the bio-Z signal. By way of example, not limitation, if body movement is detected, then (a) stimulation may be delivered in an open loop fashion (e.g., based on historical respiratory data); (b) stimulation may be delivered constantly the same or lower level; or (c) stimulation may be turned off during the period of movement. The selected stimulation response to detected movement may be preset by the physician programmer or by the patient control device. Other stimulation responses may be employed as will be described hereinafter.

[0221] In each of Figures 44 – 46, maximum and minimum peak-to-peak magnitudes (PPmax and PPmin) may be compared to distinguish hypopnea (HYP),

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obstructive sleep apnea (OSA), and central sleep apnea (CSA) events. Generally, PP values may be compared within a window defined by the event (HYP, OSA, CSA) and the recovery period thereafter. Also generally, the window in which PP values are taken excludes transitional events (e.g., gasp 456, 466). As a general alternative, peak-to-peak phases may be used instead of peak-to-peak magnitude. The hypopnea and apnea events may be flagged for the step of fiducial extraction 378 wherein data (e.g., event duration, CV, PP range, PPmin, PPmax, etc.) may be time stamped and stored with an event identifier.

[0222] A typical indication of hypopnea (HYP) and apnea (OSA, CSA) events is a recurrent event followed by a recovery. The period (T) of each event (where PP oscillates between PPmax and PPmin and back to PPmax) may be about 15 to 120 seconds, depending on the individual. The largest PP values observed during hypopneas and apneas are usually between 2 and 5 times larger than those observed during regular breathing 424 during sleep. The ratio of the PPmax to PPmin during recurrent hypopnea and apnea events is about 2 or more. During the event and recovery periods (excluding transitional events), PP values of adjacent respiratory cycles do not typically change abruptly and it is rare for the change in PP amplitude to be more than 50% of PPmax. One exception to this observation is that some people gasp 456, 466 (i.e., transitional event) as they recover from a CSA or OSA event.

[0223] The ratio of successive PP magnitudes during normal (non-event) sleep 424 is mostly random. The ratio of successive PP magnitudes during apnea and hypopnea events will tend to be a non-random sequence due to the oscillatory pattern of the PP values. Recurrent apneas and hypopneas may be diagnosed by applying a statistical test to the sequence of successive PP ratios.

[0224] The step of extracting 374 waveform data indicative of an hypopnea event 442 from a bio-Z signal 440 may be explained in more detail with reference to Figure 44. The ratio of PPmax to PPmin during recurrent hypopneas is typically between 2 and 5. This is in contrast to CSA's which have very small PPmin due to the complete cessation of breathing. This results in CSA's having PPmax to PPmin ratios larger than 5. Accordingly, hypopnea events may be detected, identified and flagged for the step of fiducial extraction

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378 wherein data (e.g., event duration, CV, PP range, PPmin, PPmax, etc.) may be time stamped and stored with an event identifier.

[0225] The step of extracting 374 waveform data indicative of an OSA event 452 from a bio-Z signal 450 may be explained in more detail with reference to Figure 45. The sharp change 456 in the bio-Z respiratory magnitude due to OSA is typically in the range of 1 to 4 times the magnitude of the peak-to-peak respiratory cycle magnitude. The sharp change 456 typically takes less than 5 seconds to occur. OSA tends to occur in a recurring sequence where the period (T) between sequential events is between 15 and 120 seconds. A one-minute period is commonly observed. According to these characteristics, OSA events may be detected, identified and flagged for the step of fiducial extraction 378 wherein data (e.g., event duration, CV, PP range, PPmin, PPmax, etc.) may be time stamped and stored with an event identifier.

[0226] The step of extracting 374 waveform data indicative of a CSA event 462 from a bio-Z signal 460 may be explained in more detail with reference to Figure 46. The behavior of the Bio-Z signal throughout recurrent CSA events differ from other hypopnea and OSA in three ways. First, during CSA there is complete cessation of respiratory activity which results in a flat Bio-Z signal. This means the ratio of PPmax to PPmin is typically greater than 5 during recurrent CSA events. The duration of the estimated respiratory cycle may also be used to distinguish between CSA from OSA and hypopnea. The lack of respiratory activity during CSA results in an inflated estimate for the respiratory cycle period. The PP typically does not vary by more than 50% for successive cycles. The respiratory cycle duration during a CSA event is more than twice as long as the duration of the respiratory cycles preceding the CSA event. Second, during CSA the Bio-Z magnitude will drift outside the PP magnitude range observed during respiration. It has been observed that with the onset of central sleep apnea (CSA) the magnitude and phase of the Bio-Z signal settle to a steady-state value outside the peak-to-peak range observed during the normal respiratory cycle during sleep. Third, upon arousal from CSA a person will typically gasp. This gasp results in a large PP. The PP of the first respiratory cycle following the CSA event and the PP observed during the CSA (which is essentially noise) will exceed 50% of PPmax.

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[0227] With continued reference to Figure 46, the flat portions 468 of the data traces are periods of respiratory cessation. Upon arousal the subject gasps 466 and the raw bio-Z signal resumes cyclic oscillation above the static impedance level observed during CSA. According to these characteristics, CSA events may be detected, identified and flagged for the step of fiducial extraction 378 wherein data (e.g., event duration, CV, PP range, PPmin, PPmax, etc.) may be time stamped and stored with an event identifier.

[0228] The step of extracting 374 waveform data indicative of sleep stage (e.g., rapid eye movement (REM) sleep vs. no-rapid eye movement (NREM) sleep) may be performed by comparing the phase difference between a first vector and a second vector wherein the first bio-Z vector is along the lung-diaphragm-liver interface (e.g., vector A-K or vector B-K) and the second bio-Z vector is about the lung(s). Examples of the first bio-Z vector include A-K, B-K, A-E1, B-E1, and A-B. Examples of the second bio-Z vector include D-F, B-D, C-G, D-E1, and C-E1. Note that some vector combinations which share a common vector endpoint such as A-E1, D-E1 and B-E1, B-D may use a common electrode and to simplify the respiratory sensing lead or leads. Typically, during NREM sleep, the two vectors are substantially in phase. During REM sleep, the diaphragm is the primary respiratory driver and a common consequence is paradoxical motion of the ribcage and diaphragm (i.e., the two vectors are substantially out of phase). This characteristic would allow for an effective monitor of a person's ability to reach REM sleep. Accordingly, REM and NREM sleep stages may be detected, identified, and flagged for the step of fiducial extraction 378 wherein characteristic data (e.g., event duration, phase, etc.) may be time stamped and stored with an event identifier.

[0229] An alternative method of detecting an OSA event is to make use of a split current electrode arrangement as shown in Figure 47 which shows the positions of three electrodes on the subject. Electrode A may be above the zyphoid, electrode B may be just above the belly button, and electrode C may be on the back a couple of inches below electrode A. Electrodes A and B are connected to a common constant current source through resistors R1 and R2. The voltage measured across the current source is a measure of the bio-impedance during normal respiration. The voltage across R1 is an indicator of the paradoxical motion associated with apnea. An unbalanced current split between R1 and

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R2 resulting in large bio-Z voltage swings is indicative of OSA. During normal respiration or even very deep breaths there is almost no effect on the apnea detection channel. Accordingly, OSA events may be detected, identified, and flagged for the step of fiducial extraction 378 wherein characteristic data (e.g., event duration, voltage swing magnitude, etc.) may be time stamped and stored with an event identifier.

[0230] Generally, the extracted 378 waveform and event data may be used for therapy tracking, for stimulus titration, and/or for closed loop therapy control. For example, data indicative of apneas and hypopneas (or other events) may be stored by the INS 50 and/or telemetered to the patient controlled 40. The data may be subsequently transmitted or downloaded to the physician programmer 30. The data may be used to determine therapeutic efficacy (e.g., apnea hypopnea index, amount of REM sleep, etc.) and/or to titrate stimulus parameters using the physician programmer 30. The data may also be used to control stimulus in a closed loop fashion by, for example, increasing stimulus intensity during periods of increased apnea and hypopnea occurrence or decreasing stimulus intensity during periods of decreased apnea and hypopnea occurrence (which may be observed if a muscle conditioning effect is seen with chronic use). Further, the data may be used to turn stimulus on (e.g., when apnea or hypopnea events start occurring or when motion artifact is absent) or to turn stimulus off (e.g., when no apnea or hypopnea events are occurring over a present time period or when motion artifact is predominant).

[0231] **Description of Stimulus Trigger Algorithms**

[0232] As mentioned previously with reference to Figure 39, the neurostimulation system described herein may operate in a closed-loop process wherein the step of delivering stimulation 390 to the targeted nerve may be a function of a sensed feedback parameter (e.g., respiration). For example, stimulation of the hypoglossal nerve may be triggered to occur during the inspiratory phase of respiration. In a health human subject, the hypoglossal nerve is triggered about 300 mS before inspiration. Accordingly, a predictive algorithm may be used to predict the inspiratory phase and deliver stimulation accordingly. Figure 48 schematically illustrates a system 480 including devices, data and processes for implementing a self-adjusting predictive trigger algorithm.

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[0233] The system components 482 involved in implementing the algorithm may include the physician programmer (or patient controller), INS and associated device memory, and the respiratory sensor(s). The sensors and device memory are the sources of real-time data and historical fiducial data which the current algorithm uses to generate a stimulation trigger signal. The data 484 utilized in implementing the algorithm may include patient specific data derived from a sleep study (i.e., PSG data), data from titrating the system post implantation, and historic and real-time respiratory data including respiratory and event fiducials. The processes 486 utilized in implementing the algorithm may include providing a default algorithm pre-programmed in the INS, patient controller or physician programmer, modifying the default algorithm, and deriving a current algorithm used to generate a trigger signal 488.

[0234] More specifically, the processes 486 utilized in implementing a predictive trigger algorithm may involve several sub-steps. First, a default algorithm may be provided to predict onset of inspiration from fiducial data. Selecting an appropriate default algorithm may depend on identifying the simplest and most robust fiducial data subsets which allow effective prediction of onset. It also may depend on a reliable means of modifying the algorithm for optimal performance. Second, modification of the default algorithm may require a reference datum. The reference datum may be the estimated onset for past respiratory cycles. It is therefore useful to precisely estimate inspiratory onset for previous respiratory cycles from historical fiducial data. This estimation of inspiratory onset for previous respiratory cycles may be specific to person, sensor location, sleep stage, sleep position, or a variety of other factors. Third, the current algorithm may be derived from real-time and historical data to yield a stimulation trigger signal 488.

[0235] As alluded to above, a trigger algorithm, such as, for example, trigger algorithm 4700 depicted in Figure 47A, may be applied to a detected respiratory signal to begin and/or control delivery of the stimulation signal. As illustrated, trigger algorithm 4700 may include a plurality of sub-routines 4701-4703 for performing various analyses on a sensed respiratory signal. These sub-routines may include, but are not limited to, performing peak detection 4701, error checking 4702, and prediction 4703, on a detected respiratory signal.

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[0236] With reference now to Figure 47D, there is depicted an exemplary sensed respiratory signal 4750. Respiratory signal 4750 may be displayed as a substantially sinusoidal waveform having a component that varies with time. As shown in Figure 47D, respiratory signal 4750 may include a plurality of peaks, such as, for example, the peak located at v_4t_4, and a plurality of valleys, such as, for example, the valley located $v^-_4t^-_4$. Therefore, as will be discussed in greater detail below, peak detection sub-routine 4701 may be applied to sensed respiratory signal 4750 to detect the peaks of signal 4750. Error checking sub-routine 4702 may be applied to signal 4750 to, among other things, ensure signal 4750 is an accurate representation of a patient's respiration and free from undesirable artifacts caused by, for example, a patient's movement or cardiac activity. Prediction sub-routine 4703 may then be applied to signal 4750 to predict when future peaks will occur in accordance with the sensed signal 4750.

[0237] With reference to Figure 47B, peak detection 4701 may include a plurality of steps 4701a-g. Step 4701a may include first detecting the peaks, such as, for example, the peak located at v_4t_4, of signal 4750. The detected peaks may be an indication of when onset of expiration occurs during the monitored respiratory cycles. Next, step 4701b may include acquiring and/or considering a new voltage V_k, where V_k may be the most recently acquired data point time T_k under consideration, where a number of recently acquired data points may be under consideration. Step 4701c may determine whether the data points under consideration meet the criteria to indicate that a minimum (min) peak has been detected. One example of such a criteria to indicate a minimum peak has been detected is if the oldest data point under consideration, V_{k+m} is less than more recent data points under consideration, (V_{k+m-1}... V_k), which can be expressed mathematically as $V_{k+m} \leq \min (V_{k+m-1}... V_k)$. Another example of such a criteria to indicate a minimum peak has been detected is if the most recent data point under consideration, V_k, is greater than all other less-recently acquired data points under consideration, (V_{k+m}... V_{k+1}), which can be expressed mathematically as $V_k \geq \max (V_{k+m}... V_{k+1})$. If the criteria for detecting a minimum peak is not met, step 4701b may be repeated to acquire and/or consider a new voltage V_k. If the criteria has been met, step 4701d may declare a minimum peak reference. Next, step 4701e may again acquire and/or consider a new voltage V_k. Subsequently, step 4701f may

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determine whether the data points under consideration meet the criteria to indicate a maximum peak has been detected. One example of such a criteria to indicate a maximum peak has been detected is if the oldest data point under consideration, V_{k+m}, is greater than more recent data points under consideration (V_{k+m-1}... V_k), which can be expressed mathematically as $V_{k+m} \geq \max (V_{k+m-1} \ldots V_k)$. Another example of such a criteria to indicate a maximum peak has been detected is if the most recent data point under consideration, V_k, is less than all other less-recently acquired data points under consideration, (V_{k+m}... V_{k+1}), which can be expressed mathematically as $V_k \leq \max (V_{k+m} \ldots V_{k+1})$. If the criteria for detecting a maximum peak is not met, step 4701e may be repeated to acquire and/or consider a new voltage V_k. If the criteria has been met,, step 4701g may declare a maximum peak, and trigger algorithm 4700 may proceed to error-checking sub-routine 4702. The declared peak will depend on the criteria used for peak detection. For example, if the criteria for detecting a peak was based on comparing V_k to less recently acquired data points, (V_{k+m}... V_{k+1}), then the peak magnitude and time would be declared to be $V_{k+m/2}$, $t_{k+m/2}$. As another example, if the criteria for detecting a peak was based on comparing the oldest considered data point, V_{k+m}, to more recently acquired data points (V_{k+m-1}... V_k), then the peak magnitude and time would be declared to be V_{k+m}, t_{k+m}.

[0238] With reference now to Figure 47C, error-checking sub-routine 4702 may include a plurality of steps 4702a-e to determine whether a sensed respiratory signal may be adequate for respiration detection. For example, step 4702a, peak correction, may include receiving information relating to the peaks detected in step 4701 and corrections, as necessary. Next, steps 4702b-e may include analyzing the sensed respiratory signal to determine whether the signal includes "noise" caused by a patient's movement (4702b), whether the signal is sub-threshold (e.g., has a relatively low amplitude) (4702c), whether the signal is sufficiently stable (4702d), and whether the inversion detection is possible with the sensed signal (4702e). If the sensed signal passes all of error-checking steps 4702b-e, trigger algorithm 4700 may proceed to prediction sub-routine 4703. However, if the sensed signal fails any of steps 4702b-e, the trigger algorithm may terminate and the pulse generator (e.g., INS 50) may either cease stimulation, continue stimulation with continuous pulses of predetermined duration, and/or continue to stimulate at the same or a fraction

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(e.g., one quarter) of the stimulation rate for the most recently measured respiratory cycle, as discussed in greater detail below.

[0239] As described above, a peak is declared for a given set of data points under consideration when a peak detection criteria is met. The declared peak itself may be used in further algorithm calculations or a more precise estimate of peak time and voltage may be calculated. The more precise estimates of peak time and voltage are referred to as the peak correction. With regard to step 4702a, peak correction may be calculated as follows:

$$\Delta V_{pk,i} = V_{pk,i} - V_{pk,i-1} \text{ for } -n \le i \le n$$

$V_{pk,0}$ is defined to be the declared peak for which a correction is being calculated. The difference in voltage between successive data points is calculated for a given number of data points, n, to either side of the declared peak.

$$\Delta V_{pk,0th} = \frac{1}{2n}\sum\left(\Delta V_{pk,i}\right)$$

The peak in signal ideally occurs when the rate of change of the signal is zero. Taking successive differences in measured voltage is an approximation to the rate of change of the signal. Linear regression is used on a range of successive differences to estimate the point in time when the rate of change is zero. Due to the fact that the data points are collected at equal increments of time, calculating the statistics $\Delta V_{pk,0th}$, $\Delta V_{pk,1st}$ and DEN allows a simple calculation based on linear regression to estimate the point in time at which the rate of change of the signal is zero.

$$\Delta V_{pk,1st} = \sum\left(i * \Delta V_{pk,i}\right) \text{ for } -n \le i \le n$$

$$\text{DEN} = \sum\left(i^2\right) \text{ for } -n \le i \le n$$

$$\text{Correction} = \Delta V_{pk,0th}\left(\frac{DEN}{\Delta V_{pk,1st}}\right)$$

Additionally, an estimated peak time after correction may be determined as follows:

$$t'_{pk,0} = t_{pk,0} + \text{Correction}$$

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[0240] With regards to step 4702e, a peak curvature estimate for inversion detection can be obtained from one of the statistics, $\Delta V_{pk,1st}$, calculated for peak correction. Maximum peaks are sharper than minimum peaks and so typically have higher values of $\Delta V_{pk,1st}$. One means of determining if a signal is inverted would be to compare the values of $\Delta V_{pk,1st}$ for a series of maximum peaks to a series of minimum peaks.

[0241] With renewed reference to Figure 47A, prediction sub-routine 4703 may include predicting the time between sequentially identified peaks with either a parametric option or a non-parametric option. The parametric option makes a prediction of the duration of the next respiratory period based on the average duration of recent respiratory cycles and the rate of change of the duration of recent respiratory cycles. The parametric option also takes advantage of the fact that data points are collected at equal increments of time which simplifies the linear regression calculation. The parametric option may be defined as follows:

$$\Delta t_i = t_i - t_{i-1}$$

Zeroth order estimate of next peak.

$$\Delta t_{0,0th} = 1/h \cdot \sum(\Delta t_i) \text{ , for } 1 \le i \le n$$

where n is the number of past respiration cycles used

First Order Estimate

$$\Delta t_{0,1st} = \sum\left(i - \left(\frac{n+1}{2}\right) * \Delta t_i\right) \text{, for } 1 \le i \le n$$

$$DEN1 = \sum\left(\left(i - \left(\frac{n+1}{2}\right)\right)^2\right) \text{, for } 1 \le i \le n$$

Predicted Interval Length for Current Respiration Cycle

$$\Delta t_{0,pred} = \Delta t_{0,0th} + \left(\frac{\Delta t_{0,1st}}{DEN1}\right) \cdot \left(\frac{n+1}{2}\right)$$

Next Predicted Offset at

$$t_{0,pred} = t_1 + \Delta t_{0,pred}$$

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Begin therapy delivery at:

$t_{therapy} = t_1 + (1 - DC) * \Delta t_{0,pred}$, where DC may be the allowable duty cycle for therapy delivery.

[0242] The non-parametric option is very similar to the parametric option in that it also estimates the duration of the next respiratory period based on the nominal duration of recent respiratory cycles and the rate of change of the duration of recent respiratory periods. The method is explained in more detail in "Nonparametric Statistic Method" by Hollander and Wolfe in sections related to the Theil statistic and the Hodges-Lehman, there disclose of which is incorporated herein by reference. The non-parametric prediction method may be defined as follows:

$\Delta t_i = t_i - t_{i-1}$

Zeroth Order Estimate

$\Delta t_{0,oth} = 1/2\, median\{\Delta t_i + \Delta t_j,\ i + \in_0 \le j \le 1,\ldots,n\}$

Where $\in_0$ is optimally 0, 1, 2 or 3

First Order Estimate

$S_{ij} = \frac{\Delta t_j - \Delta t_i}{j - i}$ $1 \le i + \in_1 < j \le n$ where $\in_1$ is optimally 0,1,2, or 3

$\Delta t_{0,1st} = median\{S_{ij}, 1 \le i \le \in_1 < j \le n\}$

Predicted Interval Length for Current Respiration cycle

$\Delta t_{0,pred} = \Delta t_{0,0th} + \Delta t_{0,1st} \cdot \left(\frac{n+1}{2}\right)$

Next Predicted Offset

$t_{0,pred} = t_1 + \Delta t_{0,pred}$

Begin Therapy Delivery at

$t_{theraphy} = t_1 + (1 - DC)) * \Delta t_{0,pred}$, where DC may be the allowable duty cycle for therapy delivery.

[0243] Stimulation may then commence at the calculated $t_{therapy}$.

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[0244] With reference to Figure 48, a self adjusting predictive algorithm may be implemented in the following manner.

[0245] The Programmer block illustrates means by which PSG-derived data may be uploaded into the device.

[0246] The Sensors and Device Memory block includes the sources of real-time data and historical fiducial variables which the current algorithm uses to generate a stimulation trigger signal.

[0247] The Patient PSG Titration Data block includes conventional polysomnographic (PSG) data obtained in a sleep study. A self-adjusting predictive algorithm utilizes a reference datum to which the algorithm can be adjusted. Onset may be defined as onset of inspiration as measured by airflow or pressure sensor used in a sleep study, for example. Estimated Onset may be defined as an estimate of Onset calculated solely from information available from the device sensors and memory. To enable the predictive algorithm to be self-adjusting, either Onset or Estimated Onset data is used. During actual use, the implanted device will typically not have access to Onset as that would require output from an airflow sensor. The device then may rely on an estimate of Onset or Estimated Onset. The calibration of Estimated Onset to Onset may be based on PSG data collected during a sleep study. The calibration may be unique to a person and/or sleep stage and/or sleep position and/or respiratory pattern.

[0248] The Historical Fiducial Variables block represents the Historical Fiducial Variables (or data) which have been extracted from the bio-Z waveform and stored in the device memory. This block assumes that the raw sensor data has been processed and is either clean or has been flagged for cardiac, movement, apnea or other artifacts. Note that fiducial data includes fiducials, mathematical combinations of fiducials or a function of one or more fiducials such as a fuzzy logic decision matrix.

[0249] The Real-Time Data and Historical Fiducial Variables block incorporates all the information content of the Historical Fiducial Variables block and also includes real-time bio-Z data.

[0250] The Default Algorithm block represents one or more pre-set trigger algorithms pre-programmed into the INS or physician programmer. The default algorithm

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used at a specific point in time while delivering therapy may be selected from a library of pre-set algorithms. The selection of the algorithm can be made automatically by the INS based on: patient sleep position (position sensor), heart rate (detectable through the impedance measuring system) or respiration rate. Clinical evidence supports that the algorithm used to predict the onset of inspiration may be dependant on sleep position, sleep state or other detectable conditions of the patient.

[0251] The Modify Algorithm block represents the process of modifying the Default Algorithm based on historical data to yield the Current Algorithm. Once the calibration of Estimated Onset to Onset is resident in the device memory it can be used to calculate Estimated Onset for past respiratory cycles from Fiducial Variables. The variable used to represent the Estimated Onset will be TEST or TEST(i) where the "i" indicates the cycle number. Note that Estimated Onset is calculated for past respiratory cycles. This means that sensor fiducial variables which either proceed or follow each Onset event may be used to calculate the Estimated Onset.

[0252] The Current Algorithm block represents the process of using the Modified Default Algorithm to predict the next inspiratory onset (Predicted Onset). The Predicted Onset for the next respiratory cycle may be calculated from real-time data and historical fiducial variables. The calculation may be based on the Modified Default Algorithm. Modification of the Modified Default Algorithm to derive the Current Algorithm may be dependent on the calibration of Estimated Onset to Onset which was input from the physician programmer and may be based on comparison of real-time bio-Z data to data collected during a PSG titration study. The Current Algorithm may use historic and/or real-time sensor fiducial variables to predict the next onset of inspiration. This predicted onset of inspiration may be referred to as Predicted Onset. The variable used to represent Predicted Onset may be TPRED or TPRED(i) where the "i" indicates the respiratory cycle.

[0253] The Stimulation Trigger Signal block represents the Current Algorithm generating a trigger signal which the device uses to trigger stimulation to the hypoglossal nerve.

[0254] Figure 49 is a table of some (not all) examples of waveform fiducials which can be extracted from each respiratory cycle waveform. For each fiducial there is a

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magnitude value and a time of occurrence. Each waveform has a set of fiducials associated with it. As a result, fiducials may be stored in the device memory for any reasonable number of past respiratory cycles. The values from past respiratory cycles which are stored in device memory are referred to as Historical Fiducial Variables.

[0255] The graphs illustrated in Figure 50 are examples of fiducials marked on bio-Z waveforms. The first of the three graphs illustrate the bio-impedance signal after it has been filtered and cleared of cardiac and motion artifacts. The first graph will be referred to as the primary signal. The second graph is the first derivative of the primary signal and the third graph is the second derivative of the primary signal. Each graph also displays a square wave signal which is derived from airflow pressure. The square wave is low during inspiration. The falling edge of the square wave is onset of inspiration.

[0256] Due to the fact that it may be difficult to identify onset of inspiration in real-time from respiratory bio-impedance, a goal is to construct an algorithm which can reliably predict onset of inspiration "T" for the next respiratory cycle from information available from the current and/or previous cycles. A reliable, distinct and known reference point occurring prior to onset of inspiration, "T", is "A", the peak of the primary signal in the current cycle. As can be seen in Figure 50, the upper peak of the bio-Z waveform "A" approximately corresponds to the onset of expiration "O." A dependent variable $t_{T\text{-}PK}$ is created to represent the period of time between the positive peak of the primary signal for the current cycle, t.Vmax(n), indicated by "A_n" on the graph, and onset of inspiration for the next cycle, t.onset(n+1), indicated by "T" on the graph. The variable $t_{T\text{-}PK}$ may be defined as:

[0257] $t_{T\text{-}PK} = t.onset(n+1) - t.Vmax(n)$

[0258] Note that t.Vmax could be replaced by any other suitable fiducial in defining a dependent variable for predicting onset.

[0259] A general model for a predictive algorithm may be of the following form:

[0260] $t_{T\text{-}PK} = f$(fiducials extracted from current and/or previous cycles)

[0261] A less general model would be to use a function which is a linear combination of Fiducial Variables and Real-Time Data.

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[0262] The following fiducials may be both highly statistically significant and practically significant in estimating T:

[0263] t.Vmax(n) = the time where positive peak occurs for the current cycle;

[0264] t.dV.in(n) = the time of most positive 1st derivative during inspiration for the current cycle; and

[0265] t.Vmax(n-1) = the time of positive peak for the previous cycle.

[0266] This model can be further simplified by combining the variables as follows:

[0267] $\Delta t.pk(n) = t.Vmax(n) - t.Vmax(n-1)$

[0268] $\Delta t.in(n) = t.Vmax(n) - t.dV.in(n)$

[0269] Either $\Delta t.pk(n)$ or $\Delta t.in(n)$ is a good predictor of Onset.

[0270] The following example uses $\Delta t.pk(n)$. The time from a positive peak until the next inspiration onset can be estimated by:

[0271] $T_{pred} = t.Vmax(n) + k0 + k1*\Delta t.pk(n)$

[0272] The coefficients k0 and k1 would be constantly modified by optimizing the following equation for recent historical respiratory cycles against T_{est}:

[0273] $T_{est} = t.Vmax(n) + k0 + k1*\Delta t.pk(n)$

[0274] Thus, the predictive trigger time T_{pred} may be determined by adding $t_{T\text{-}PK}$ to the time of the most recent peak (PK) of the bio-Z signal, where:

[0275] $t_{T\text{-}PK} = k0 + k1*\Delta t.pk(n)$

[0276] The predictive equation we are proposing is based on the fact that the very most recent cycle times should be negatively weighted. Regression analysis supports this approach and indicates a negative weighting is appropriate for accurate prediction of onset. Thus, predicting onset is more effective if the most recent historical cycle time is incorporated into an algorithm with a negative coefficient.

[0277] As noted above, stimulation may be delivered for only a portion of the respiratory cycle, such as, for example, during inspiration. Additionally, it may be desirable to begin stimulation approximately 300 milliseconds before the onset of inspiration to more closely mimic normal activation of upper airway dilator muscles. However, predicting and/or measuring inspiration, in particular, the onset of inspiration, may be relatively

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challenging. Thus, since the onset of expiration may be relatively easy to measure and/or predict (as discussed in greater detail below) when an adequate measure of respiration is available, it is contemplated that stimulation may be triggered as a function of expiration onset.

[0278] Turning now to Figure 50A, there is depicted an exemplary respiratory waveform 5500 for two complete respiratory cycles A and B. In analyzing exemplary waveform 5500, it may be determined that peaks M of the waveform 5500 may indicate onset of the expiratory phases of respiration cycles A and B. Furthermore, it may be discovered that peaks M occur at regular intervals of approximately 3-4 seconds. Thus, it may be relatively easy to predict the occurrence of subsequent peaks M, and consequently, the onset of expiration for future respiratory cycles.

[0279] Therefore, in order to deliver a stimulus to a patient in accordance with the principles of the present disclosure, the start of stimulation may be calculated by first predicting the time intervals between the start of expiration for subsequently occurring respiratory cycles. Next, in order to capture the entire inspiratory phase, including the brief pre-inspiratory phase of approximately 300 milliseconds, stimulation may be started at the time N that is prior to the next onset of expiration by approximately 30% to 50% of the time between subsequently occurring expiratory phases. Stimulating less than 30% or more than 50% prior to the next expiratory phase may result in an inadequate stimulation period and muscle fatigue, respectively.

[0280] In some embodiments, however, it is contemplated that an adequate measure of respiration may not be available, such as, for example, when a relied upon signal has failed. In these embodiments, it is contemplated that the implanted neurostimulator system may be configured to respond in one or more of the following three ways. First, the implanted neurostimulator may completely cease stimulation until an adequate signal is acquired. Second, the neurostimulator may deliver continuous simulation pulses of predetermined durations (e.g., up to 60 seconds) until an adequate signal is acquired; or if an adequate signal is not acquired in this time, the stimulation will be turned off. Third, the neurostimulator may continue to stimulate at the same or a fraction (e.g., one quarter) of the stimulation rate for the most recently measured respiratory cycle. That is to say, the

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neurostimulator may deliver stimulation pulses of relatively long durations at a frequency that is less than the frequency of stimulation utilized with an adequate measure of respiration. Alternatively, the neurostimulator may deliver stimulation pulses of relatively short durations at a frequency that is greater than the frequency used with an adequate measure of respiration.

[0281] **Description of an Exemplary Stimulation Pulse**

[0282] Turning now to Figure 50B, there is depicted an exemplary stimulation pulse waveform 5000 that may be emitted from an INS in accordance with the principles of the present disclosure. Typically, exemplary stimulation pulse waveform 5000 may include a square wave pulse train having one or more square wave pulses 5001 of approximately 1 to 3 volts in amplitude, a duration of approximately 100 ms, and a frequency of approximately 30 Hz, assuming a 1000 ohm impedance at the electrodes and a constant current or voltage.

[0283] In some embodiments, exemplary stimulation pulse waveform 5000 may include a bi-phasic charge balanced waveform square pulses 5001 and 5002, as depicted in Figure 50B. Square pulse 5002 may be included in waveform 5000 to, among other things, promote efficient stimulation and/or mitigate electrode corrosion. However, square pulse 5002 may be excluded from waveform 5000 as desired. Furthermore, although the depicted exemplary waveform 5000 includes square pulse 5002 that exactly balances the stimulation wave pulse 5001, in certain circumstances, square pulse 5002 may not exactly balance the stimulation wave pulse 5001, and may not be a square pulse.

[0284] In some embodiments, exemplary stimulation pulse waveform 5000 may include the delivery of a low amplitude (e.g., below the stimulation threshold), long duration, pre-stimulation pulse 5004. The pre-stimulation pulse 5004 may include any suitable low amplitude, long duration pulse, and may be provided approximately 0.5 ms before the delivery of a first stimulation pulse 5001.

[0285] Pre-stimulation pulse 5004 may facilitate selectively stimulating certain fibers of a nerve, such as, for example, the hypoglossal nerve or the superior laryngeal nerve. In particular, when stimulating the hypoglossal nerve, the presence of a pre-stimulation pulse, such as, for example, pulse 5004, before a stimulation pulse (e.g., the bi-phasic stimulation pulse 5001 depicted in Figure 50B) may serve to saturate the large

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diameter fibers of the nerve so as to allow the stimulation pulse 5001 to only affect (e.g., stimulate) the smaller diameter fibers of the nerve. In circumstances where a nerve (e.g., the hypoglossal nerve) may be stimulated for extended periods of time, a pre-stimulation pulse 5004 may be selectively introduced to waveform 5000, so as to permit selective switching between stimulating the large and small diameter fibers of the nerve, in order to reduce muscle fatigue. Similarly, in situations where OSA may be treated by stimulating the superior laryngeal nerve to open the upper airway through a reflex mechanism, the presence of pre-stimulation pulse 5004 may serve to saturate the larger diameter efferent fibers so as to allow the stimulation pulse 5001 to only affect the smaller diameter afferent fibers of the nerve.

[0286] **Description of External (Partially Implanted) System**

[0287] With reference to Figures 51A and 51B, an example of an external neurostimulator system inductively coupled to an internal/implanted receiver is shown schematically. The system includes internal/implanted components comprising a receiver coil 910, a stimulator lead 60 (including lead body 62, proximal connector and distal nerve electrode 64). Any of the stimulation lead designs and external sensor designs described in more detail herein may be employed in this generically illustrated system, with modifications to position, orientation, arrangement, integration, etc. made as dictated by the particular embodiment employed. The system also includes external components comprising a transmit coil 912 (inductively linked to receiver coil 910 when in use), an external neurostimulator or external pulse generator 920 (ENS or EPG), and one or more external respiratory sensors 916/918.

[0288] As illustrated, the receiver coil 910 is implanted in a subcutaneous pocket in the pectoral region and the stimulation lead body 62 is tunneled subcutaneously along the platysma in the neck region. The nerve electrode 64 is attached to the hypoglossal nerve in the submandibular region.

[0289] The transmitter coil 912 may be held in close proximity to the receiver coil 910 by any suitable means such as an adhesive patch, a belt or strap, or an article of clothing (e.g., shirt, vest, brazier, etc.) donned by the patient. For purposes of illustration, the transmitter coil 912 is shown carried by a t-shirt 915, which also serves to carry the ENS

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920 and respiratory sensor(s) 916, 918. The ENS 920 may be positioned adjacent the waist or abdomen away from the ribs to avoid discomfort while sleeping. The respiratory sensor(s) 916, 918 may be positioned as a function of the parameter being measured, and in this embodiment, the sensors are positioned to measure abdominal and thoracic/chest expansion which are indicative of respiratory effort, a surrogate measure for respiration. The external components may be interconnected by cables 914 carried by the shirt or by wireless means. The shirt may incorporate recloseable pockets for the external components and the components may be disconnected from the cables such that the reusable components may be removed from the garment which may be disposed or washed.

[0290] The transmitting coil antenna 912 and the receiving coil antenna 910 may comprise air core wire coils with matched wind diameters, number of wire turns and wire gauge. The wire coils may be disposed in a disc-shaped hermetic enclosure comprising a material that does not attenuate the inductive link, such as a polymeric or ceramic material. The transmitting coil 912 and the receiving coil 910 may be arranged in a co-axial and parallel fashion for coupling efficiency, but are shown side-by-side for sake of illustration only.

[0291] Because power is supplied to the internal components via an inductive link, the internal components may be chronically implanted without the need for replacement of an implanted battery, which would otherwise require re-operation. Examples of inductively powered implantable stimulators are described in U.S. Patent No. 6,609,031 to Law et al., U.S. Patent No. 4,612,934 to Borkan, and U.S. Patent No. 3,893,463 to Williams, the entire disclosures of which are incorporated herein by reference.

[0292] With reference to Figures 51C – 51G, alternative embodiments of an external neurostimulator system inductively coupled to an internal/implanted receiver are schematically shown. These embodiments are similar to the external embodiment described above, with a few exceptions. In these embodiments, the receiver coil 910 is implanted in a positioned proximate the implanted stimulation lead body 62 and nerve electrode 64. The receiver coil 910 may be positioned in a subcutaneous pocket on the platysma muscle under the mandible, with the lead body 62 tunneling a short distance to the nerve electrode 64 attached to the hypoglossal nerve. Also in these embodiments, the respiratory sensor(s)

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916/918 may be integrated into the ENS 920 and attached to a conventional respiratory belt 922 to measure respiratory effort about the abdomen and/or chest. An external cable 914 connects the ENS 920 to the transmitter coil 912.

[0293] In the embodiment of Figure 51D, the transmitter coil 912 is carried by an adhesive patch 924 that may be placed on the skin adjacent the receiver coil 910 under the mandible. In the embodiment of Figure 51E, the transmitter coil 912 is carried by an under-chin strap 926 worn by the patient to maintain the position of the transmitter coil 912 adjacent the receiver coil 910 under the mandible. In the embodiment of Figure 51F, the receiver coil 910 may be positioned in a subcutaneous pocket on the platysma muscle in the neck, with the lead body 122 tunneling a slightly greater distance. The transmitter coil 912 may be carried by a neck strap 928 worn by the patient to maintain the position of the transmitter coil 912 adjacent the receiver coil 910 in the neck.

[0294] With reference to Figures 51G – 51K, additional alternative embodiments of an external neurostimulator system inductively coupled to an internal/implanted receiver are schematically shown. These embodiments are similar to the external embodiment described above, with a few exceptions. As above, the receiver coil 910 may be positioned in a subcutaneous pocket on the platysma muscle under the mandible, with the lead body 62 tunneling a short distance to the nerve electrode 64 attached to the hypoglossal nerve. However, in these embodiments, the ENS 920 (not shown) may be located remote from the patient such as on the night stand or headboard adjacent the bed. The ENS 920 may be connected via a cable 930 to a large transmitter coil 912 that is inductively coupled to the receiver coil 910. The respiratory sensor 916 may comprise a conventional respiratory belt 922 sensor to measure respiratory effort about the abdomen and/or chest, and sensor signals may be wirelessly transmitted to the remote ENS 920. As compared to other embodiments described above, the transmitter coil 912 is not carried by the patient, but rather resides in a proximate carrier such as a bed pillow, under a mattress, on a headboard, or in a neck pillow, for example. Because the transmitter coil 912 is not as proximate the receiver coil as in the embodiments described above, the transmitter coil may be driven by a high powered oscillator capable of generating large electromagnetic fields.

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[0295] As shown in Figure 51H, the transmitter coil 912 may be disposed in a bed pillow 934. As shown in Figure 51I, the transmitter coil 912 may comprise a series of overlapping coils disposed in a bed pillow 934 that are simultaneously driven or selectively driven to maximize energy transfer efficiency as a function of changes in body position of the patient corresponding to changes in position of the receiver coil 910. This overlapping transmitter coil arrangement may also be applied to other embodiments such as those described previously wherein the transmitter coil is carried by an article donned by the patient. In Figure 51J, two or more transmitter coils 912 are carried by orthogonal plates 936 arranged as shown to create orthogonal electromagnetic fields, thereby increasing energy transfer efficiency to compensate for movement of the patient corresponding to changes in position of the receiver coil 910. Figure 51J also illustrates a non-contact respiratory sensor 916 arrangement as utilized for detecting sudden infant death syndrome (SIDS). As shown in Figure 51K, two orthogonal transmitter coils 912 are located on each side of a neck pillow 938, which is particularly beneficial for bilateral stimulation wherein a receiver coil 910 may be located on either side of the neck.

[0296] With reference to Figures 51L (front view) and 51M (rear view), external respiratory effort sensors 916/918 are schematically shown incorporated into a stretchable garment 945 donned by the patient. The sensors 916/918 generally include one or more inductive transducers and an electronics module 942. The inductive transducers may comprise one or more shaped (e.g., zig-zag or sinusoidal) stranded wires to accommodate stretching and may be carried by (e.g., sewn into) the garment 945 to extend around the patient's abdomen and chest, for example. As the patient breathes, the patient's chest and/or abdomen expands and contracts, thus changing the cross-sectional area of the shape (i.e., hoop) formed by the wire resulting in changes in inductance. The electronics module may include an oscillator (LC) circuit with the inductive transducer (L) comprising a part of the circuit. Changes in frequency of the oscillator correspond to changes in inductance of the shaped wires which correlate to respiratory effort. The electronics module may be integrated with an ENS (not shown) or connected to an ENS via a wired or wireless link for triggering stimulus as described previously.

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[0297] The garment 945 may include features to minimize movement artifact and accommodate various body shapes. For example, the garment 945 may be form-fitting and may be sleeveless (e.g., vest) to reduce sensor artifacts due to arm movement. Further, the garment 945 may be tailored to fit over the patient's hips with a bottom elastic band which helps pull the garment down and keep the sensors 916/918 in the proper location.

[0298] **Description of a Specific External (Partially Implanted) Embodiment**

[0299] With reference to Figures 52A – 52G a specific embodiment utilizing an external neurostimulator system inductively coupled to an internal/implanted receiver is schematically shown. With initial reference to Figure 52A, the illustrated hypoglossal nerve stimulator includes several major components, namely: an implantable electronics unit that derives power from an external power source; a stimulation delivery lead that is anchored to the nerve or adjacent to the nerve and provides electrical connection between the electronics unit and the nerve, an external (non-implanted) power transmitting device that is inductively coupled with the implant to convey a powering signal and control signals; a power source for the external device that is either small and integrated into the body-worn coil and transmitter or is wired to the transmitter and transmit induction coil and can be powered by primary or secondary batteries or can be line powered; and a respiratory sensor such as those described previously.

[0300] These components may be configured to provide immediate or delayed activation of respiration controlled stimulation. Initiation of the stimulation regimen may be by means of activation of an input switch. Visual confirmation can be by an LED that shows adequate signal coupling and that the system is operating and is or will be applying stimulation. As a means of controlling gentleness of stimulation onset and removal, either pulse width ramping of a constant amplitude stimulation signal can be commanded or amplitude of a constant pulse width stimulation signal or a combination thereof can be performed.

[0301] The electrical stimulation signal is delivered by the stimulation lead that is connected to the implanted nerve stimulator and attached to or in proximity of a nerve. The implanted electronics unit receives power through a magnetically coupled inductive link. The operating carrier frequency may be high enough to ensure that several cycles (at least

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10) of the carrier comprise the output pulse. The operating frequency may be in a band of frequencies approved by governmental agencies for use with medical instruments operating at high transmitted radio frequency (RF) power (at least 100milliwatts). For example, the operating frequency may be 1.8MHz, but 13.56 MHz is also a good candidate since it is in the ISM (Industrial/ Scientific/ Medical) band. The non-implanted (external) transmitter device integrates respiration interface, waveform generation logic and transmit power driver to drive an induction coil. The power driver generates an oscillating signal that drives the transmitter induction coil and is designed to directly drive a coil of coil reactance that is high enough or can be resonated in combination with a capacitor. Power can come from a high internal voltage that is used to directly drive the transmit induction coil or power can come from a low voltage source applied to a tap point on the induction coil.

[0302] With reference to Figures 52B – 52E, the waveform generation logic may be used to modulate the carrier in such a way that narrow gaps in the carrier correspond to narrow stimulation pulses. When stimulator pulses are not needed, interruptions to the carrier are stopped but the carrier is maintained to ensure that power is immediately available within the stimulator upon demand. Presence or absence of electrical nerve stimulation is based on respiration or surrogates thereof. The transmitted signal may comprise a carrier of about 1.8MHz. To control the implanted electronics unit to generate individual nerve stimulation pulses, the carrier signal is interrupted. The duration of the interruption is about equal to the duration of the output stimulation pulse. The stimulation pulses may be about 110 microseconds in duration and are repeated at a rate of approximately 33 per second. In addition, multiple pulses can be transmitted to logic within the implant to control stimulation pulse amplitude, pulse width, polarity, frequency and structure if needed. Further, onset and removal of stimulation can be graded to manage patient discomfort from abruptness. Grading may comprise pulse width control, signal amplitude control or a combination thereof.

[0303] An indicator (not shown) may be used to show when the transmitter is properly positioned over the implant. The indicator may be a part of the transmitter or by way of communication with the transmitter, or a part of related patient viewable equipment. Determination of proper position may be accomplished by monitoring the transmitter power

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output loading relative to the unloaded power level. Alternatively, the implant receive signal level transmitted back by a transmitter within the implant may be monitored to determine proper positioning. Or, the implant receive signal level that is communicated back to the transmitter by momentarily changing the loading properties presented to the transmitter, such a shorting out the receive coil may be monitored to determine proper positioning. Such communication may be by means of modulation such as pulse presence, pulse width, pulse-to-pulse interval, multi-pulse coding.

[0304] The transmitter may be powered by an internal primary power source that is used until it is exhausted, a rechargeable power source or a power source wired to a base unit. In the case of the wired base unit, power can be supplied by any combination of battery or line power.

[0305] The respiration interface may transduce sensed respiratory activity to an on-off control signal for the transmitter. Onset of stimulation may be approximately correlated slightly in advance of inspiration and lasts through the end of inspiration, or onset may be based on anticipation of the next respiration cycle from the prior respiration cycle or cycles. The respiration sensor may comprise any one or combination of devices capable of detecting inspiration. The following are examples: one or more chest straps; an impedance sensor; an electromiographical measurement of the muscles involved with respiration; a microphone that is worn or is in proximity to the patients' face; a flow sensor; a pressure sensor in combination with a mask to measure flow; and a temperature sensor to detect the difference between cool inspired air versus warmed expired air.

[0306] The circuit illustrated in Figure 52F may be used for the implanted electronics unit. There are five main subsystems within the design: a receive coil, a power rectifier, a signal rectifier, an output switch and an output regulator. The signal from the inductive link is received by L1 which is resonated in combination with C1 and is delivered to both the power and signal rectifiers. Good coupling consistent with low transmitter coil drive occurs when the transmit coil diameter is equal to the receive coil diameter. When coil sizes are matched, coupling degrades quickly when the coil separation is about one coil diameter. A large transmit coil diameter will reduce the criticality of small coil spacing and

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coil-to-coil coaxial alignment for maximum signal transfer at the cost of requiring more input drive power.

[0307] The power rectifier may comprise a voltage doubler design to take maximum advantage of lower signal levels when the transmit to receive coil spacing is large. The voltage doubler operates with an input AC voltage that swing negative (below ground potential) causes D1 to conduct and forces C2 to the maximum negative peak potential (minus a diode drop). As the input AC voltage swings away from maximum negative, the node of C2, D1, D2 moves from a diode drop below ground to a diode drop above ground, forward biasing diode D2. Further upswing of the input AC voltage causes charge accumulated on C2 to be transferred through D2 to C3 and to "pump up" the voltage on C3 on successive AC voltage cycles. To limit the voltage developed across C3 so that an over-voltage condition will not cause damage, and Zener diode, D3 shunts C3. Voltage limiting imposed by D3 also limits the output of the signal rectifier section. The power rectifier has a long time constant, compared to the signal rectifier section, of about 10 milliseconds.

[0308] The signal rectifier section may be similar in topology to the power rectifier except that time constants are much shorter – on the order of 10 microseconds – to respond with good fidelity to drop-outs in the transmitted signal. There is an output load of 100K (R1) that imposes a controlled discharge time constant. Output of the signal rectifier is used to switch Q1, in the output switching section, on and off.

[0309] The output switching section compares the potential of C3 to that across C5 by means of the Q1, Q2 combination. When there is a gap in the transmitted signal, the voltage across C5 falls very rapidly in comparison with C3. When the voltage difference between C5 and C3 is about 1.4 volts, Q1 and Q2 turn on. Q1 and Q2 in combination form a high gain amplifier stage that provides for rapid output switching time. R3 is intended to limit the drive current supplied to Q2, and R2 aids in discharging the base of Q2 to improve the turn-off time.

[0310] In the output regulator section, the available power rectifier voltage is usually limited by Zener diode D3. When the coil separation becomes suboptimal or too large the power rectifier output voltage will be come variable as will the switched voltage available at the collector of Q2. For proper nerve stimulation, it may be necessary to

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regulate the (either) high or variable available voltage to an appropriate level. An acceptable level is about 3 volts peak. A switched voltage is applied to Zener diode D6 through emitter follower Q3 and bias resistor R5. When the switched voltage rises to a level where D6 conducts and develops about 0.6 volts across R4 and the base-emitter junction of Q4, Q4 conducts. o Increased conduction of Q4 is used to remove bias from Q3 through negative feedback. Since the level of conduction of Q4 is a very sensitive function of base to emitter voltage, Q4 provides substantial amplification of small variations in D6 current flow and therefore bias voltage level. The overall result is to regulate the bias voltage applied to Zener diode D6. Output is taken from the junction of the emitter of Q3 and D6 since that point is well regulated by the combination of Zener diode breakdown voltage combined with the amplification provided by Q4. In addition to good voltage regulation a the junction of the emitter of Q3 and D6, the output is very tolerant of load current demand since the conductivity of Q3 will be changed by shifts in the operating point of Q4. Due to amplification by Q3 and Q4, the circuit can drive a range of load resistances. Tolerable load resistances above 1000 ohms and less than 200 ohms. The regulator has the advantage of delivering only the current needed to operate the load while consuming only moderate bias current. Further, bias current is only drawn during delivery of the stimulation pulse which drops to zero when no stimulation is delivered. As a comparison, a simple series resistance biased Zener diode requires enough excess current to deliver a stimulation pulse and still maintain adequate Zener bias. As a further comparison, conventional integrated circuit regulators, such as three terminal regulators are not designed to well regulate and respond quickly to short input pulses. Experiment shows that three-terminal regulators exhibit significant output overshoot and ramp-up time upon application of an input pulse. This can be addressed by applying a constant bias to a regulator circuit or even moving the regulator before the output switching stage but this will be at the cost of constant current drain and subsequently reduced range.

[0311] The implanted electronics unit may be used to manage the loss of control and power signals. With this design, more than enough stimulation power is stored in C3 to supply multiple delivered stimulation pulses. This design is intended to ensure that the voltage drop is minimal on any individual pulse. One of the consequences is that when

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signal is lost, the circuit treats the condition as a commanded delivery of stimulation and will apply a single, extended duration, energy pulse until the full stored capacity of C3 is empty. An alternative method may be to use an indirect control modulation to command delivery of a nerve stimulation pulse through logic and provide for a time-out that limits pulse duration.

[0312] To stimulate tissue, a modified output stage may be used to mitigate electrode corrosion and establish balanced charging. The output stage is illustrated in Figure 52G and includes a capacitive coupling between the ground side of the stimulator and tissue interface in addition to a shunt from the active electrode to circuit ground for re-zeroing the output coupling capacitor when an output pulse is not being actively delivered.

[0313] **Description of Alternative Screening Methods**

[0314] Screening generally refers to selecting patients that will be responsive to the therapy, namely neurostimulation of the upper airway dilator nerves and/or muscles such as the hypoglossal nerve that innervates the genioglossus. Screening may be based on a number of different factors including level of obstruction and critical collapse pressure (Pcrit) of the upper airway, for example. Because stimulation of the hypoglossal nerve affects the genioglossus (base of tongue) as well as other muscles, OSA patients with obstruction at the level of the tongue base and OSA patients with obstruction at the level of the palate and tongue base (collectively patients with tongue base involvement) may be selected. Because stimulation of the hypoglossal nerve affects upper airway collapsibility, OSA patients with airways that have a low critical collapse pressure (e.g., Pcrit of less than about 5cm water) may be selected. Pcrit may be measured using pressure transducers in the upper airway and measuring the pressure just prior to an apnea event (airway collapse). Alternatively, a surrogate for Pcrit such as CPAP pressure may be used. In this alternative, the lowest CPAP pressure at which apnea events are mitigated may correlate to Pcrit.

[0315] The critical collapse pressure (Pcrit) may be defined as the pressure at which the upper airway collapses and limits flow to a maximal level. Thus, Pcrit is a measure of airway collapsibility and depends on the stability of the walls defining the upper airway as well as the surrounding pressure. Pcrit may be more accurately defined as the pressure

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inside the upper airway at the onset of flow limitation when the upper airway collapses. Pcrit may be expressed as:

[0316] Pcrit = Pin – Pout

[0317] where

[0318] Pin = pressure inside the upper airway at the moment of airway collapse; and

[0319] Pout = pressure outside the upper airway (e.g., atmospheric pressure).

[0320] Other screening methods and tools may be employed as well. For example, screening may be accomplished through acute testing of tongue protruder muscle contraction using percutaneous fine wire electrodes inserted into the genioglossus muscle, delivering stimulus and measuring one or more of several variables including the amount of change in critical opening pressure, the amount of change in airway caliber, the displacement of the tongue base, and/or the retraction force of the tongue (as measured with a displacement and/or force gauge). For example, a device similar to a CPAP machine can be used to seal against the face (mask) and control inlet pressure down to where the tongue and upper airway collapse and occlude during inspiration. This measurement can be repeated while the patient is receiving stimulation of the geneoglossus muscle (or other muscles involved with the patency of the upper airway). Patients may be indicated for the stimulation therapy if the difference in critical pressure (stimulated vs. non-stimulated) is above a threshold level.

[0321] Similarly, a flexible optical scope may be used to observe the upper airway, having been inserted through the mask and nasal passage. The difference in upper airway caliber between stimulation and non-stimulation may be used as an inclusion criterion for the therapy. The measurement may be taken with the inlet air pressure to the patient established at a pre-determined level below atmospheric pressure to better assess the effectiveness of the stimulation therapy.

[0322] Another screening technique involves assessing the protrusion force of the tongue upon anterior displacement or movement of the tongue with and without stimulation while the patient is supine and (possibly) sedated or asleep. A minimum increase in protrusion force while under stimulation may be a basis for patient selection.

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[0323] For example, with reference to Figure 53, a non-invasive oral appliance 530 may be worn by the patient during a sleep study that can directly measure the protrusion force of the tongue as a basis for patient selection. The oral appliance 530 may include a displacement probe 532 for measuring tongue movement protrusion force by deflection (D). The oral appliance 530 may also include a force sensor 534 for measuring the force (F) applied by protrusion of the tongue. The sensors in the displacement probe 532 and the force sensor 534 may be connected to measurement apparatus by wires 536.

[0324] Figure 54 illustrates another example of a non-invasive oral appliance 540 that may be worn by the patient during a sleep study to directly measure the protrusion force of the tongue as a basis for patient selection. The oral appliance 540 includes a displacement sensor 542 for measuring tongue movement and a force sensor for measuring tongue protrusion force. The displacement sensor and the force sensor may be connected to measurement apparatus by wires 546.

[0325] Oral appliances 530 and 540 could be worn during a sleep study and would measure the tongue protrusion force during (and just prior to) an apnea event when the protruder muscle tone is presumed to be inadequate to maintain upper airway patency. The protrusion force measured as the apnea is resolved by the patient will increase as the patient changes sleep state and the airway again becomes patent. The force difference may be used as a basis for patient selection.

[0326] Another screening technique involves the use of an oral appliance with sub-lingual surface electrodes contacting the base of the tongue or fine wire electrodes inserted into the genioglossus muscle to stimulate the tongue protruder muscle(s) synchronous with respiration during a sleep study. The oral appliance may be fitted with a drug delivery system (e.g., drug eluting coating, elastomeric pump, electronically controlled pump) for topical anesthesia to relieve the discomfort of the electrodes.

[0327] For example, with reference to Figure 55, an oral appliance 550 includes a pair of small needle intramuscular electrodes 552 that extend into the genioglossus. The electrodes 552 are carried by flexible wires 554 and may be coupled to an external pulse generator (not shown) by wires 556. The electrodes 552 may be supported by a drug (e.g., anesthetic) eluting polymeric member 558.

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[0328] Alternatively, with reference to Figure 56, an oral appliance 560 includes a cathode electrode 562 guarded by two anode electrodes 564 carried by a soft extension 565 that extends under the tongue. The surface electrodes 562 and 564 contact the floor of the mouth under the tongue to indirectly stimulate the genioglossus. The electrodes 562 and 564 may be coupled to an external pulse generator (not shown) by wires 566. The extension 565 may incorporate holes 568 through which a drug (e.g., anesthetic) may be eluted.

[0329] Oral appliances 550 and 560 may be used during a sleep study and stimulation of the target tissue can be performed synchronous with respiration and while inlet airflow pressure can be modulated. The ability to prevent apneas/hypopneas can be directly determined. Also the critical opening pressure with and without stimulation can be determined. Alternatively or in addition, the intramuscular or surface electrodes may be used to measure genioglossus EMG activity, either with or without stimulation. On any of theses bases, patient selection may be made.

[0330] Patient selection may also be applied to the respiratory sensors to determine if the respiratory sensors will adequately detect respiration for triggering stimulation. For example, in the embodiment wherein bio-Z is used to detect respiration using an implanted lead 70, skin surface or shallow needle electrodes may be used prior to implantation to determine if the signal will be adequate. This method may also be sued to determine the preferred position of the electrodes (i.e., optimal bio-Z vector). This may be done while the patient is sleeping (i.e., during a sleep study) or while the patient is awake.

[0331] **Description of Alternative Intra-operative Tools**

[0332] Intra-operatively, it may be desirable to determine the correct portion of the nerve to stimulate in order to activate the correct muscle(s) and implant the nerve cuff electrode accordingly. Determining the correct position may involve stimulating at different locations along the length or circumference of the nerve and observing the effect (e.g., tongue protrusion). In addition or in the alternative, and particularly in the case of field steering where multiple combinations of electrode contacts are possible, it may be desirable to determine optimal electrode or filed shape combinations.

[0333] An example of an intra-operative stimulating tool 570 is shown in Figures 57A and 57B. In this embodiment, the tool 570 includes a first shaft 571 with a distal half-

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cuff 573. Tool 570 further includes a second shaft 575 with a proximal movable collar 574 and a distal half-cuff 575. Stimulating tool 570 includes multiple electrodes 572 on half-cuff 573 and/or half-cuff 575 that may be arranged in an array or matrix as shown in Figure 57C, which is a view taken along line A-A in Figure 57B. The half-cuffs 573 and 575 may be longitudinally separated for placement about a nerve and subsequently closed such that the half-cuffs 573 and 575 gently grasp the nerve. The electrodes 575 may be sequenced through a series of electrode/field shape combinations to optimize (lower) the critical opening pressure, airway caliber, tongue protrusion force or other acute indicia of therapeutic efficacy.

[0334] The tool 570 may be part of an intra-operative system including: (1) tool 570 or other tool with one or more stimulating electrodes that are designed to be easily handled by the surgeon during implant surgery; (2) an external pulse generator which triggers off of a respiration signal; (3) a feedback diagnostic device that can measure critical closing pressure intra-operatively; and (4) an algorithm (e.g., firmware or software in the programmer) that is design to automatically or manually sequence through a series of electrode configurations that will identify the best placement of electrode cuffs on the nerves and configuration of electrode polarity and amplitude settings. Information from the intra-operative system may greatly speed the process of identifying where to place the electrode cuff(s) on the hypoglossal nerve and what field steering may be optimal or necessary to provide efficacy.

[0335] In certain circumstances, such as, when treating a child or a small adult, it may be difficult to implant a nerve cuff electrode of the present disclosure about a nerve in a patient's body. Accordingly, it may be desirable to provide a tool capable of facilitating temporary expansion of a nerve cuff electrode of the present disclosure, so as to slip the nerve cuff electrode around a patient's nerve. Turning now to Figures 58A-58B, there is depicted a tool 5800 for temporarily expanding a nerve cuff electrode in accordance with the principles of the present disclosure. Tool 5800 may include a substantially scissor-like configuration having a first element 5801 and a second element 5802 pivotably secured together by a suitable fastener, such as, for example, pivot pin 5803, acting as a fulcrum. Elements 5801 and 5802 may be substantially similar to each other or may differ as

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necessary. In the depicted embodiment, elements 5801 and 5802 may include levers having distal effecting portions 5804, 5805 and proximal actuating portions 5806, 5807.

[0336] Proximal actuating portions 5806, 5807 may be of any suitable length and may be connected to respective handles (not shown), which may be used to operate tool 5800. Alternatively, proximal actuating portions 5806, 5807 themselves may be used to operate tool 5800. Distal effecting portions 5804, 5805 may include any suitable configuration to achieve the desired effect. For example, each portion 5804, 5805 may include a substantially curved configuration. Additionally, a distal end of each portion 5804, 5805 may be provided with a fastening mechanism, such as, for example, hook-like projection 5804a, 5805a, for facilitating connection of tool 5800 to a nerve cuff electrode. As shown in Figures 58A-58B, hook-like projections 5804a, 5805a may be configured to be disposed in differing parallel planes, such that projections 5804a, 5805a may be spaced (offset) horizontally from one another. In use, distal effecting portions 5804, 5805 may be opened and closed as proximal actuating portions 5806, 5807 may be rotated about pivot pin 5803.

[0337] In embodiments where tool 5800 may be used to temporarily expand a nerve cuff electrode for implantation purposes, the nerve cuff electrode, e.g., nerve cuff electrode 5810, may be provided with one more geometric configurations for facilitation connection with tool 5800. In the depicted embodiment, nerve cuff electrode 5810 may be provided with extensions 5811, 5812 for facilitating connection with tool 5800. Each extension 5811, 5812 may be provided with openings 5811a, 5812a, respectively, for receiving hook-like projections 5804a, 5805a, so as to operably couple nerve cuff electrode 5811 with tool 5800.

[0338] **Description of Miscellaneous Alternatives**

[0339] The implanted neurostimulation system may be configured so that stimulation of the nerve is set at a relatively low level (i.e., low voltage amplitude, narrow pulse width, lower frequency) so as to maximize battery life of the INS and to minimize the chances that the electrical stimulation will cause arousal from sleep. If apneas/hypopneas are detected, then the electrical stimulation can be increased progressively until the apneas/hypopneas are no longer detected, up to a maximum pre-set stimulation level. This

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auto titration may automatically be reset to the low level after the patient is awakened and sits up (position detector) or manually reset using the patient controller. The stimulation level may be automatically reduced after a period of time has elapsed with no (or few) apneas/hypopneas detected.

[0340] The stimulation level (i.e., voltage amplitude, pulse width, frequency) may be adjusted based on changes in respiration rate. Respiration rate or patterns of rate change may be indicative of sleep state. A different power level based on sleep state may be used for minimal power consumption, minimal unwanted stimulation (sensory response), etc., while providing adequate efficacy.

[0341] The electrical field shape used to stimulate the target nerve can be changed while the system is proving therapy based on feedback indicating the presence (or lack) of apneas/hypopneas. The electrical field shape for an implanted system can be changed by adjusting the polarity, amplitude and other stimulation intensity parameters for each of the electrodes within the nerve stimulating cuff. An algorithm within the INS may change the currently operating electrical field shape if the presence of apneas/hypopneas is detected, and then wait a set period of time to determine if the new configuration was successful in mitigating the apneas/hypopneas before adjusting the field shape again. Additionally, the system may be designed to keep a log of the most successful stimulation patterns and when they were most likely to be effective. This may allow the system to "learn" which settings to be used during what part of the night, for example, or with specific breathing patterns or cardiac signal patterns or combinations thereof.

[0342] The proportion of stimulation intensity of two electrode cuffs used to stimulate a nerve can be modulated while the system is providing therapy based on feedback indicating the presence (or lack) of apneas/hypopneas. For example, one nerve stimulating electrode cuff may be place on the more proximal section of the hypoglossal nerve, while a second is placed more distally. The proximal cuff will be more likely to stimulate branches of the hypoglossal nerve going to muscles in the upper airway involved with tongue or hyoid retrusion while the more distal electrode cuff will more likely stimulate only the muscles involved with tongue/hyoid protrusion. Research suggests that to best maintain upper airway patency, stimulating both protrudes and retruders (in the right

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proportion) may be more effective that stimulating protruders alone. Software within the INS may change the currently operating proportion of electrical stimulation going to the distal electrode cuff in proportion to that going to the proximal cuff based on the presence of apneas/hypopneas detected. The system may then wait a set period of time to determine if the new configuration was successful in mitigating the apneas/hypopneas before adjusting the system again. Additionally, the system software may be designed to keep a log of the most successful stimulation proportion and when they were most likely to be effective. This may allow the system to "learn" which settings to be used during what part of the night, for example, or with specific breathing patterns or cardiac signal patterns or combinations thereof.

[0343] The system described above may modulate electrical stimulation intensity proportion based on electromyogram (EMG) feedback from the muscles in the upper airway being stimulated or others in the area. This feedback may be used to determine the correct proportion of stimulation between protruders and retruders. The correct ratio of EMG activity between retruders and protruders may be determined during a sleep study for an individual, may be determined to be a constant for a class of patients or may be "learned" my the implanted system by using the detection of apneas/hypopneas as feedback.

[0344] A library of electrical stimulation parameter settings can be programmed into the INS. These settings listed in the library may be selected by the patient manually using the patient programmer based on, for example: (1) direct patient perception of comfort during stimulation; (2) a log of the most successful settings compiled by the software in the INS (assumes apnea/hypopnea detection capability); (3) a sleep physician's or technician's assessment of the most effective stimulation as determined during a sleep study; and/or (4) a list of the most effective parameters produced for a particular class of patient or other.

[0345] The electrical stimulation parameters described above may be adjusted based on patient position as detected by a position sensor within the INS. The best setting for a given position may be determined by, for example: (1) a log of the most successful settings compiled or learned by the software in the INS (assumes apnea/hypopnea detection capability); (2) a sleep physician's or technician's assessment of the most effective

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stimulation as determined during a sleep study; and/or (3) a list of the most effective parameters produced for a particular class of patient or other.

[0346] To avoid fatigue using a normal duty cycle or to extend the time that the upper airway is opened through neurostimulation, different parts of the genioglossus muscle and/or different muscles involved with establishing patency of the upper airway can be alternately stimulated. For example, using two or more nerve or muscle electrode cuffs, the left and right side genioglossus muscles can be alternately stimulated, cutting the effective duty cycle on each muscle in half. In addition, different protruder muscles on the ipsilateral side such as the geniohyoid and the genioglossus muscle can be alternately stimulated to the same effect. This may also be accomplished through one electrode cuff using field steering methods that selectively stimulated the fascicles of the hypoglossal nerve going to one group of protruders alternating with stimulating the fascicles leading to a different protruder muscle group. This method may also be used to alternately stimulate one group of muscle fibers within the genioglossus muscle with the compliment of muscle fibers in the same muscle group.

[0347] To increase the ability of the upper airway to open during a (sensed) apnea/hypopnea through neurostimulation, different parts of the genioglossus muscle and/or different muscles involved with establishing patency of the upper airway can be simultaneously stimulated. For example, using two or more nerve or muscle electrode cuffs, the left and right side genioglossus muscles can be simultaneously stimulated, greatly increasing the protrusion forces. In addition, different protruder muscles on the ipsilateral side such as the geneohyoid and the genioglossus muscle can be simultaneously stimulated to the same effect. This may also be accomplished through one electrode cuff using field steering methods that selectively stimulated the fascicles of the hypoglossal nerve going to one group of protruders simultaneously with stimulating the fascicles leading to a different protruder muscle group. This may be achieved with one electrode cuff using field steering on a more proximal location on the hypoglossal nerve or two or more electrode cuffs, one on each branch going to a muscle involved with maintaining muscle patency.

[0348] A sensor inside the INS (or elsewhere in system implanted) may detect body position and automatically shut off stimulation when patient sits up or stands up. This will

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prevent unwanted stimulation when patient is no longer sleeping. The device may automatically restart the stimulation after the sensor indicates the patient is again horizontal, with or without a delay. The system may also be configured so that the stimulation can only be restarted using the patient controller, with, or without a delay.

[0349] The respiration signal using impedance and/or EMG/ENG are easily capable of determining heart rate. The stimulation may be interrupted or turned off when the heart rate falls outside out a pre-determined acceptable range. This may be an effective safety measure that will decrease the chance that hypoglossal nerve stimulation will interfere with mitigating physiological processes or interventional emergent medical procedures.

[0350] Respiration waveforms indicating apneas/hypopneas or of other clinical interest may be recorded and automatically telemetered to a bed-side receiver unit or patient programmer. Respiration waveforms indicating frequent apneas/hypopneas, abnormal breathing patterns, irregular heart rate/rhythm may be recorded and automatically telemetered to a bed-side deceiver unit or patient programmer causing an alarm to be issued (audible/visible). The INS status such as low battery or system malfunction may also trigger an alarm.

[0351] Electrical stimulation intensity could be ramped up for each respiration cycle by increasing amplitude or pulse width from 0 to a set point to prevent sudden tongue protrusion or sudden airway opening causing the patient to wake up. During inspiration, the system may deliver approximately 30 pulses per second for a length of time of one to one and one half seconds, totaling between about 30 and 45 pulses per respiration cycle. Prior to delivery of these 30 to 45 pulses, amplitude of each individual therapy pulse (in an added group of pulses) could be ramped up from 0 to a set point at a rate of < 10% of the amplitude intended for the active duty cycle or 200 mS, whichever is less. The pulse width of each individual therapy pulse could be ramped up from 0 to a set point at a rate of <10% of the active duty cycle or 200 mS, whichever is less. Each of these ramp methods would require a predictive algorithm that would stimulate based on the previous inspiration cycle.

[0352] Nerves innervating muscles that are involved with inspiration, such as the hypoglossal nerve, have been shown to have greater electrical activity during apnea or hypopnea. This signal cannot be easily measured while simultaneously stimulating the same

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nerve. One method of stimulating and sensing using the same lead is to interleave a sensing period within the stimulation pulse bursts during the duty cycle. In other words, the sensing period may occur between pulses within the stimulation pulse train. This approach may be used with electrodes / leads that directly stimulate and alternately sense on a nerve involved with inspiration or on a muscle involved with inspiration or a combination of the two. The approach may allow sensing of apnea/hypopnea, as well as therapeutic stimulation.

[0353] From the foregoing, it will be apparent to those skilled in the art that the present invention provides, in exemplary non-limiting embodiments, devices and methods for nerve stimulation for OSA therapy. Further, those skilled in the art will recognize that the present invention may be manifested in a variety of forms other than the specific embodiments described and contemplated herein. Accordingly, departures in form and detail may be made without departing from the scope and spirit of the present invention as described in the appended claims.

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WHAT IS CLAIMED IS:

1. A stimulation lead having a distal electrode configured for attachment to a nerve, the lead comprising:

a lead body including a proximal portion and a distal portion, the proximal portion configured to be connected to a pulse generator and the distal portion connected to the distal electrode, wherein the proximal portion includes a first flexibility and the distal portion includes a second flexibility different from the first flexibility; and

an anchoring portion operably connected to the proximal portion and the distal portion between the proximal portion and the distal portion, the anchoring portion configured for attachment to tissue to relieve stress applied to the electrode by movements of a patient.

2. The stimulation lead of claim 1, wherein the distal portion is more flexible than the proximal portion.

3. The stimulation lead of claim 1, wherein the lead body includes a lumen containing a plurality of conductors.

4. The stimulation lead of claim 3, wherein the plurality of conductors include braided conductors coiled along a longitudinal axis of the lead.

5. The stimulation lead of claim 1, wherein the anchoring portion is adapted to be sutured to the tissue.

6. The stimulation lead of claim 1, wherein the lead body includes a sigmoid shape having a plurality of flexible undulations disposed in a plane.

7. A method of manufacturing a sigmoid shaped lead body of a chronically implantable stimulation lead, the method comprising:

extruding silicone in a semi cross-linked state;

placing the semi cross-linked extruded silicone in a sigmoid-shaped mold; and

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allowing the semi cross-linked extruded silicone to become fully cross-linked.

8. The method of claim 7, wherein an oven is used facilitate converting the semi cross-linked extruded silicone to fully cross-linked silicone.

9. The method of claim 7, wherein the lead body defines a lumen therein.

10. The method of claim 7, wherein the semi-cured silicone is extruded in a substantially straight configuration.

11. A chronically implantable stimulation lead comprising:

a lead body having a plurality of undulations for accommodating deflection of the lead body when the lead body is subjected to stresses imparted by a patient's body movements, wherein the lead body is configured to elongate by approximately 40% from an initial unstressed state, and bend by approximately 15% about a bend radius of approximately 1 centimeter, for at least 300,000 cycles.

12. The chronically implantable stimulation lead of claim 11, wherein the lead body includes a sigmoid shape.

13. A method of stimulating a hypoglossal nerve, the method comprising:

implanting a plurality of electrode contacts proximal the hypoglossal nerve, wherein the plurality of electrode contacts include a cathode electrode contact disposed in between two anode electrode contacts, the first anode electrode contact being spaced from the cathode electrode contact by a first distance, and the second anode electrode contact being spaced from the cathode electrode contact by a second distance larger than the first distance.

14. The method of claim 13, wherein efferent fibers of the hypoglossal nerve are stimulated while afferent fibers of the hypoglossal nerve are not stimulated.

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15. The method of claim 13, wherein the second distance is approximately two to three times larger than the first distance.

16. The method of claim 13, wherein the first anode electrode contact is disposed distally of the cathode electrode contact, and the second anode electrode contact is disposed proximally of the cathode electrode contact.

17. The method of claim 16, wherein efferent fibers of the hypoglossal nerve are stimulated while afferent fibers of the hypoglossal nerve are not stimulated.

18. A method of stimulating a superior laryngeal nerve, the method comprising:

implanting a plurality of electrode contacts proximal the superior laryngeal nerve, wherein the plurality of electrode contacts include a cathode electrode contact disposed in between two anode electrode contacts, the first anode electrode contact being spaced from the cathode electrode contact by a first distance, and the second anode electrode contact being spaced from the cathode electrode contact by a second distance larger than the first distance.

19. The method of claim 18, wherein afferent fibers of the superior laryngeal nerve are stimulated while efferent fibers of the superior laryngeal nerve are not stimulated.

20. The method of claim 18, wherein the second distance is approximately two to three times larger than the first distance.

21. The method of claim 18, wherein the first anode electrode contact is disposed proximally of the cathode electrode contact, and second anode electrode contact is disposed distally of the cathode electrode contact.

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22. The method of claim 21, wherein afferent fibers of the superior laryngeal nerve are stimulated while efferent fibers of the superior laryngeal nerve are not stimulated.

23. A method of selectively stimulating fibers of a hypoglossal nerve, the method comprising:

implanting a nerve cuff electrode on the hypoglossal nerve, the nerve cuff electrode including a plurality of serially disposed, spaced electrode contacts, wherein the nerve cuff electrode is configured to stimulate relatively small diameter fibers of the hypoglossal nerve when a first combination of the plurality of serially disposed electrode contacts is activated, and wherein the nerve cuff electrode is configured to stimulate relatively large diameter fibers of the hypoglossal nerve when a second combination of the plurality of serially disposed electrode contacts is activated.

24. The method of claim 23, wherein a distance between adjacent electrode contacts of the second combination is greater than a distance between adjacent electrode contacts of the first combination.

25. The method of claim 23, wherein the electrode contacts of the nerve cuff electrode are configured to switch between an anode electrode contact and a cathode electrode contact.

26. The method of claim 23, wherein the nerve cuff electrode is configured to stimulate afferent fibers of the hypoglossal nerve when the first combination is activated, and wherein the nerve cuff electrode is configured to stimulate efferent fibers of the hypoglossal nerve when the second combination is activated

27. A method of selectively stimulating afferent or efferent fibers of the superior laryngeal nerve, the method comprising:

implanting a nerve cuff electrode proximal the superior laryngeal nerve, the nerve cuff electrode including a plurality of serially disposed, spaced electrode contacts, wherein

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the nerve cuff electrode is configured to stimulate relatively small diameter fibers of the superior laryngeal nerve when a first combination of the plurality of serially disposed electrode contacts is activated, and wherein the nerve cuff electrode is configured to stimulate relatively large diameter fibers of the superior laryngeal nerve when a second combination of the plurality of serially disposed electrode contacts is activated.

28. The method of claim 27, wherein a distance between adjacent electrode contacts of the second combination is greater than a distance between adjacent electrode contacts of the first combination.

29. The method of claim 27, wherein the electrode contacts of the nerve cuff electrode are configured to switch between an anode electrode contact and a cathode electrode contact.

30. The method of claim 27, wherein the nerve cuff electrode is configured to stimulate afferent fibers of the superior laryngeal nerve when the first combination is activated, and wherein the nerve cuff electrode is configured to stimulate efferent fibers of the superior laryngeal nerve when the second combination is activated.

31. A method of electrically stimulating a patient's hypoglossal nerve having relatively small and relatively large diameter fibers, the method comprising:

implanting a plurality of electrode contacts adjacent the hypoglossal nerve;

delivering a saturation pulse to the electrode contacts to substantially saturate the relatively large diameter fibers of the nerve; and

delivering a stimulation pulse to the electrode contacts to stimulate the relatively small diameter fibers of the nerve, wherein the stimulation pulse has an amplitude that is larger than the saturation pulse.

32. The method of claim 31, wherein the stimulation pulse has a shorter duration than the saturation pulse.

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33. The method of claim 31, wherein the saturation pulse is delivered approximately 0.5 ms before delivery of the stimulation pulse.

34. The method of claim 31, wherein delivering the stimulation pulse does not stimulate the relatively large diameter fibers.

35. A method of electrically stimulating a patient's superior laryngeal nerve having efferent and afferent fibers, the method comprising:

implanting a plurality of electrode contacts adjacent the superior laryngeal nerve;

delivering a saturation pulse to the electrode contacts to substantially saturate the efferent fibers of the nerve; and

delivering a stimulation pulse to the electrode contacts to stimulate the afferent fibers of the nerve, wherein the stimulation pulse has an amplitude that is larger than the saturation pulse.

36. The method of claim 35, wherein the stimulation pulse has a shorter duration than the saturation pulse.

37. The method of claim 35, wherein the saturation pulse is delivered approximately 0.5 ms before delivery of the stimulation pulse.

38. The method of claim 35, wherein delivering the stimulation pulse does not stimulate the relatively large diameter fibers.

39. A method of treating obstructive sleep apnea, the method comprising:

chronically implanting an electrode on a cranial root of a patient's cranial nerve XI proximal of a portion innervating a levator veli palatini muscle of a patient's soft palate; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, to the nerve via the electrode to mitigate obstruction of an upper airway of the patient.

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40. The method of claim 39, wherein delivering the stimulus elevates the patient's soft palate.

41. The method of claim 39, wherein delivering the stimulus includes selectively stimulating only fibers of the nerve that innervate the levator veli palatini muscle.

42. A method of treating obstructive sleep apnea, the method comprising:

chronically implanting an electrode on a cranial root of a patient's cranial nerve XI proximal of a portion innervating a palatoglossal muscle of a patient; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, to the nerve via the electrode to mitigate obstruction of an upper airway of the patient.

43. The method of claim 42, wherein delivering the stimulus pulls the soft palate inferiorly.

44. The method of claim 42, wherein delivering the stimulus includes selectively stimulating only fibers of the nerve that innervate the palatoglossal muscle.

45. A method of treating obstructive sleep apnea, the method comprising:

chronically implanting an electrode on a patient's glossopharyngeal nerve proximal of a portion innervating a stylopharyngeus muscle of a patient; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, to the nerve via the electrode to mitigate obstruction of an upper airway of the patient.

46. The method of claim 45, wherein delivering the stimulus includes selectively stimulating only fibers of the nerve that activate the stylopharyngeus muscle.

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47. The method of claim 45, wherein delivering the stimulus dilates the lateral walls of the pharynx.

48. A method of treating obstructive sleep apnea, the method comprising:

chronically implanting an electrode on a patient's superior laryngeal nerve proximal a portion innervating sensory fibers capable of triggering a reflex causing dilation of an upper airway; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, to the nerve via the electrode to mitigate obstruction of an upper airway of the patient.

49. The method of claim 118, wherein delivering the stimulus includes electrically stimulating only the sensory fibers of the nerve.

50. A method of treating obstructive sleep apnea, the method comprising:

implanting an electrode on a nerve innervating an upper airway dilator muscle;

monitoring respiration based on a sensed bio-impedance parameter using an implanted bio-impedance sensor, wherein the bio-impedance sensor includes an electrode array having a plurality of electrodes positioned translaterally across a patient's thoracic cavity; and

periodically delivering a stimulus, based on the sensed bio-impedance parameter, to the nerve via the electrode to mitigate obstruction of a patient's upper airway.

51. A method of selecting between electrodes for measuring bio-impedance, the method comprising:

providing first, second, and third electrodes spaced from each other;

chronically implanting the electrodes;

measuring a first bio-impedance between the first and second electrodes;

measuring a second bio-impedance between the second and third electrodes;

comparing the first and second bio-impedance measurements; and

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selecting one of either the first and the second bio-impedance measurements as a preferred indicator of respiration.

52. The method of claim 51, wherein the second electrode is spaced from the first electrode by a first distance, the second electrode is spaced from the third electrode by a second distance, and the first electrode is spaced from the third electrode by a third distance larger than both the first distance and the second distance.

53. The method of claim 52, further comprising measuring bio-impedance between the first and third electrodes if the bio-impedance measured between the first and second electrodes and between the second and third electrodes are not adequate indicators of the patient's respiration.

54. A method of selecting between electrodes for measuring bio-impedance, the method comprising:

providing first, second, and third electrodes spaced from each other;

chronically implanting the electrodes;

measuring a first bio-impedance between the first and second electrodes;

measuring a second bio-impedance between the second and third electrodes;

comparing the first and second bio-impedance measurements; and

selecting the second bio-impedance measurements as a preferred indicator of respiration if the first bio-impedance measurement is not an adequate indicator of respiration.

55. A method of selecting between electrodes for measuring bio-impedance, the method comprising:

providing first, second, and third electrodes spaced from each other;

chronically implanting the electrodes;

measuring a first bio-impedance between the first and second electrodes;

measuring a second bio-impedance between the second and third electrodes;

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comparing the first and second bio-impedance measurements; and

switching to the second bio-impedance measurement as a preferred indicator of respiration when the first bio-impedance is no longer an adequate indication of respiration.

56. A method of selecting between electrodes for measuring bio-impedance, the method comprising:

providing first, second, and third electrodes spaced from each other;

chronically implanting the electrodes;

measuring a first bio-impedance between the first and second electrodes;

measuring a second bio-impedance between the second and third electrodes;

measuring a third bio-impedance between the first and third electrodes

comparing the first, second, and third bio-impedance measurements;

selecting one of the first, second, and third bio-impedance measurements as a preferred indicator of respiration;

scanning the first, second, and third bio-impedance measurements for a secondary indicator of respiration, before the bio-impedance measurement selected as the preferred indicator of respiration becomes an inadequate indicator of respiration; and

selecting the bio-impedance measurement designated the secondary indicator of respiration if the bio-impedance measurement designated as the preferred indicator of respiration is not an adequate indicator of respiration.

57. A method of selecting a vector producing a signal adequate to be an indicator of respiration, the method comprising:

sampling a plurality of short distance vectors first to determine if any of the short distance vectors are producing a signal sufficiently adequate to be an indicator of respiration, wherein a short distance vector includes a path between two electrodes spaced by a first distance;

sampling a plurality of intermediate distance vectors if the short distance vectors are not producing a signal sufficiently adequate to be an indicator of respiration, wherein

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intermediate distance vector includes a path between two electrodes spaced by a second distance larger than the first distance; and

sampling a plurality of long distance vectors if the intermediate distance vectors are not producing a signal sufficiently adequate to be an indicator of respiration, wherein a long distance vector includes a path between a two electrodes spaced by a third distance larger than the second distance.

58. The method of claim 57, further comprising:

selecting a vector producing a signal sufficiently adequate to be an indicator of respiration; and

stimulating nerve innervating an upper airway dilator muscle via a chronically implanted an electrode on the nerve.

59. A method of switching between a plurality of sensed signals, the method comprising:

providing a plurality of sensed signals to a channel selection switch;

identifying a plurality of fiducials for each of the plurality of sensed signals;

analyzing the fiducials of each of the plurality of sensed signals to determine which of the sensed signals is the best indicator of a patient's respiration;

identifying the sensed signal that is the best indicator of a patient's respiration as a primary signal;

storing the identified fiducials for at least the signals not identified as the primary signal;

analyzing the stored fiducials to determine if any of the signals not identified as the primary signal are a better indicator of a patient's respiration than the primary signal;

identifying the signal that is the better indicator of a patient's respiration as the secondary signal; and

switching to the secondary signal for respiration detection.

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60. The method of claim 59, wherein each of the plurality of sensed signals is a bio-impedance measurement.

61. A method of monitoring a chronically implanted stimulation lead, the method comprising:

providing an implantable electrical stimulator having an impedance sensing circuit for sensing a parameter indicative of respiration;

providing an impedance sensor connected to the impedance sensing circuit;

providing a stimulation lead connected to the stimulator, the stimulation lead including a distal electrode;

providing a switching circuit operably coupled to the impedance sensing circuit; and

via the switching circuit, selectively coupling the impedance sensing circuit to the stimulation lead.

62. The method of claim 61, wherein the impedance sensing circuit measures an impedance within the stimulation lead.

63. The method of claim 61, wherein the impedance sensing circuit measures a tissue impedance at the distal electrode.

64. A device for treating obstructive sleep apnea, comprising:

a chronically implantable lead with a distally disposed electrode;

a chronically implantable neurostimulator operably connected to the lead;

a chronically implantable respiratory sensor operably connected to the neurostimulator; and

a patient controller for adjusting a functionality of the device, wherein the patient controller includes an alarm clock.

65. An electrode for delivering an electrical stimulation to a tissue, the electrode comprising:

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a body configured to be disposed substantially adjacent the tissue;

a plurality of electrodes disposed on the body and configured to be in electrical communication with the tissue, wherein one of the plurality of electrodes is configured to deliver a charge density that is different from a charge density of the remaining plurality of electrodes, when each of the plurality of electrodes is subjected to substantially the same stimulation pulse.

66. The method of claim 65, wherein the charge density of the one electrode is higher than the charge density of the remaining plurality of electrodes.

67. The method of claim 65, wherein the charge density of the one electrode is lower than the charge density of the remaining plurality of electrodes.

68. The method of claim 65, wherein the one electrode includes a surface area that is different from the remaining plurality of electrodes.

69. The method of claim 65, wherein the one electrode includes a material having a conductance different from a conductance of a material of the remaining plurality of electrodes.

70. A method of treating obstructive sleep apnea, the method comprising:

chronically implanting an electrode on a nerve innervating an upper airway dilator muscle;

sensing a measure of respiration for a plurality of respiratory cycles including inspiratory and expiratory phases;

identifying the respiratory cycle period;

analyzing the measure of respiration to identify the onset of the expiratory phase for each respiratory cycle;

predicting the onset of a future expiratory phase; and

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beginning stimulation of the nerve a fraction of a respiratory cycle period before the onset of the future expiratory phase.

71. The method of claim 70, wherein the fraction ranges between $\frac{30}{100}$ and $\frac{50}{100}$.

72. The method of claim 70, wherein fraction is selectively adjustable.

73. The method of claim 70, wherein the measure of respiration is bio-impedance.

74. A method of treating obstructive sleep apnea, the method comprising:

obtaining a respiration waveform for a respiratory cycle including inspiratory and expiratory phases;

identifying the respiratory cycle period;

identifying the onset of the expiratory phase for the respiratory cycle;

predicting the onset of a future expiratory phase; and

stimulating a nerve to cause dilation of a patient's upper airway, wherein stimulation of the nerve begins a fraction of a respiratory cycle period before the onset of the future expiratory phase.

75. The method of claim 74, wherein fraction is selectively adjustable.

76. The method of claim 74, wherein identifying the onset of the expiratory phase includes identifying a peak of the respiration waveform.

77. A method of treating obstructive sleep apnea, comprising:

chronically implanting an electrode on a nerve innervating an upper airway dilator muscle;

obtaining a respiration signal;

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providing a signal to the electrode at a rate to stimulate the patient's nerve, based on the obtained respiration signal;

determining that the respiration signal has experienced a loss; and

continuing stimulation of the nerve at substantially the rate before the respiratory signal was lost.

78. A method of treating obstructive sleep apnea, comprising:

chronically implanting an electrode on a nerve innervating an upper airway dilator muscle;

obtaining a respiration signal;

providing a signal to the electrode at a rate to stimulate the patient's nerve, based on the obtained respiration signal;

determining that the respiration signal has experienced a loss; and

continuing stimulation of the nerve at a rate that is a fraction of the rate before the respiratory signal was lost.

79. A method of treating obstructive sleep apnea, comprising:

chronically implanting an electrode on a hypoglossal nerve at a site to stimulate a tongue protruder muscle and a tongue retruder muscle; and

periodically delivering a stimulus to the nerve via the electrode to mitigate obstruction of the upper airway,

wherein the stimulus is configured to selectively activate the tongue protruder muscle more than or before the tongue retruder muscle.

80. A method as in claim 79, wherein stimulus is triggered based on a sensed parameter indicative of respiration.

81. A method as in claim 79, wherein electrical filed steering is used for selective activation.

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82. A method of treating obstructive sleep apnea, comprising:

chronically implanting a first electrode cuff on a hypoglossal nerve at a first site to stimulate a tongue protruder muscle;

chronically implanting a second electrode on the hypoglossal nerve at a second site, proximal of the first site, to stimulate a tongue retruder muscle; and

periodically delivering a stimulus to the first and second nerve sites via the electrodes to mitigate obstruction of the upper airway.

wherein the stimulus is configured to selectively activate the tongue protruder muscle more than or before the tongue retruder muscle.

83. A method as in claim 82, wherein stimulus is triggered based on a sensed parameter indicative of respiration.

84. A method of treating obstructive sleep apnea as in claim 82, wherein the stimulus is configured to selectively activate the tongue protruder muscle more than or before the tongue retruder muscle.

85. A method of treating obstructive sleep apnea, comprising:

chronically implanting a first electrode on a hypoglossal nerve;

chronically implanting a second electrode on an ansa cervicalis nerve; and

periodically delivering a stimulus to the nerves via the electrodes to mitigate obstruction of the upper airway.

86. A method of treating obstructive sleep apnea, comprising:

chronically implanting a first electrode on a first nerve;

chronically implanting a second electrode on a second nerve, different from the first nerve; and

periodically delivering a stimulus to the nerves via the electrodes to mitigate obstruction of the upper airway.

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87. A method of treating obstructive sleep apnea, comprising:

chronically implanting a first electrode on a nerve;

chronically implanting a second electrode in a muscle; and

periodically delivering a stimulus via the electrodes to mitigate obstruction of the upper airway.

88. A system for treating sleep apnea, comprising:

a lead having a lead body, a distal electrode and a tether connected to the lead body proximal of the electrode, wherein the electrode is configured for chronic implantation on a nerve and the tether is configured for connection to tissue other than the nerve to relieve stress applied to the nerve; and

a pulse generator configured for chronic implantation and connected to the lead to periodically delivering a stimulus to the nerve.

89. A system as in claim 88, wherein the tether is connected to the lead body at a junction proximal of the electrode, and wherein the lead body is more flexible distal of the junction.

90. A method of treating obstructive sleep apnea, comprising:

providing a lead having a lead body, a distal electrode, and a tether connected to the lead body proximal of the electrode;

chronically implanting the electrode on a hypoglossal nerve;

connecting the tether to tissue other than the nerve, wherein the tether is configured to relieve stress applied to the nerve; and

periodically delivering a stimulus to the nerve via the electrode to mitigate obstruction of the upper airway.

91. A chronically implantable lead having a lead body, a distal electrode configured for attachment to a nerve, and a tether connected to the lead body adjacent the electrode, the

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tether configured for attachment to tissue other than the nerve to relieve stress applied to the nerve.

92. A chronically implantable lead as in claim 91, wherein the lead body is more flexible distal of the tether.

93. A chronically implantable lead having a lead body, a distal electrode configured for attachment to a nerve, and a tether connected to the electrode, the tether configured for attachment to tissue other than the nerve to relieve stress applied to the nerve.

94. A method of treating obstructive sleep apnea, comprising:

providing a lead having a lead body, a distal electrode, and a tether connected to the lead body proximal of the electrode, the lead body having a sigmoid shape, the lead body carrying a plurality of coiled conductors therein;

chronically implanting the electrode on a hypoglossal nerve;

connecting the tether to tissue other than the nerve, wherein the tether is configured to relieve stress applied to the nerve;

chronically implanting the sigmoid shaped lead body in the neck; and

periodically delivering a stimulus to the nerve via the electrode to mitigate obstruction of the upper airway.

95. A method of treating obstructive sleep apnea, comprising:

providing an electrode comprising a cuff having a relatively long side and a relatively short side; and

chronically implanting the electrode on a portion of a hypoglossal nerve such that the relatively short side of the cuff extends around a deep side of the nerve; and

delivering a stimulus to the hypoglossal nerve via the electrode to mitigate obstruction of the upper airway.

96. A method as in claim 95 wherein a cathode is disposed on the short side of the cuff.

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97. A method as in claim 96 wherein two anodes are disposed on the long side of the cuff and positioned diametrically opposite and longitudinally spaced relative to the cathode.

98. A method as in claim 95 wherein a cathode and two anodes are disposed on the long side of the cuff.

99. A method as in claim 95 wherein the short side of the cuff includes a removable strap extending therefrom to facilitate placement around the deep side of the nerve.

100. A method of treating obstructive sleep apnea, comprising:

providing an electrode comprising a cuff having a relatively long side and a relatively short side, wherein three or more electrode contacts are disposed on an inside surface of the cuff;

chronically implanting the electrode on a portion of a hypoglossal nerve such that the relatively short side of the cuff extends around a deep side of the nerve;

selectively delivering stimulus to two or more of the electrodes to steer an electrical field in the cuff and selectively activate fascicles in the nerve.

101. A chronically implantable nerve electrode comprising a split cylindrical cuff having a relatively long semi-cylindrical side and a relatively short semi-cylindrical side, wherein three or more electrode contacts are disposed on an inside surface of the cuff and configured to steer an electrical field in the cuff and selectively activate fascicles in a nerve.

102. A chronically implantable lead having a lead body, a nerve cuff, an electrode carried by the cuff, and a wire connected to the electrode and longitudinally extending through the lead body, wherein the wire is connected to the electrode off-axis relative to the position of the wire in the lead body.

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103. A chronically implantable nerve electrode comprising a complaint sheet wrap configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet, wherein the sheet includes a plurality of radially and longitudinally distributed fenestrations to accommodate nerve swelling and/or over tightening.

104. A chronically implantable nerve electrode comprising a complaint sheet wrap configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet, wherein one of the opposite portions comprises one or more narrow strips integral with the sheet to accommodate nerve swelling and/or over tightening.

105. A chronically implantable nerve electrode comprising a complaint sheet wrap configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet, wherein the opposite portions are offset from the nerve and a thickened portion of the sheet fills the offset space to accommodate nerve swelling and/or over tightening.

106. A chronically implantable nerve electrode comprising a complaint sheet wrap configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet, wherein the sheet includes a plurality of radially distributed slits extending partly through the thickness of the sheet to accommodate nerve swelling and/or over tightening.

107. A chronically implantable nerve electrode comprising a complaint sheet wrap configured to be wrapped about a nerve and secured thereto by connecting opposite portions of the sheet, wherein the sheet includes a plurality of longitudinally extending and radially distributed convolutions to accommodate nerve swelling and/or over tightening.

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108. A chronically implantable nerve electrode comprising a semi-cylindrical portion carrying a plurality of electrode contacts, and one or more separate strips configured to be wrapped around a nerve and connected to the semi-cylindrical portion to reduce dissection on one side of the nerve.

109. A chronically implantable nerve electrode comprising a relatively long semi-cylindrical portion carrying a plurality of anodes, and a relatively short integral semi-cylindrical portion carrying a cathode, the short semi-cylindrical portion configured to be wrapped around a nerve and connected to the long semi-cylindrical portion to reduce dissection on one side of the nerve.

110. A chronically implantable nerve electrode comprising a relatively long semi-cylindrical portion carrying a cathode and a pair of guarding anodes, and a relatively short integral semi-cylindrical portion carrying an anode, the short semi-cylindrical portion configured to be wrapped around a nerve and connected to the long semi-cylindrical portion to reduce dissection on one side of the nerve.

111. A chronically implantable nerve electrode array comprising a plurality of independent cuff electrodes each with independent leads, each cuff electrode comprising a compliant wrap with a removable tow strap.

112. A chronically implantable nerve electrode array comprising at least three independent cuff electrode configured to be arranged adjacent each other along a nerve with a middle cuff electrode comprising a cathode and two end cuff electrodes comprising anodes, each cuff electrode with independent leads.

113. A chronically implantable nerve cuff electrode comprising a slit cylinder configured to be wrapped around a nerve with opposite portions connected to each other to secure the cuff around the nerve, and a plurality of radially spaced electrode contacts to facilitate field steering.

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114. A chronically implantable nerve cuff electrode comprising a slit cylinder configured to be wrapped around a nerve with opposite portions connected to each other to secure the cuff around the nerve, wherein the longitudinal ends have a tapered thickness to reduce mechanical abrasion.

115. A chronically implantable nerve electrode comprising a housing configured to be connected to a nerve, the housing having a receptacle configured to removably receive a cylindrical lead with ring electrodes, the housing also having windows configured to align with the ring electrodes and permit electrical exposure of the ring electrodes to the nerve.

116. A method of treating obstructive sleep apnea, comprising:

forming an access site to a hypoglossal nerve;

providing a paddle-shaped lead having a distally disposed nerve electrode with the electrode exposed on one side of the paddle-shape and insulted on the other;

inserting the lead into the access site; and

advancing the lead distally along the hypoglossal nerve such that the electrode extends beyond the access site and the exposed side of the electrode is positioned to face the hypoglossal nerve.

117. A method of treating obstructive sleep apnea, comprising:

providing a tubular introducer;

positioning a distal end of the introducer adjacent a hypoglossal nerve;

providing a lead with a distally disposed nerve electrode;

inserting the lead through the introducer; and

advancing the lead distally through the introducer such that the electrode extends beyond the distal end of the introducer and is positioned adjacent the hypoglossal nerve.

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118. A method of treating obstructive sleep apnea, comprising:

chronically implanting one or more electrodes on a hypoglossal nerve innervating a tongue protruder muscle;

determining respiration based on a sensed parameter other than efferent signals on the hypoglossal nerve;

periodically delivering a stimulus, based on the sensed parameter, to the nerve via the electrode to mitigate obstruction of the upper airway; and

tracking obstruction of the upper airway by sensing efferent signals on the hypoglossal nerve via the one or more electrodes.

119. A method of treating obstructive sleep apnea, comprising:

providing a chronically implantable lead with a distal disposed electrode and a proximally disposed receiver;

chronically implanting the electrode on a hypoglossal nerve innervating a tongue protruder muscle;

providing a neurostimulator connected to a transmitter and a respiratory sensor, each of which is carried by an article configured to be donned by a person;

sensing respiration using the respiratory sensor; and

wirelessly transmitting a signal from the transmitter to the receiver to cause a stimulus to be delivered to the nerve via the electrode as a function of the sensed respiration to mitigate obstruction of the upper airway.

120. A method as in claim 119 wherein the article comprises a belt.

121. A method as in claim 119 wherein the article comprises a vest.

122. A method as in claim 119 wherein the article comprises a shirt.

123. A method as in claim 119 wherein a plurality of respiratory sensors are carried by the article.

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124. A method of treating obstructive sleep apnea, comprising:

providing a chronically implantable lead with a distal disposed electrode and a proximally disposed receiver;

chronically implanting the electrode on a hypoglossal nerve innervating a tongue protruder muscle;

chronically implanting the receiver in a neck region;

providing a neurostimulator coupled to a transmitter, wherein the transmitter is carried by an article configured to be donned by a person about the neck; and

wirelessly transmitting a signal from the transmitter to the receiver to cause a stimulus to be delivered to the nerve via the electrode to mitigate obstruction of the upper airway.

125. A method of treating obstructive sleep apnea, comprising:

chronically implanting one or more electrodes on a hypoglossal nerve innervating a tongue protruder muscle;

determining respiration based on a bio-impedance parameter using an implanted bio-impedance sensor;

periodically delivering a stimulus, based on the sensed parameter, to the nerve via the electrode to mitigate obstruction of the upper airway;

detecting one or more types of respiratory events using the implanted bio-impedance sensor; and

adjusting a parameter of the stimulus to increase efficacy as a function of sensed respiratory events.

126. A method as in claim 125 wherein the respiratory event comprises an episode of obstructive sleep apnea.

127. A method as in claim 125 wherein the respiratory event comprises an episode of central sleep apnea.

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128. A method as in claim 125 wherein the respiratory event comprises an episode of hypopnea.

129. A method of treating obstructive sleep apnea, comprising:

chronically implanting one or more electrodes on a hypoglossal nerve innervating a tongue protruder muscle;

determining respiration using an implanted sensor;

periodically delivering a stimulus, based on sensed respiration, to the nerve via the electrode to mitigate obstruction of the upper airway;

detecting one or more types of respiratory events using the implanted sensor; and

adjusting a parameter of the stimulus to increase efficacy as a function of sensed respiratory events.

130. A method as in claim 129 wherein the respiratory event comprises an episode of obstructive sleep apnea.

131. A method as in claim 129 wherein the respiratory event comprises an episode of central sleep apnea.

132. A method as in claim 129 wherein the respiratory event comprises an episode of hypopnea.

133. A method of treating obstructive sleep apnea, comprising:

chronically implanting one or more electrodes on a hypoglossal nerve innervating a tongue protruder muscle;

determining respiration based on a bio-impedance parameter using an implanted bio-impedance sensor, wherein the bio-impedance sensor includes an electrode array positioned across a lung-diaphragm-liver interface; and

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periodically delivering a stimulus, based on the sensed parameter, to the nerve via the electrode to mitigate obstruction of the upper airway.

134. A method of treating obstructive sleep apnea, comprising:

chronically implanting one or more electrodes on a hypoglossal nerve innervating a tongue protruder muscle;

determining respiration using an implanted sensor;

periodically delivering a stimulus, based on sensed respiration, to the nerve via the electrode to mitigate obstruction of the upper airway;

detecting one or more types of respiratory events using the implanted sensor; and

logging the respiratory events for subsequent download by an external device.

135. A method as in claim 134 wherein the implanted sensor comprises a bio-impedance sensor.

136. A method as in claim 134 wherein the respiratory event comprises an episode of obstructive sleep apnea.

137. A method as in claim 134 wherein the respiratory event comprises an episode of central sleep apnea.

138. A method as in claim 134 wherein the respiratory event comprises an episode of hypopnea.

139. A method of treating obstructive sleep apnea, comprising:

chronically implanting a first electrode on a first nerve innervating an upper airway muscle;

chronically implanting a second electrode on a second nerve innervating an upper airway muscle;

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wherein the first nerve is one a right side and the second nerve is on a left side; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, alternately to the nerves via the electrodes to mitigate obstruction of the upper airway.

140. A method of treating obstructive sleep apnea by delivering a stimulus to activate an upper airway dilator muscle, wherein the stimulus is delivered according to an algorithm that triggers stimulation to occur during inspiration predicted as a function of expiration onset.

141. A method of treating a patient with obstructive sleep apnea, comprising:

a. evaluating the patient to determine of the level of obstruction in the upper airway; and
b. treating the patient by delivering a stimulus to activate a tongue protruder muscle if the level of obstruction occurs at the level of the tongue.

142. A method as in claim 141, wherein the screening method includes visually determining the level of obstruction using a scope.

143. A method of treating a patient with obstructive sleep apnea, comprising:

c. evaluating the patient to determine of the minimum positive airway pressure required to mitigate obstruction; and
d. treating the patient by delivering a stimulus to activate a tongue protruder muscle if the minimum pressure is less than a threshold amount.

144. A method of treating obstructive sleep apnea, comprising:

forming an access site to a hypoglossal nerve;

providing a stimulation probe having at least a cathode and an anode disposed on a distal end thereof;

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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stimulating the nerve at different sites along the nerve;

selecting an optimal site for chronic stimulation; and

chronically implanting an electrode on the hypoglossal nerve at the optimal site to deliver a stimulus to the nerve via the electrode to mitigate obstruction of the upper airway.

145. A method of treating a patient with obstructive sleep apnea, comprising:

e. chronically implanting a respiration sensor on a right lateral side of the patient to reduce cardiac noise; and

f. chronically implanting an electrode on a hypoglossal nerve to deliver a stimulus to the nerve via the electrode to mitigate obstruction of the upper airway.

146. A method as in claim 145, wherein the respiration sensor comprises a bio-impedance sensor including a plurality of electrodes disposed on the right laterl side of the patient.

147. A method of treating obstructive sleep apnea, comprising:

chronically implanting an electrode on a nerve at a site to stimulate an upper airway dilator muscle;

chronically implanting a receiver circuit connected to the electrode, the receiver circuit including a capacitor for storing electrical energy used for stimulation of the nerve;

providing an external transmitter inductively coupled to the receiver;

transmitting a carrier signal from the transmitter to the receiver to provide electrical energy stored by the capacitor; and

periodically interrupting the carrier signal to cause stimulation to be delivered to the nerve via the electrode to mitigate obstruction of the upper airway.

148. A method of treating a patient with obstructive sleep apnea, comprising:

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g. providing a pulse generator including a position sensor that disables stimulation when the patient is not a prone position;
h. chronically implanting an electrode on a hypoglossal nerve; and
i. delivering a stimulus from the pulse generator to the nerve via the electrode only when the patient is in a prone position to mitigate obstruction of the upper airway during sleep.

149. A method of treating a patient with obstructive sleep apnea, comprising:
j. providing a pulse generator to deliver a stimulation signal and detect a sense signal;
k. chronically implanting an electrode on a nerve innervating a muscle of the upper airway; and
l. interleaving delivery of the stimulation signal and detection of the sense signal on the electrode.

150. A method of treating obstructive sleep apnea, comprising:

chronically implanting an electrode on a patient's nerve proximal of a portion innervating palate musculature; and

periodically delivering a stimulus, based on a sensed parameter indicative of respiration, to the nerve via the electrode to mitigate obstruction of an upper airway of the patient.

151. The method of claim 150, wherein the palate musculature includes the tensor veli palatine muscle.

152. The method of claim 150, wherein the patient's nerve includes the mandibular nerve.

Exhibit 1002
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00815

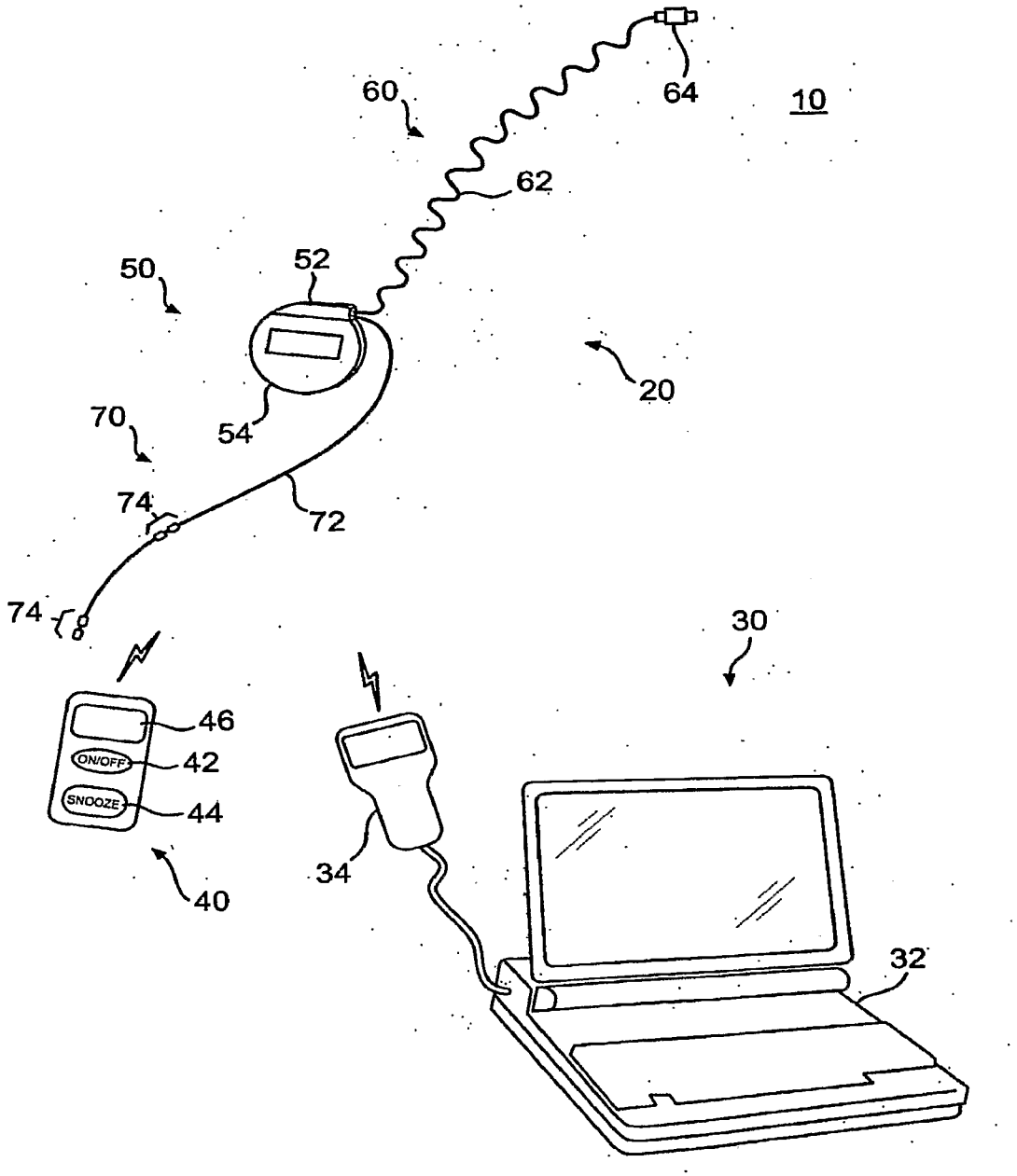


FIG. 1

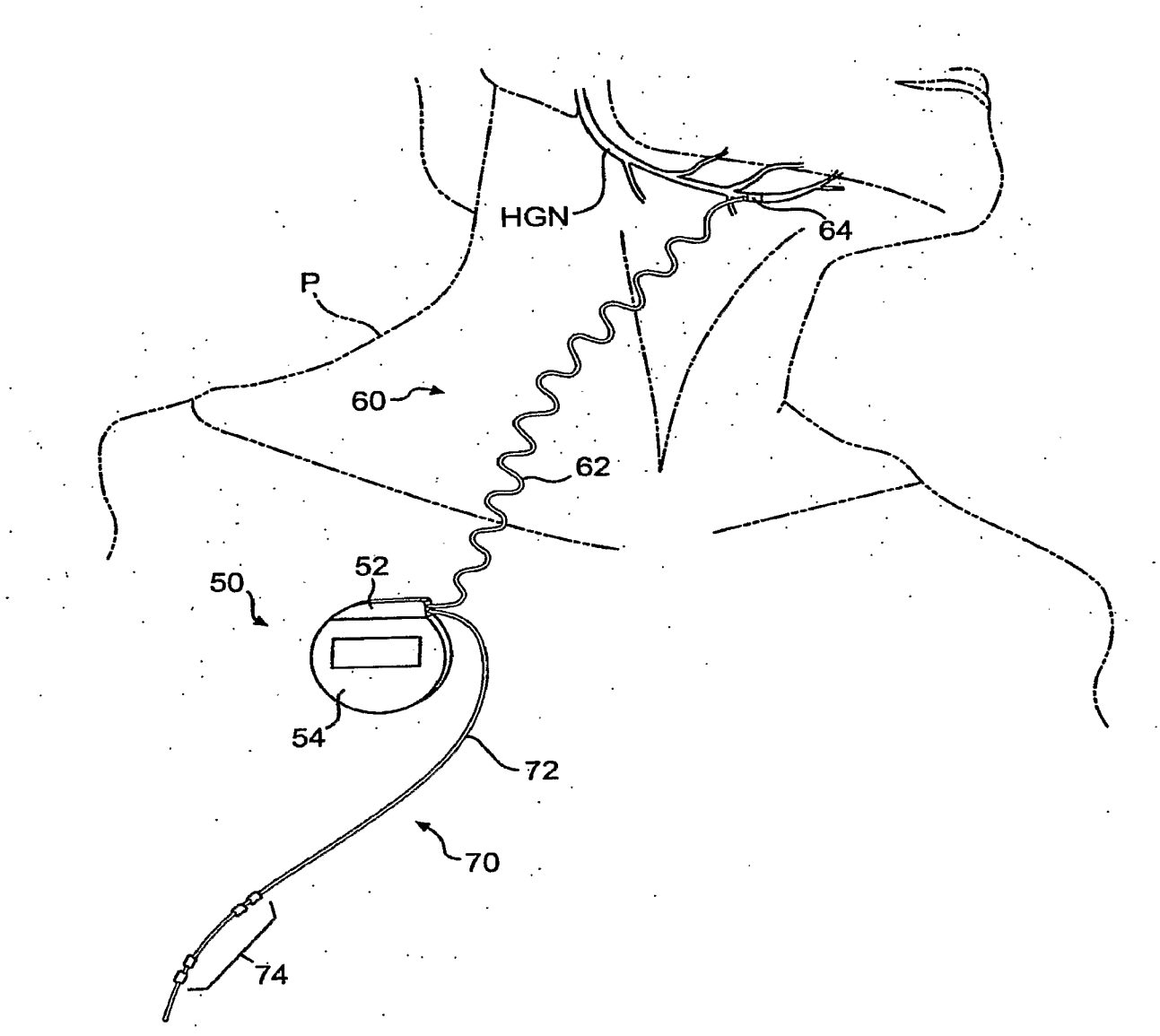


FIG. 2

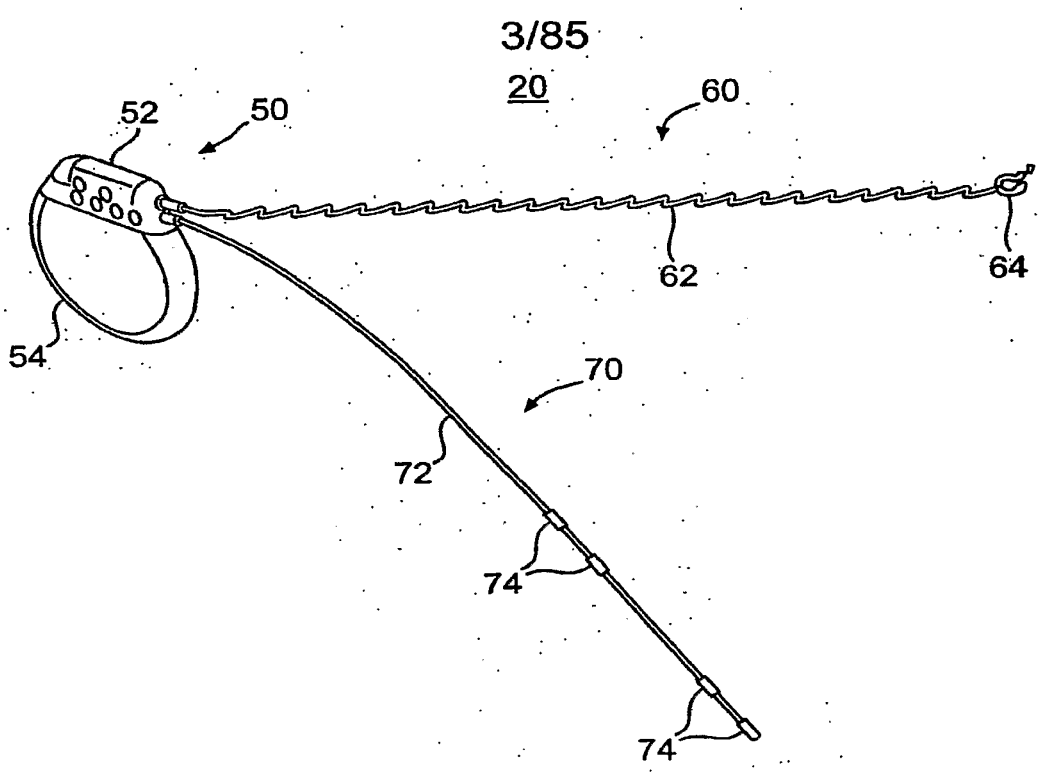


FIG. 3

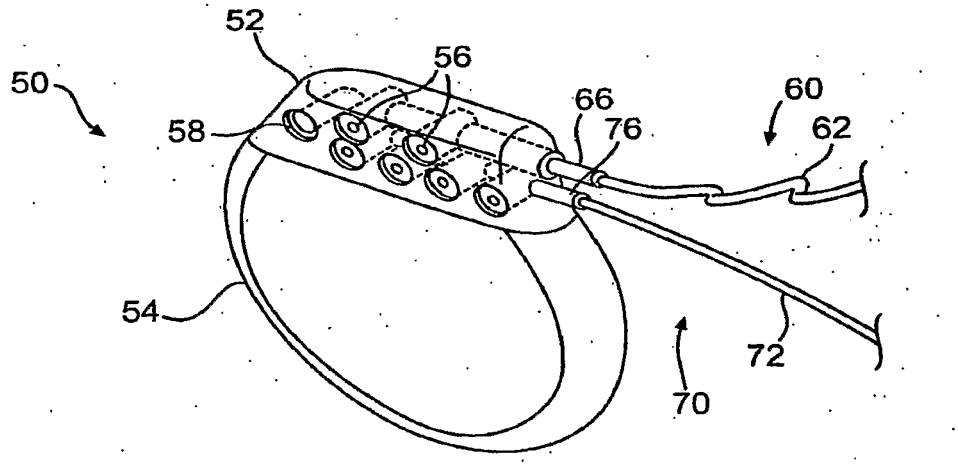


FIG. 4

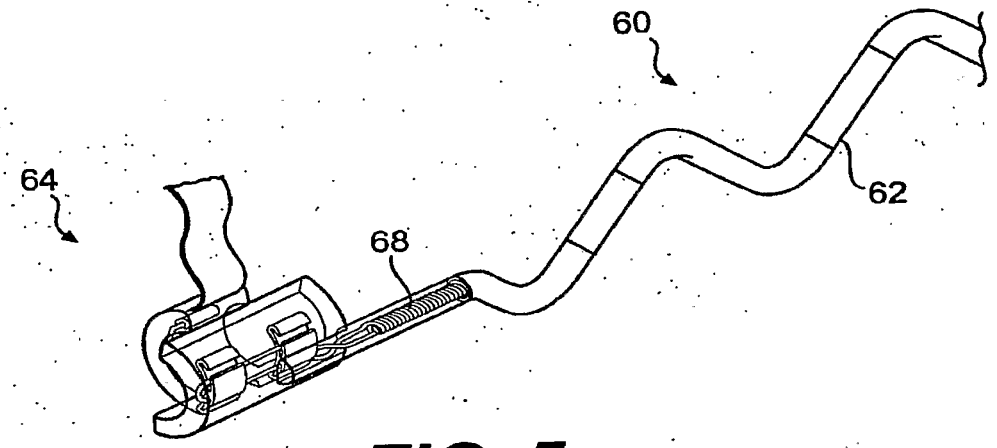


FIG. 5

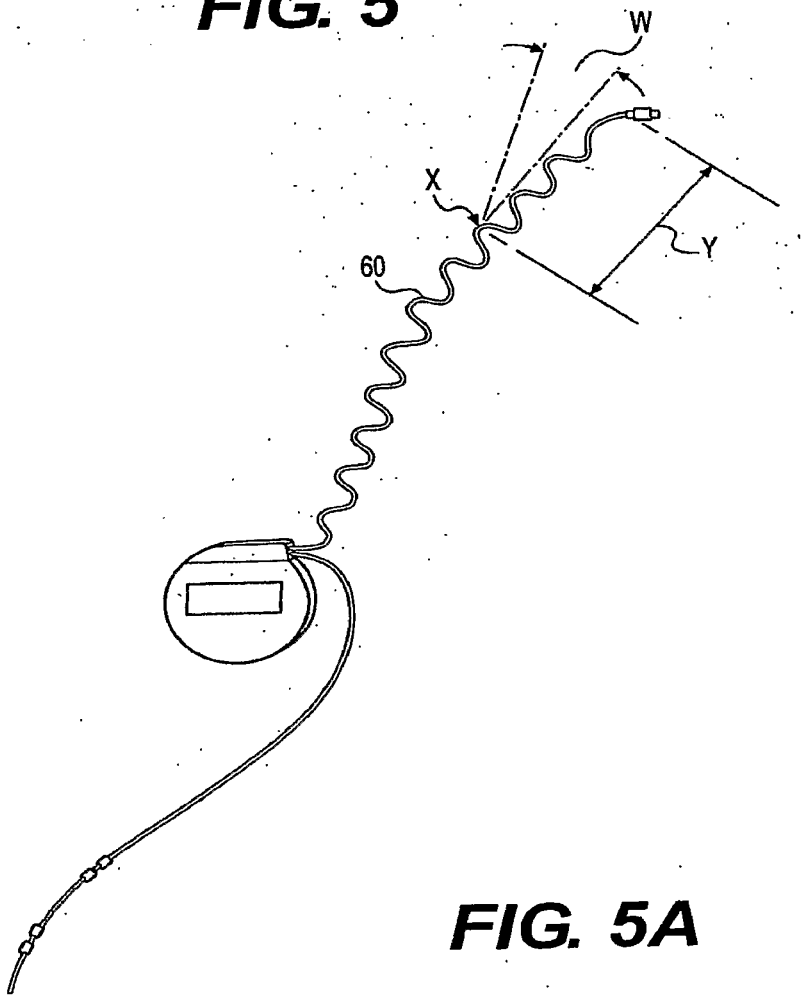


FIG. 5A

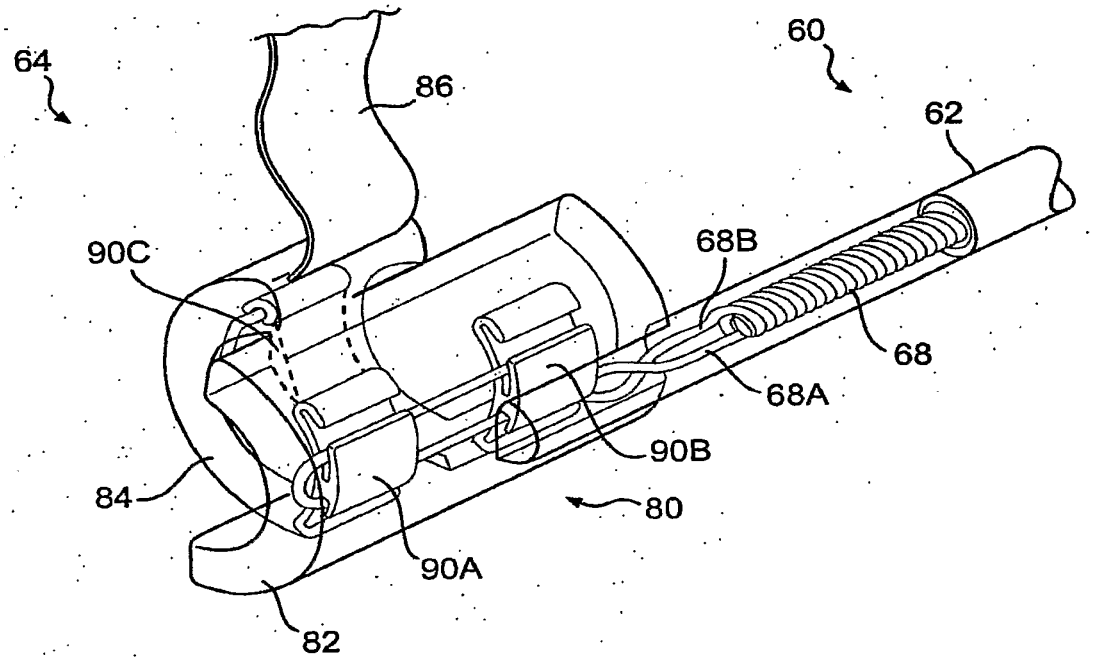


FIG. 6

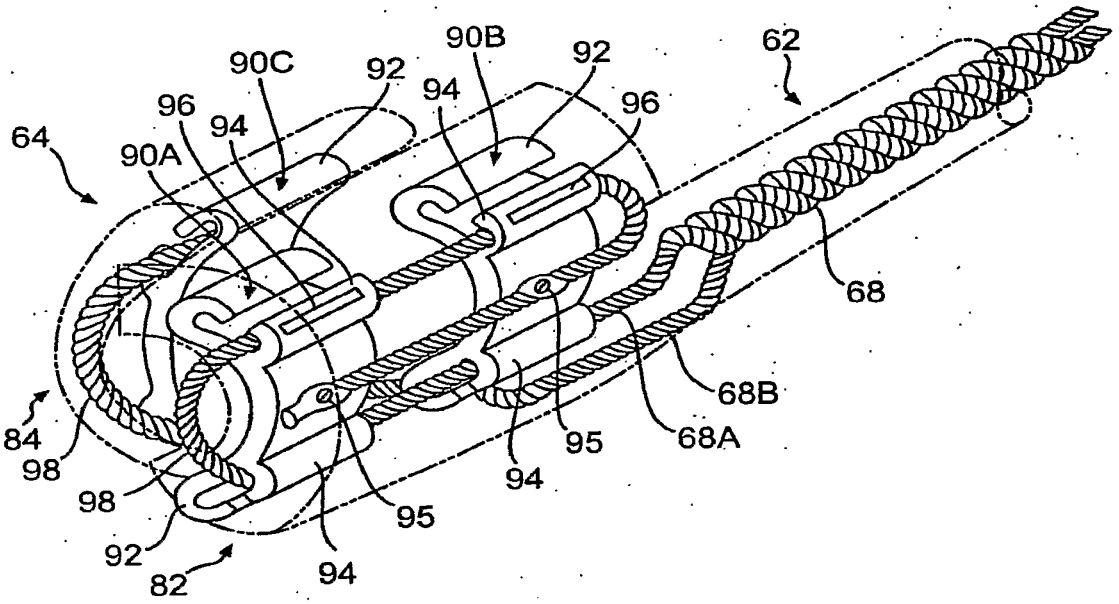

64
90A
96
94
90C
92
90B
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96
62
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68B
68A
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82
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FIG. 7

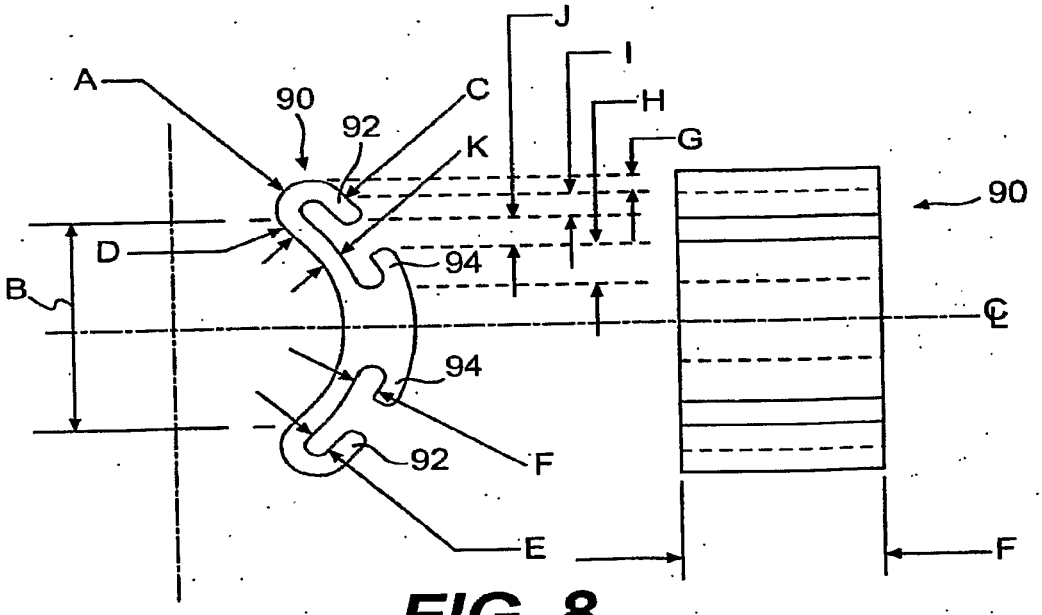

A
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J
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H
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D
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F
E
F

FIG. 8

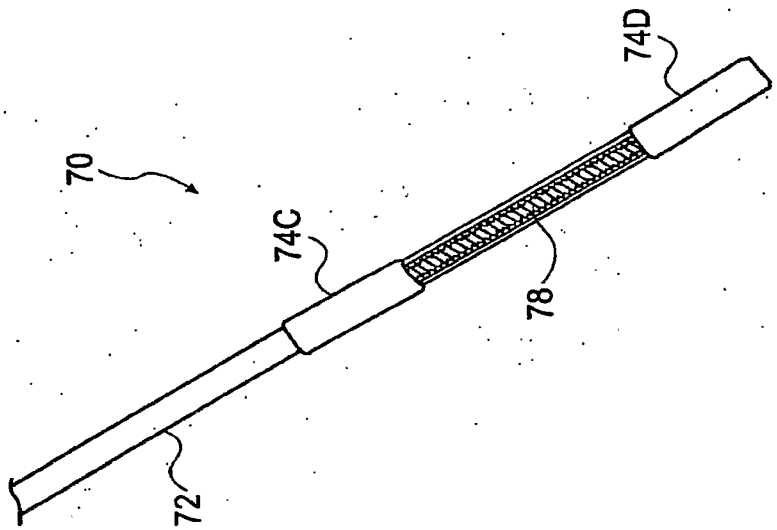


FIG. 9B

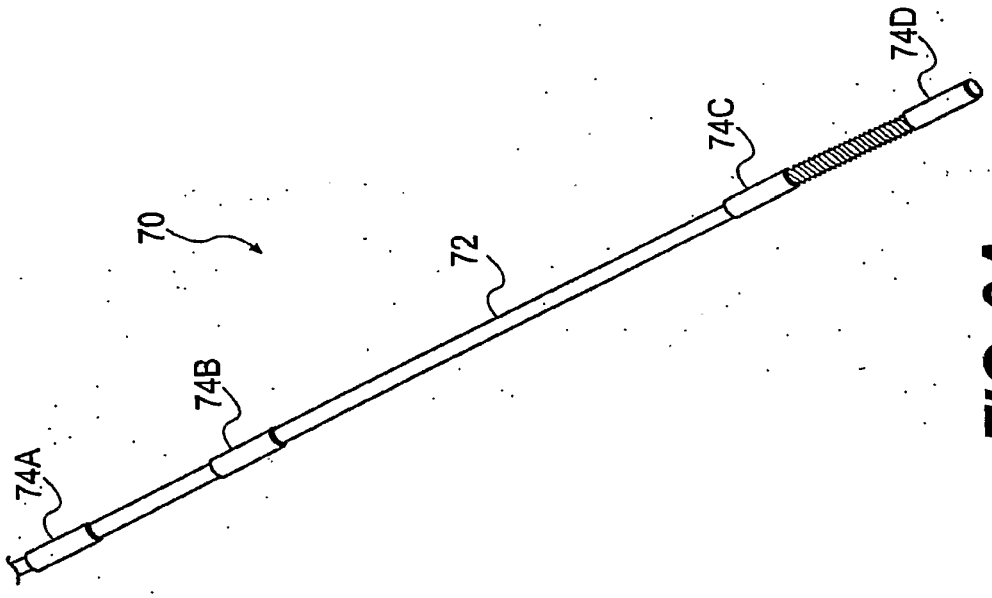


FIG. 9A

FIG. 10

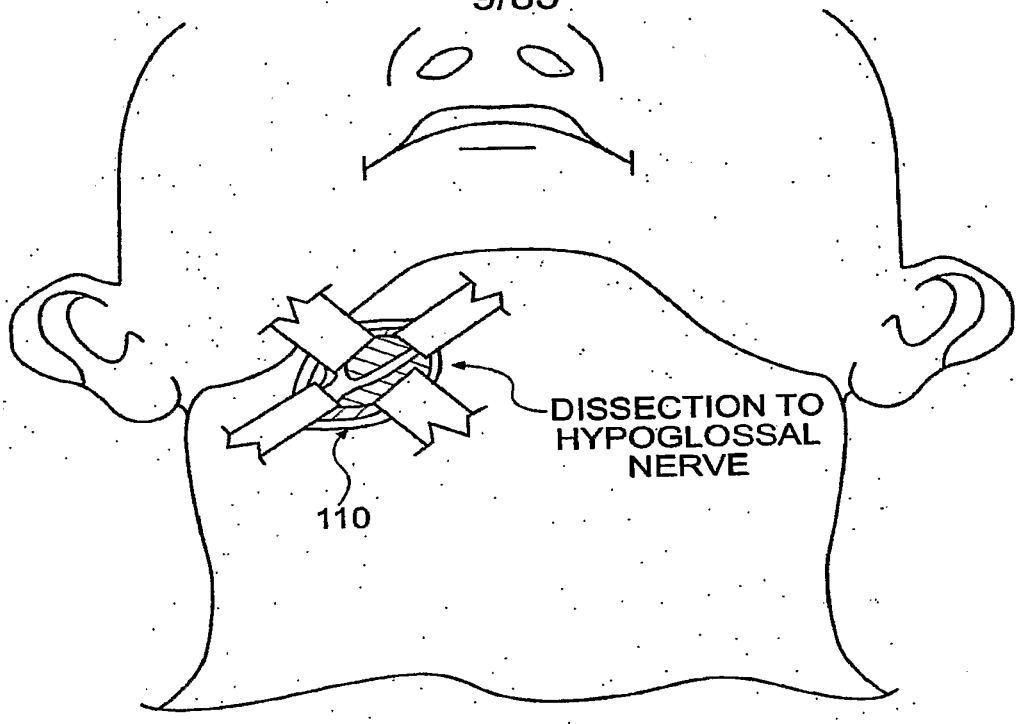


FIG. 11A

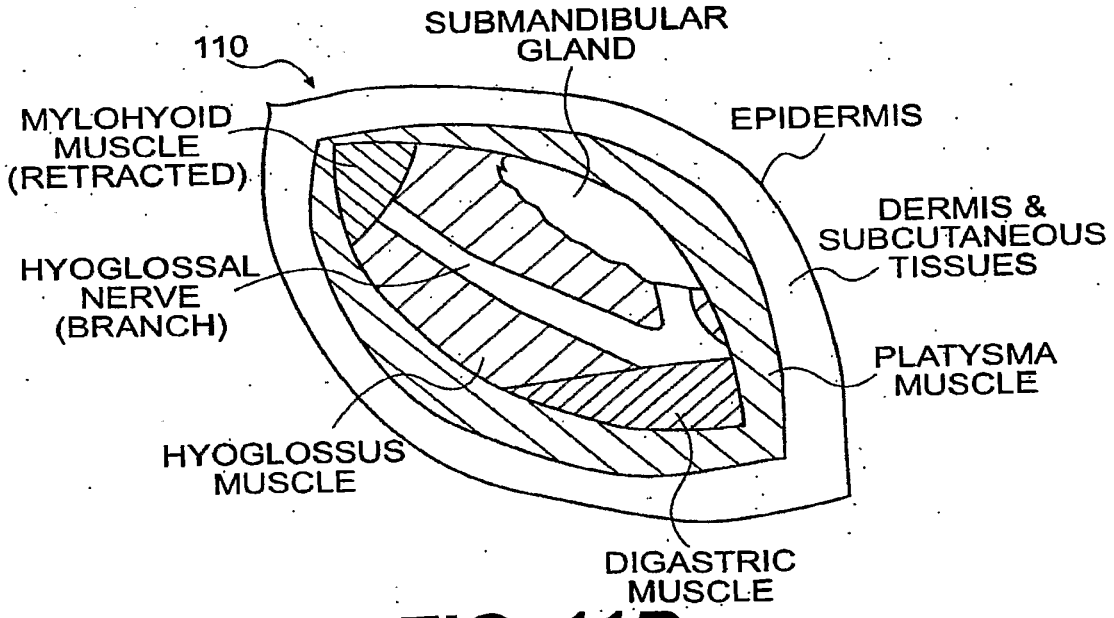


FIG. 11B

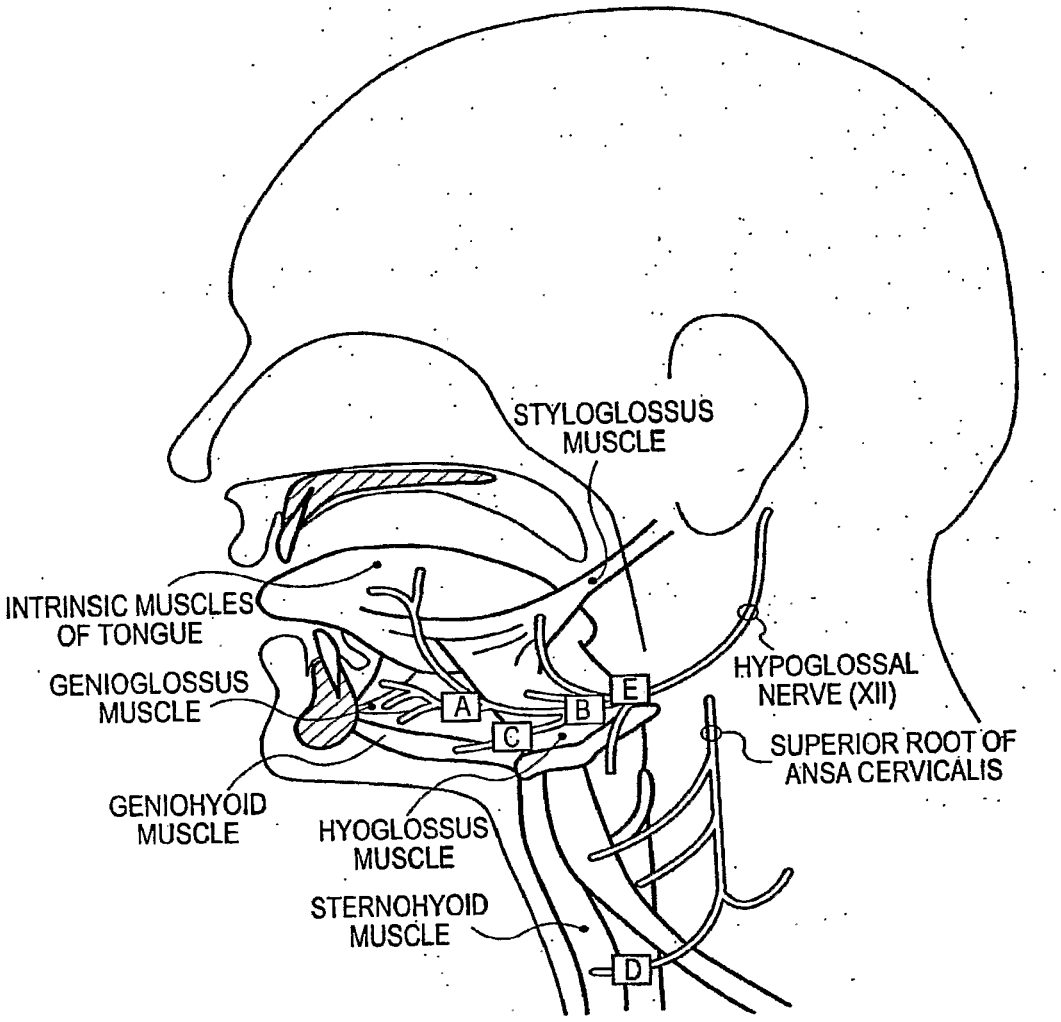

STYLOGLOSSUS MUSCLE
INTRINSIC MUSCLES OF TONGUE
GENIOGLOSSUS MUSCLE
GENIOHYOID MUSCLE
HYOGLOSSUS MUSCLE
STERNOHYOID MUSCLE
HYPOGLOSSAL NERVE (XII)
SUPERIOR ROOT OF ANSA CERVICALIS
A
B
C
D
E

FIG. 12

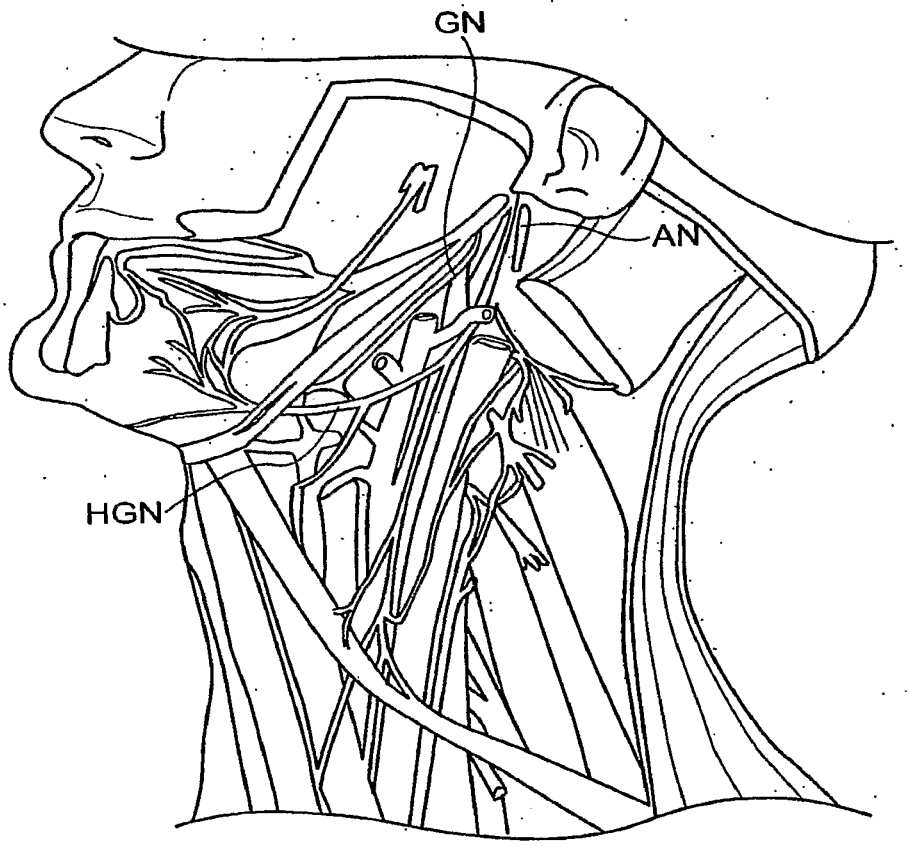


FIG. 12A

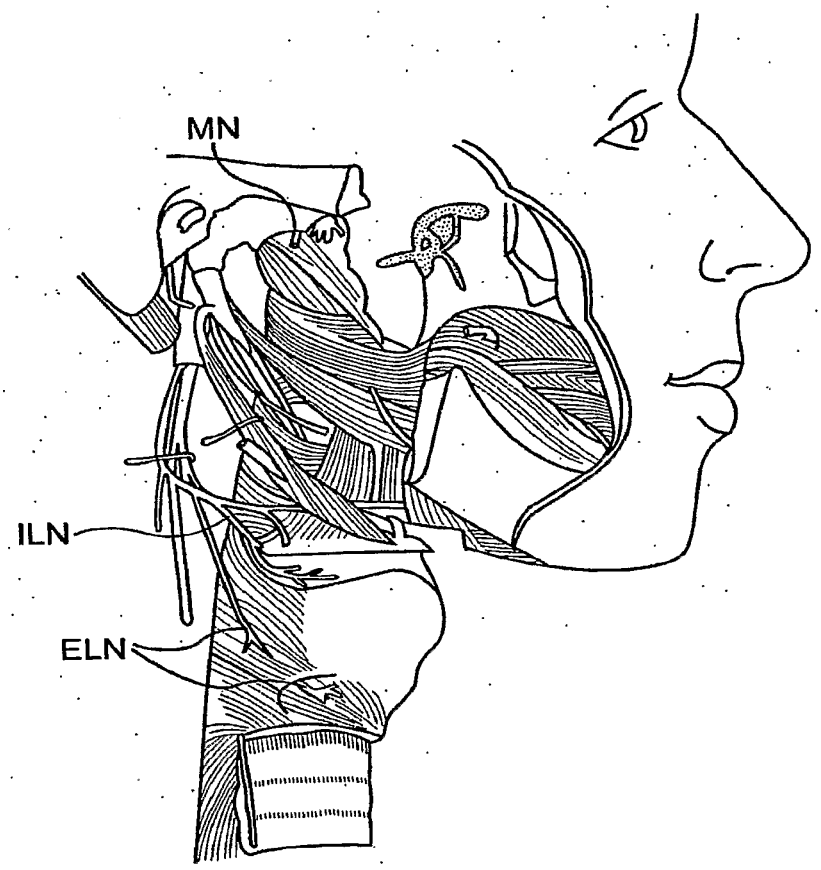


FIG. 12B

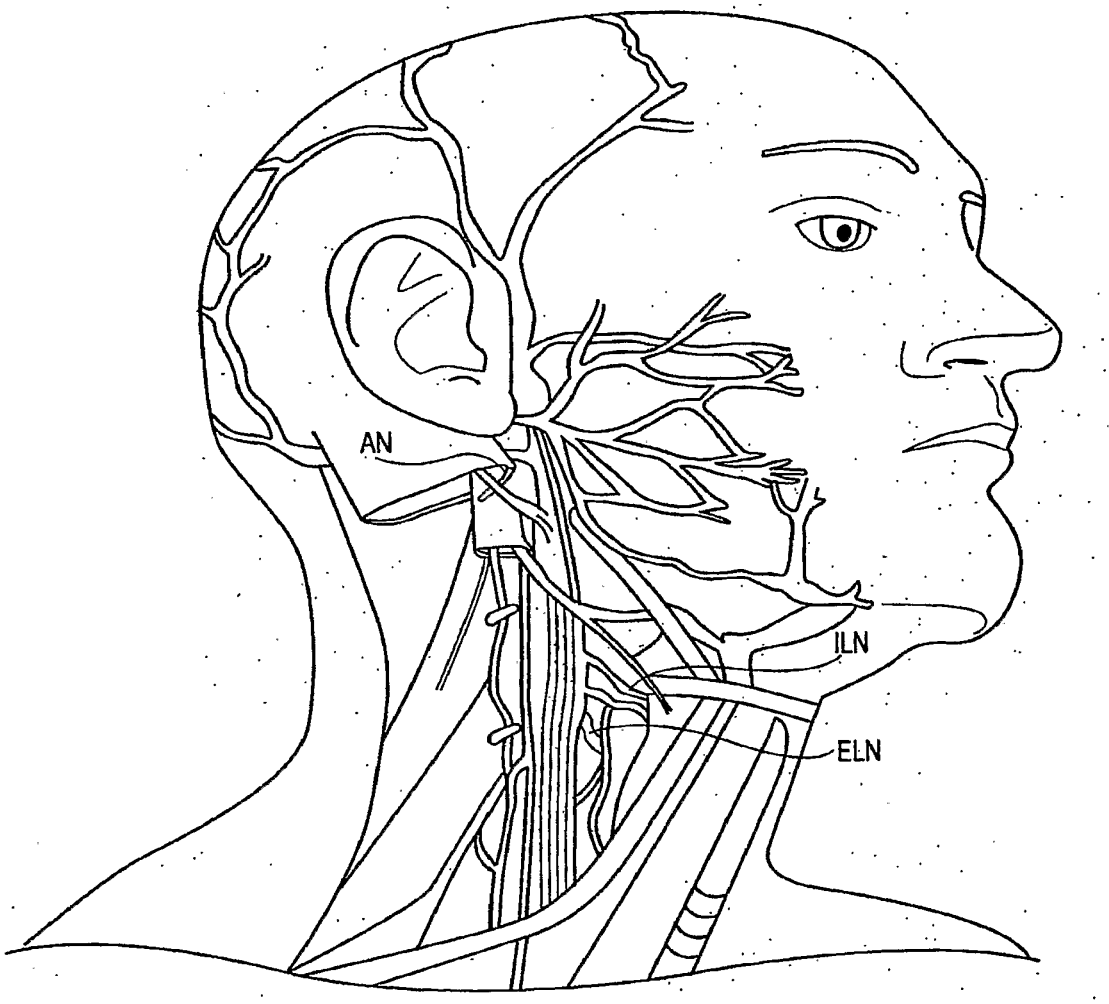


FIG. 12C

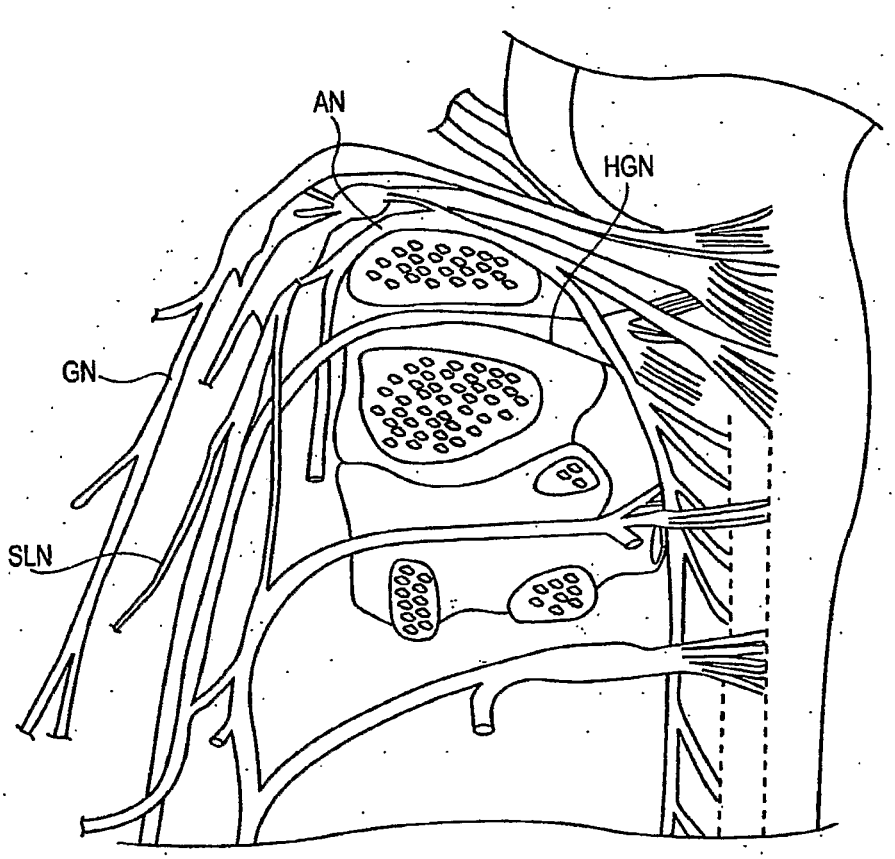


FIG. 12D

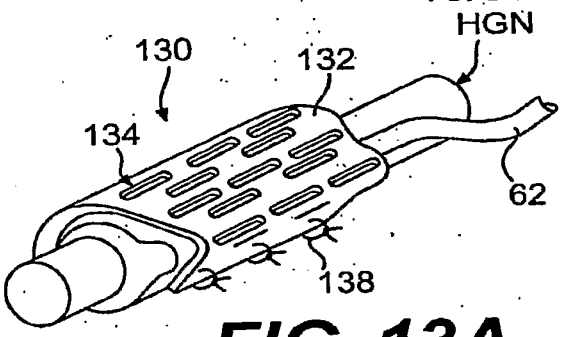


FIG. 13A

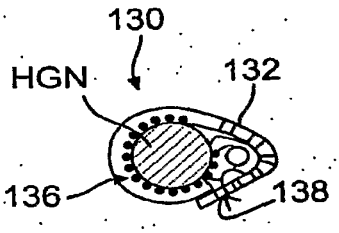


FIG. 13B

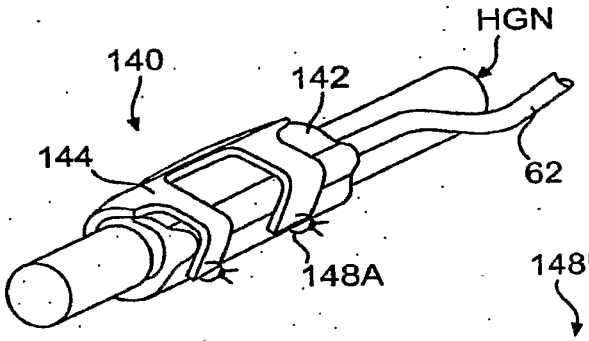


FIG. 14A

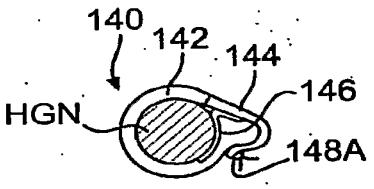


FIG. 14B

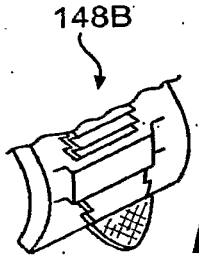


FIG. 14C

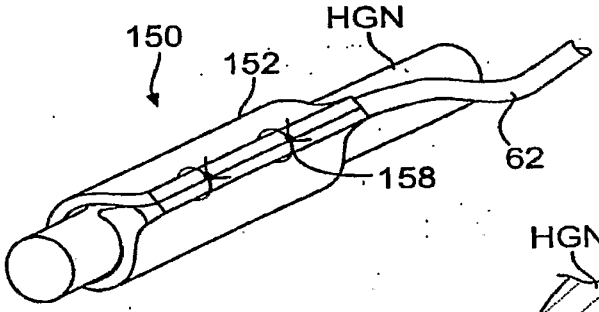


FIG. 15A

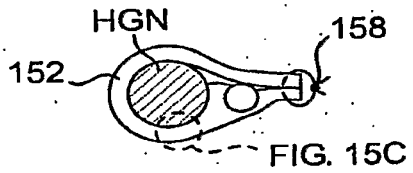


FIG. 15B

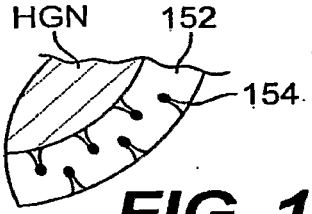


FIG. 15C

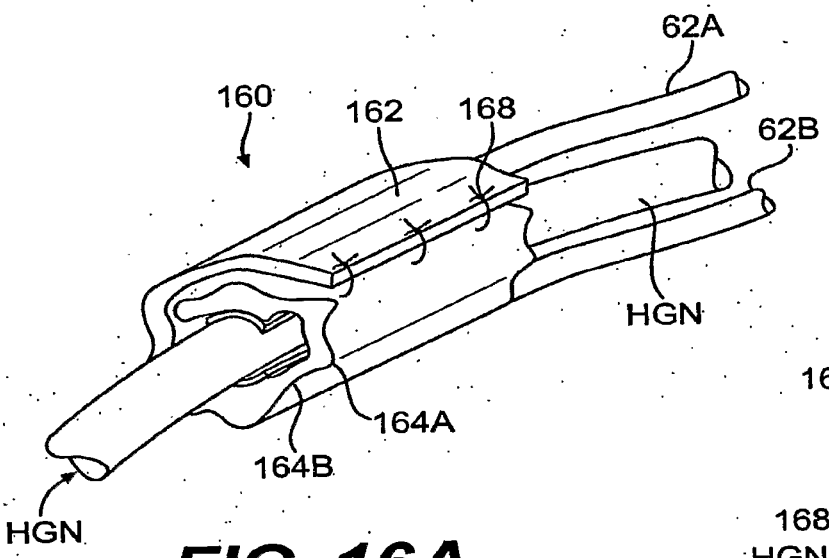


FIG. 16A

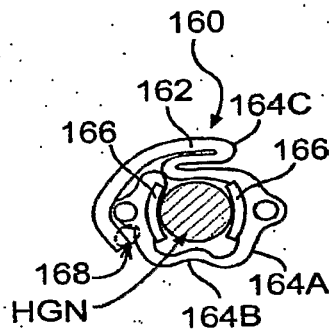


FIG. 16B

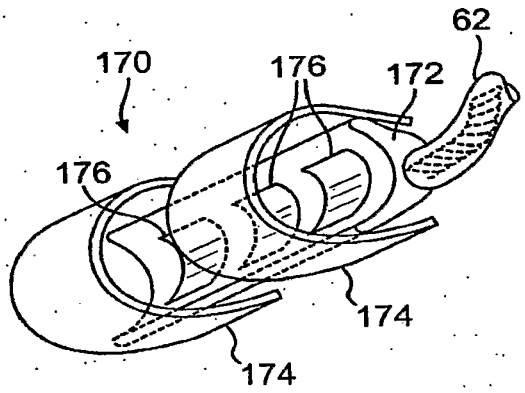


FIG. 17

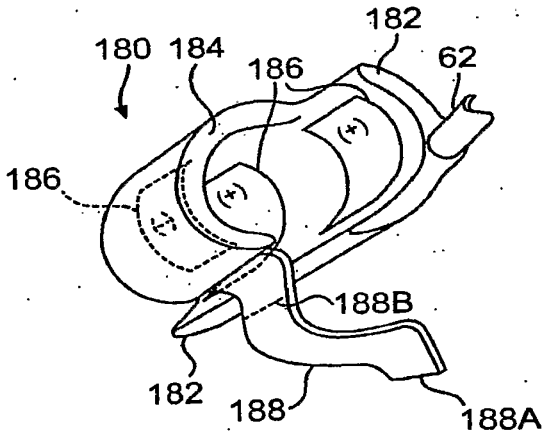


FIG. 18

FIG. 16C

FIG. 16D

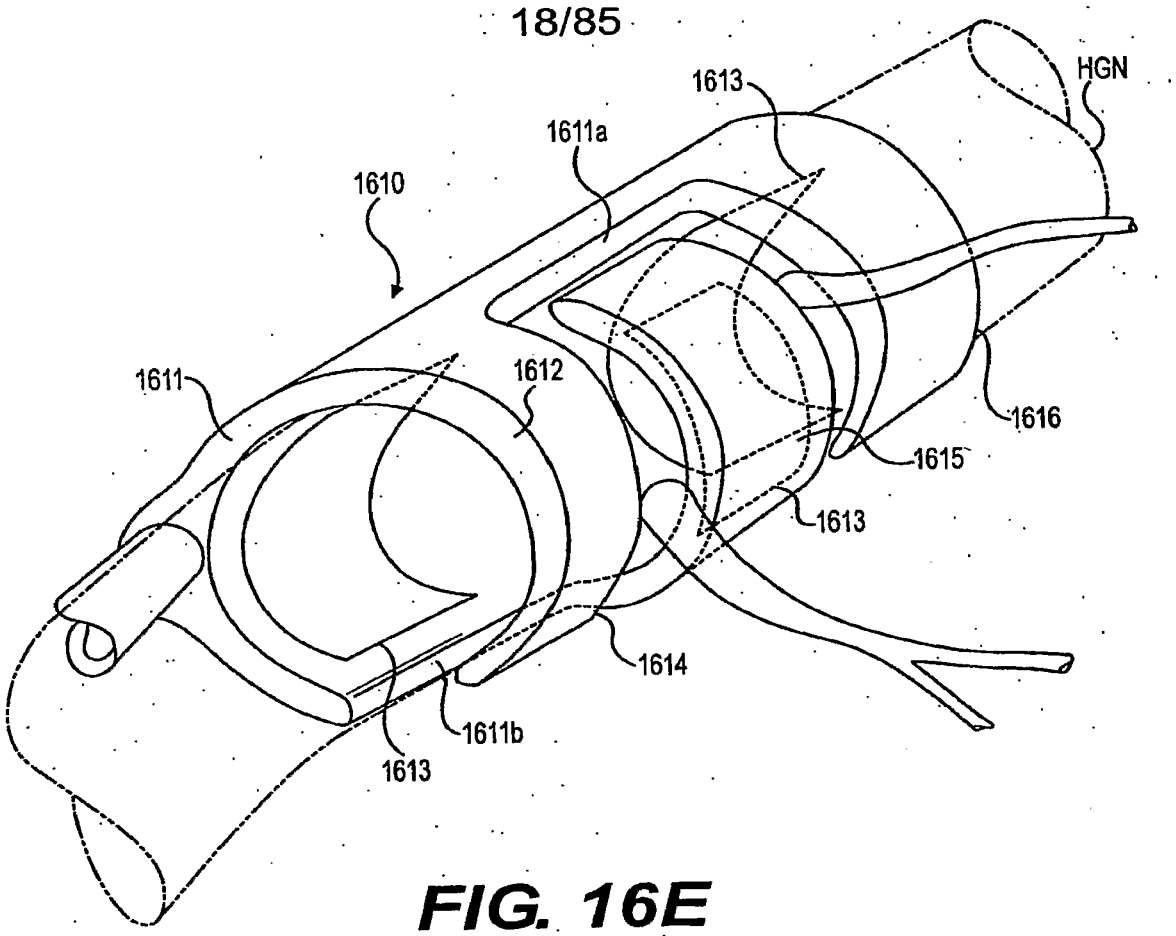


FIG. 16E

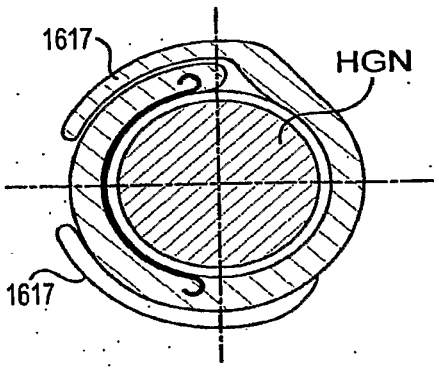


FIG. 16F

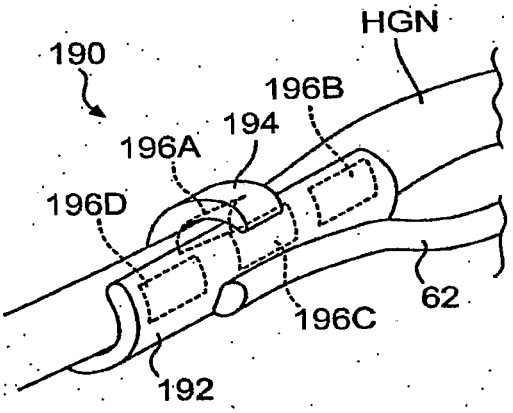


FIG. 19A

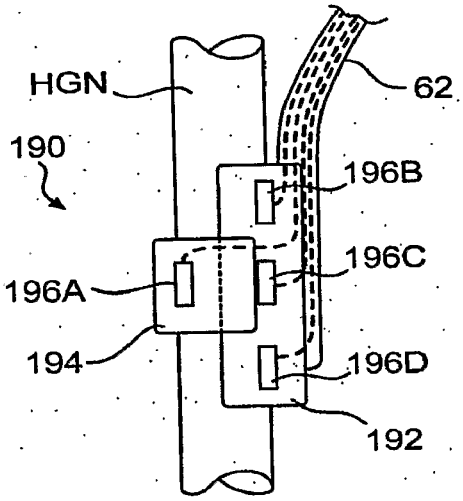


FIG. 19B

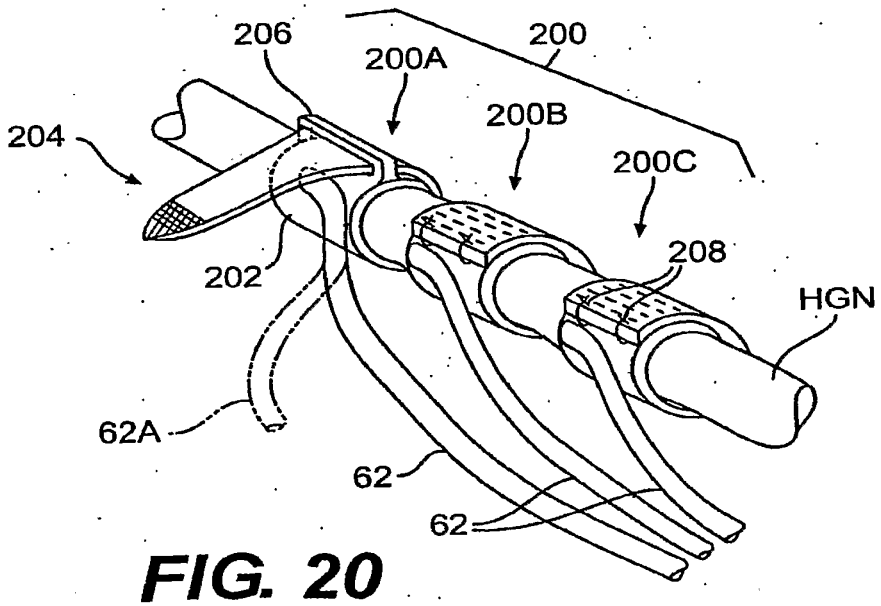


FIG. 20

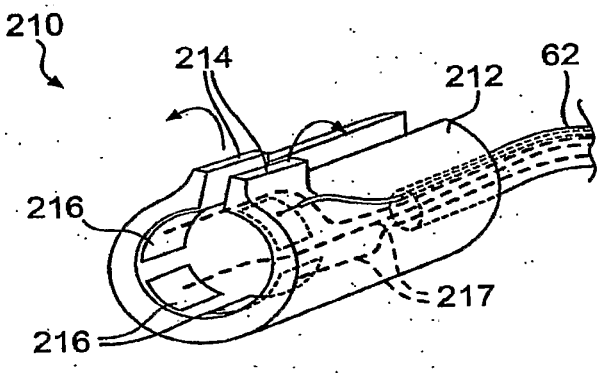


FIG. 21A

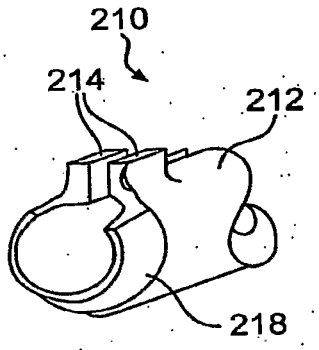


FIG. 21B

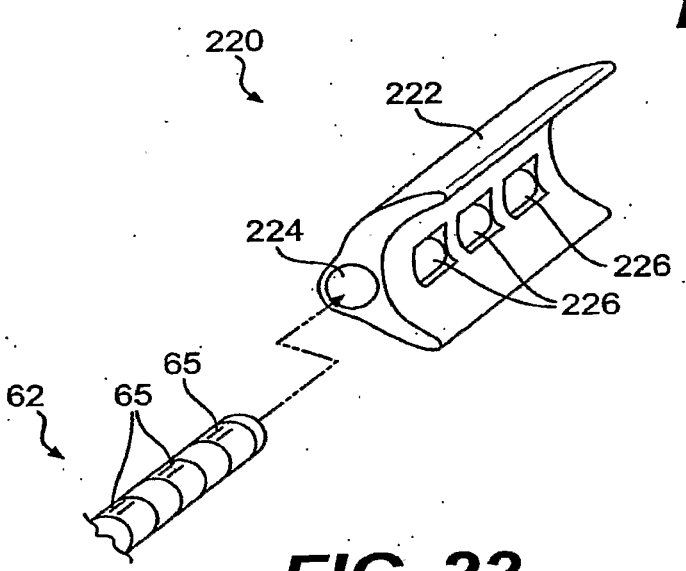


FIG. 22

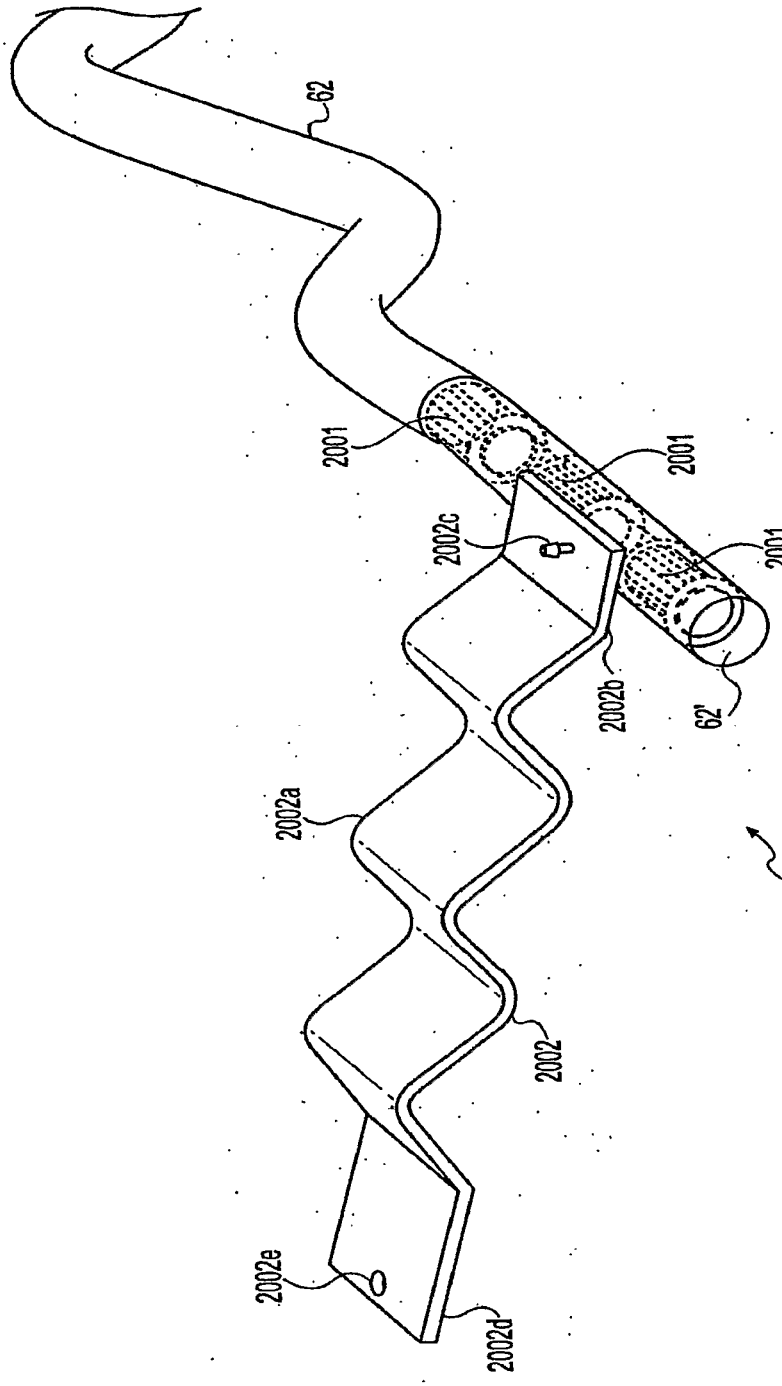


FIG. 22A

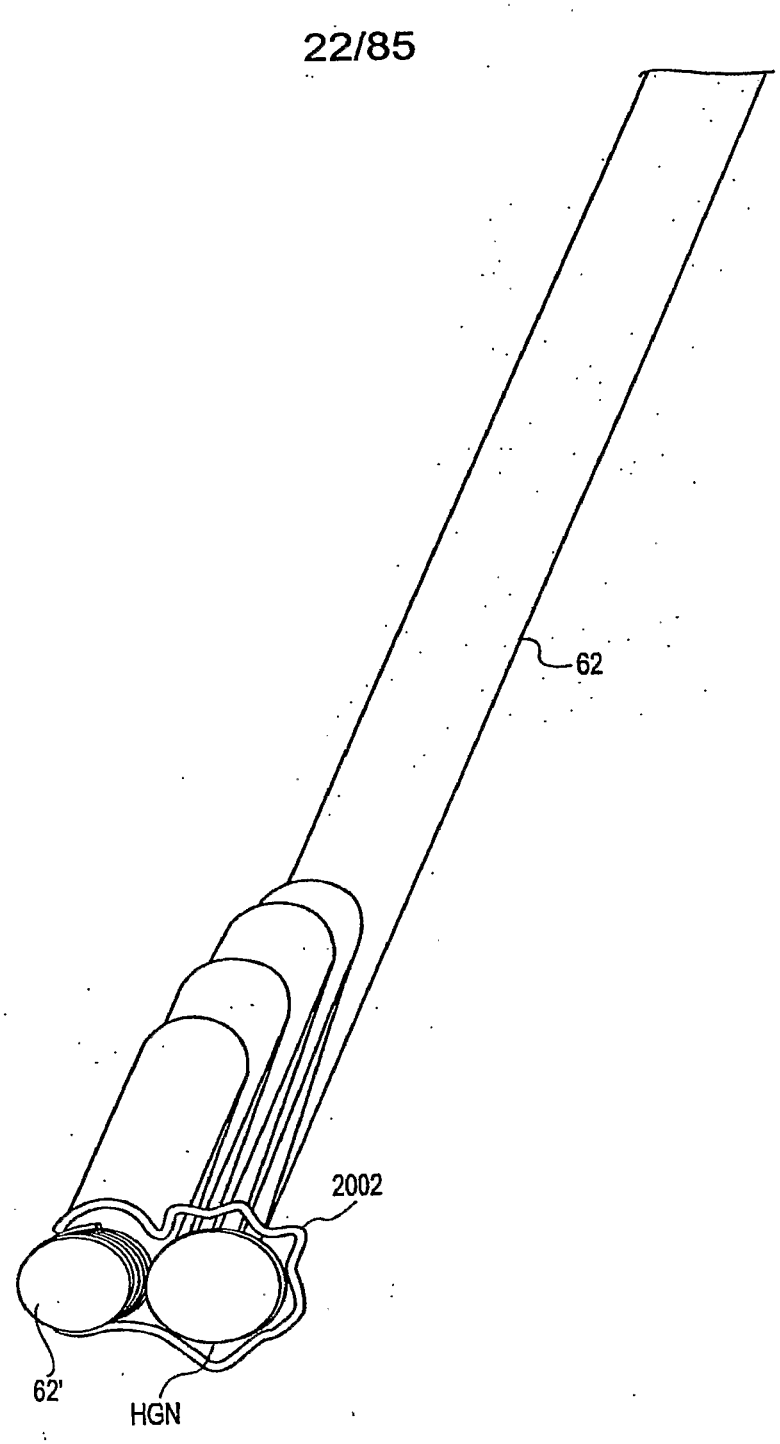


FIG. 22B

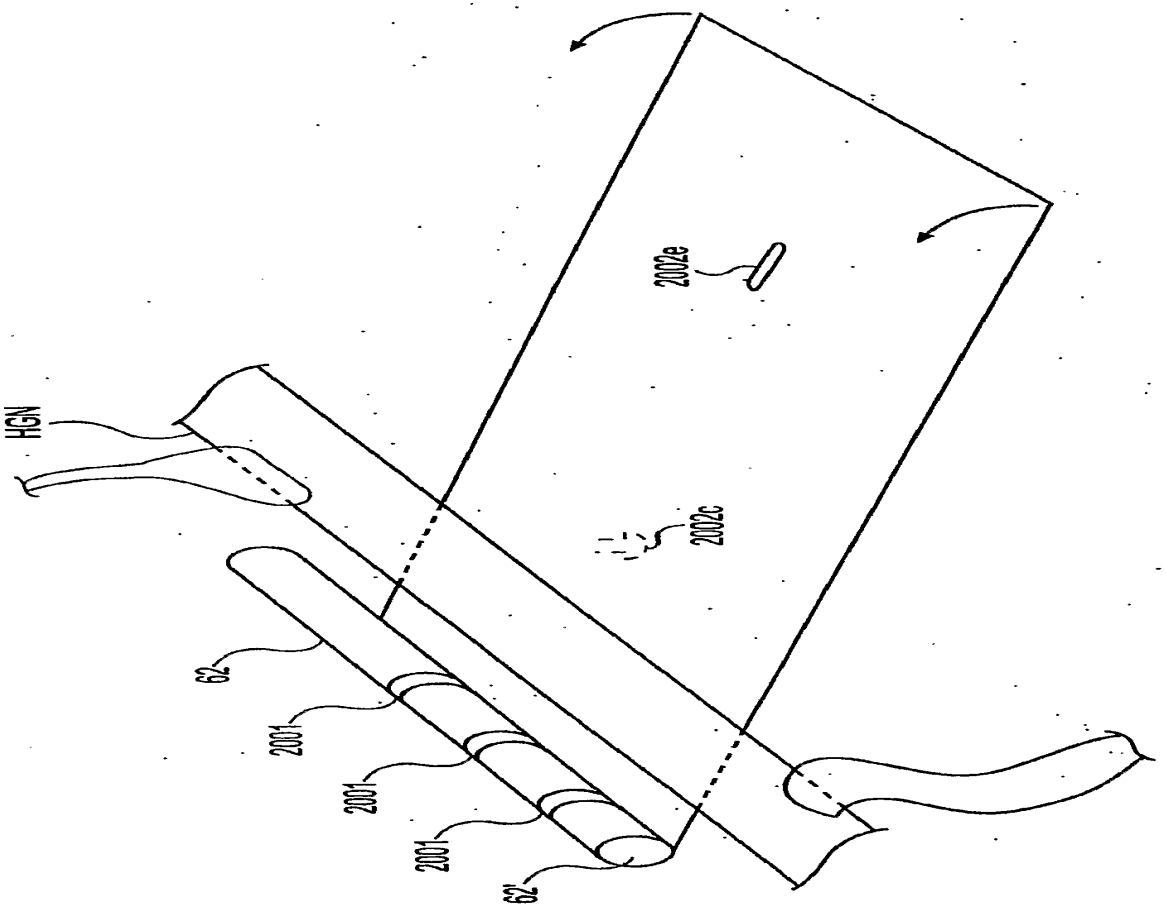


FIG. 22C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00838

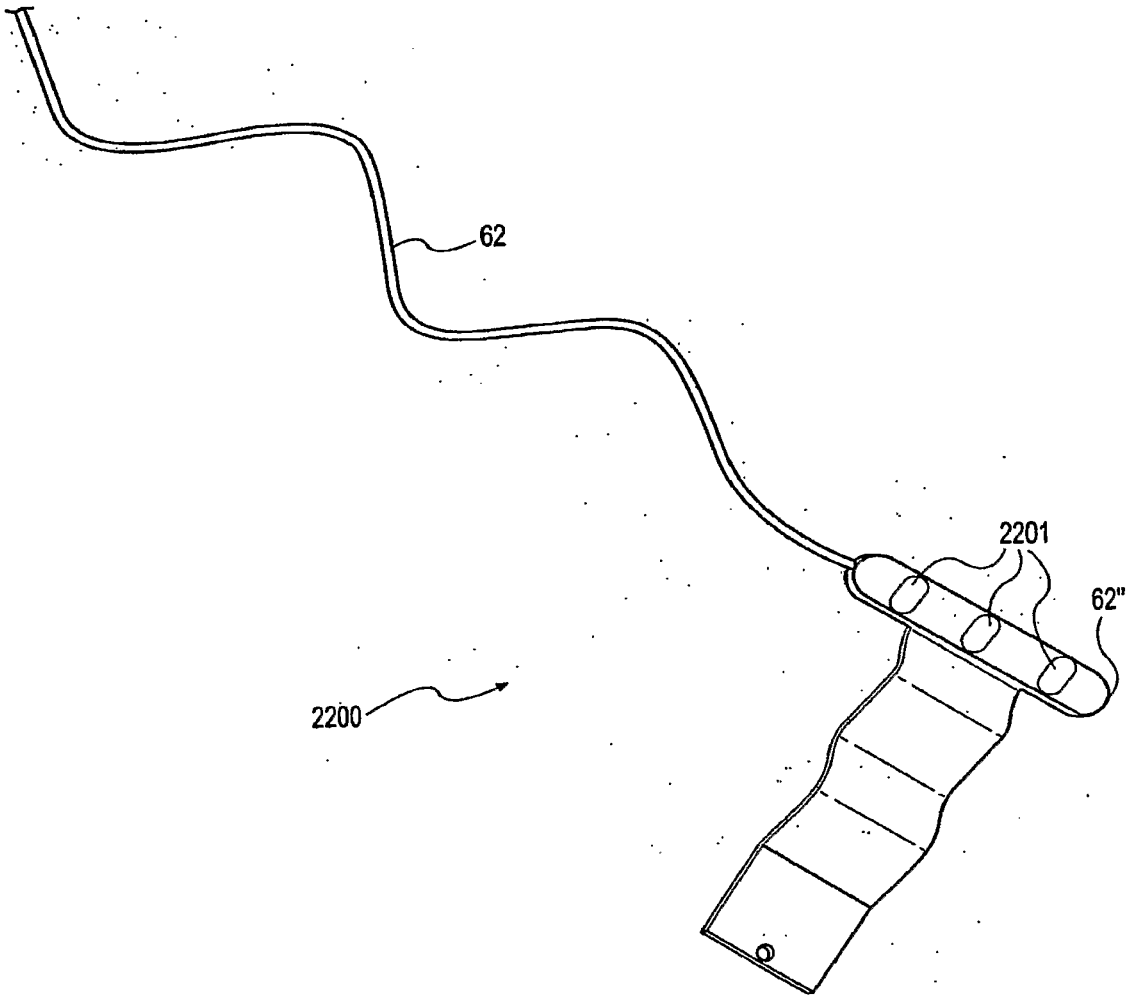


FIG. 22D

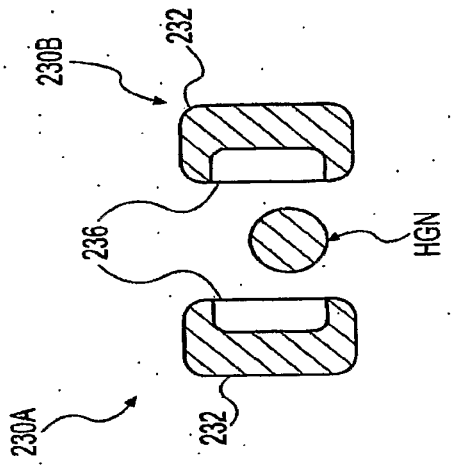


FIG. 23B

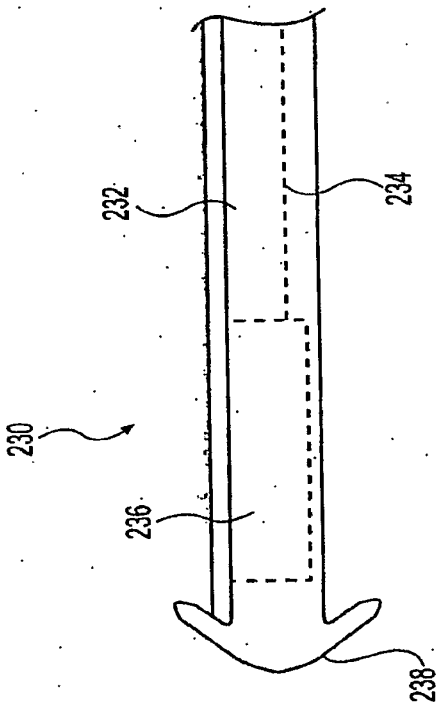


FIG. 23A

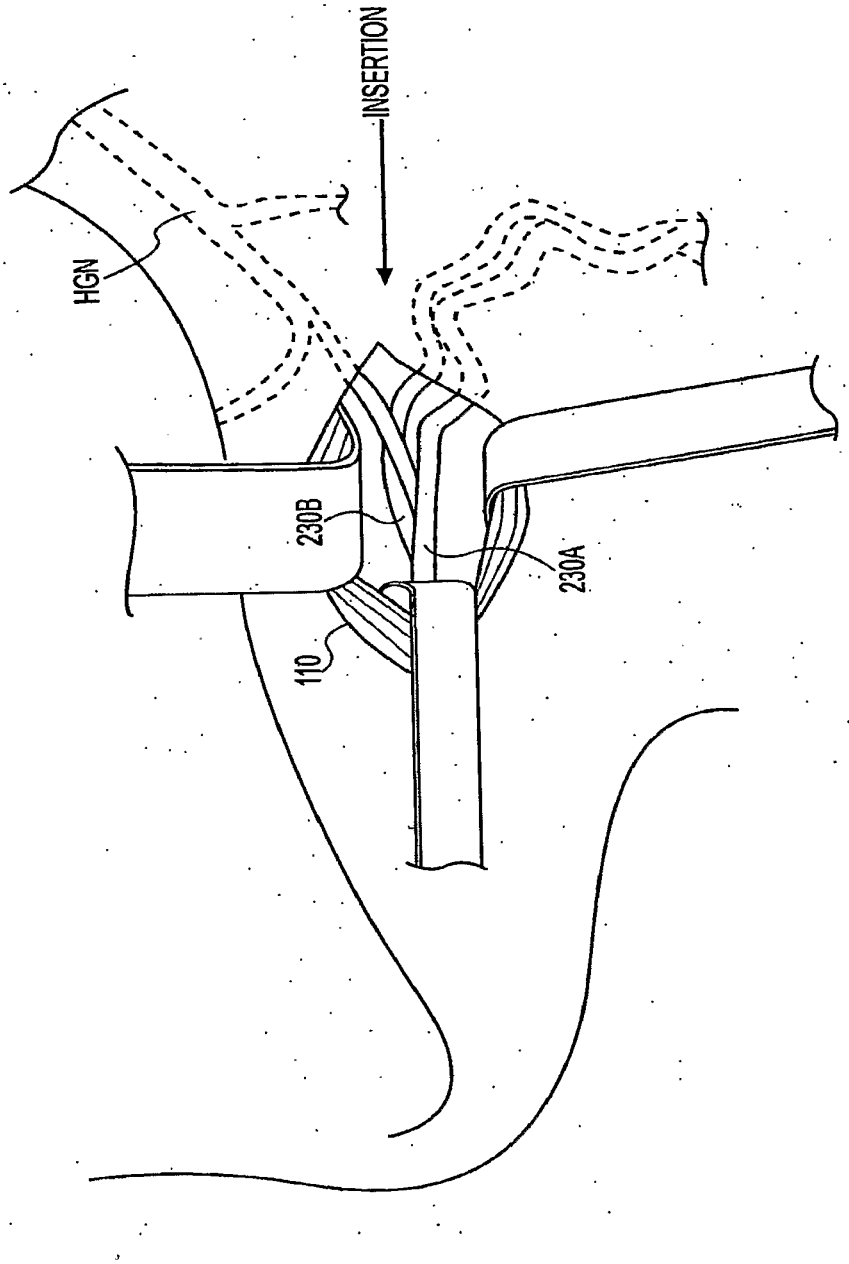


FIG. 23C

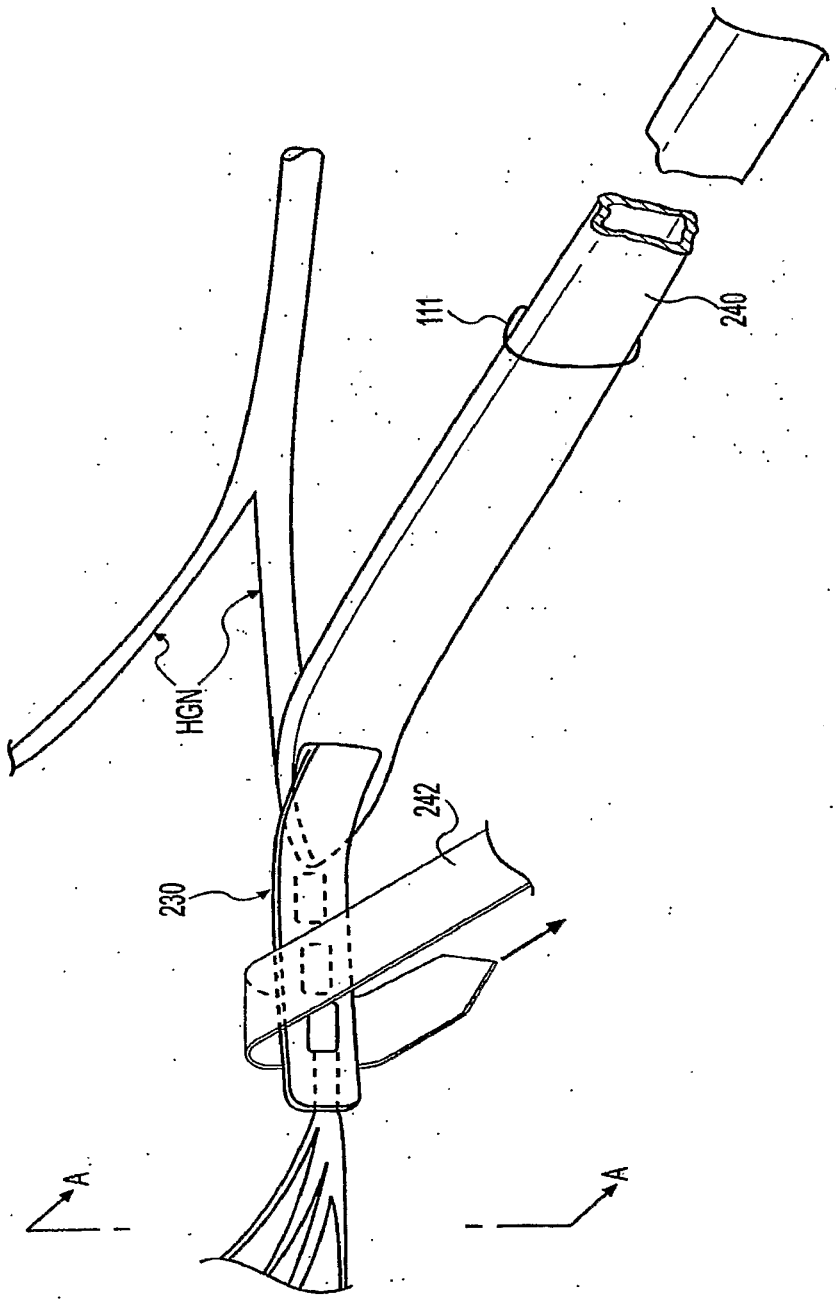


FIG. 24A

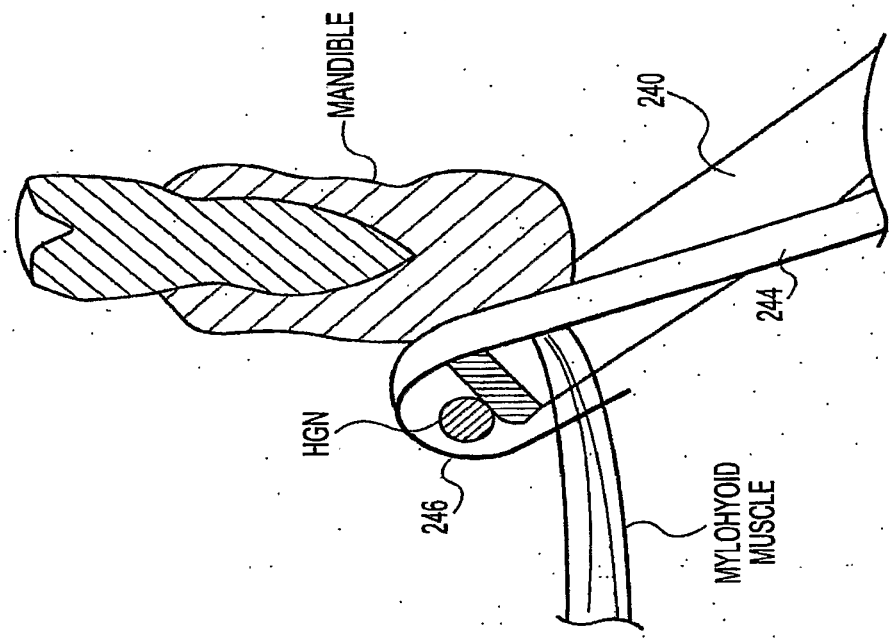


FIG. 24C

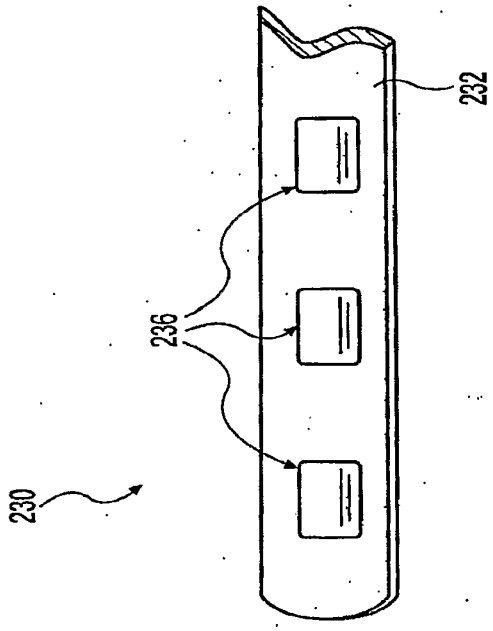


FIG. 24B

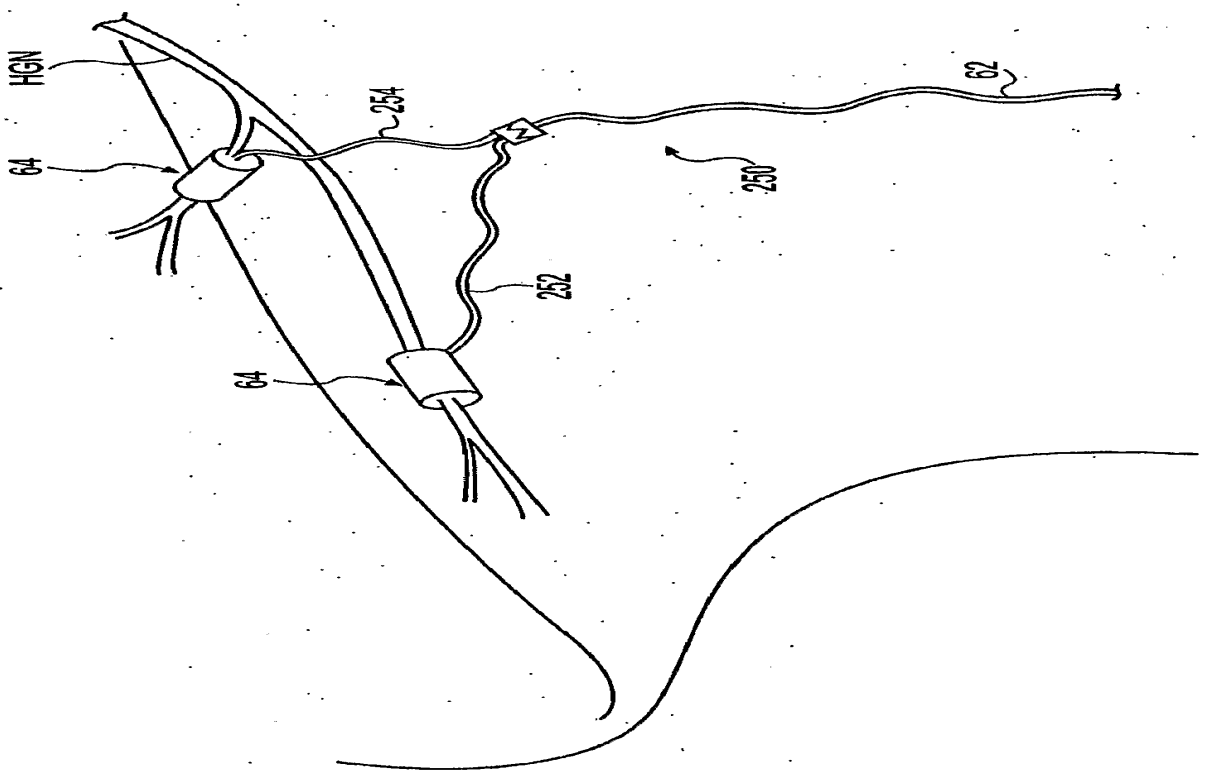


FIG. 25

Exhibit 1002
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00844

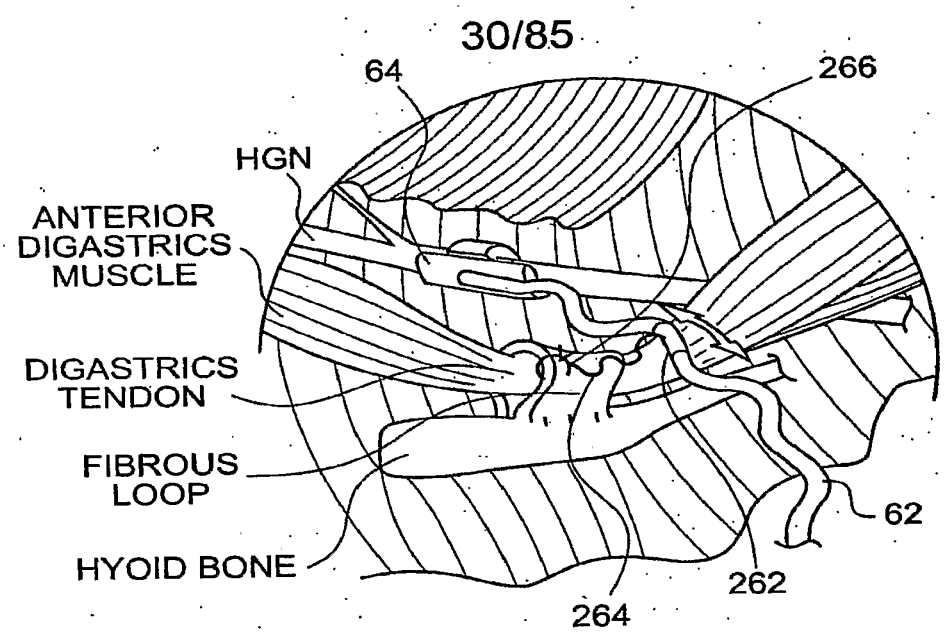


FIG. 26A

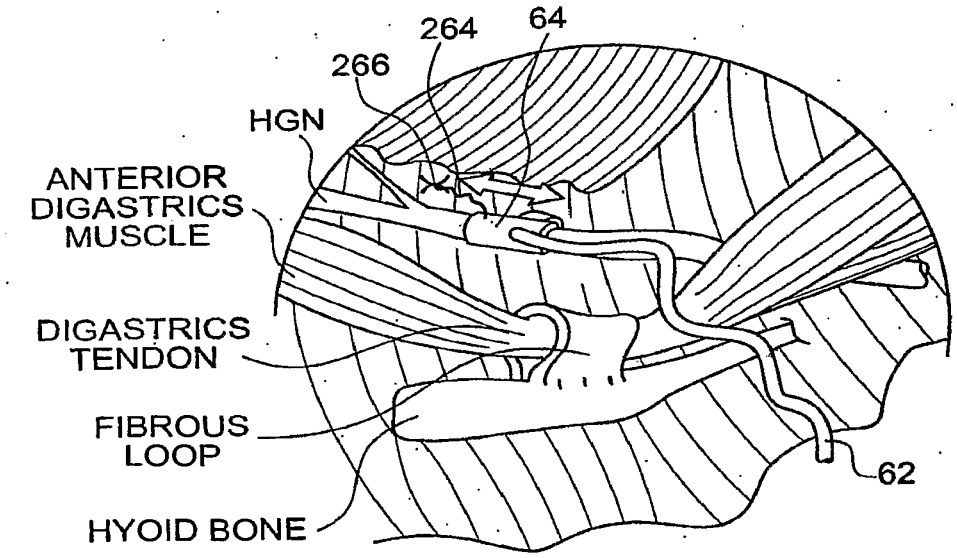


FIG. 26B

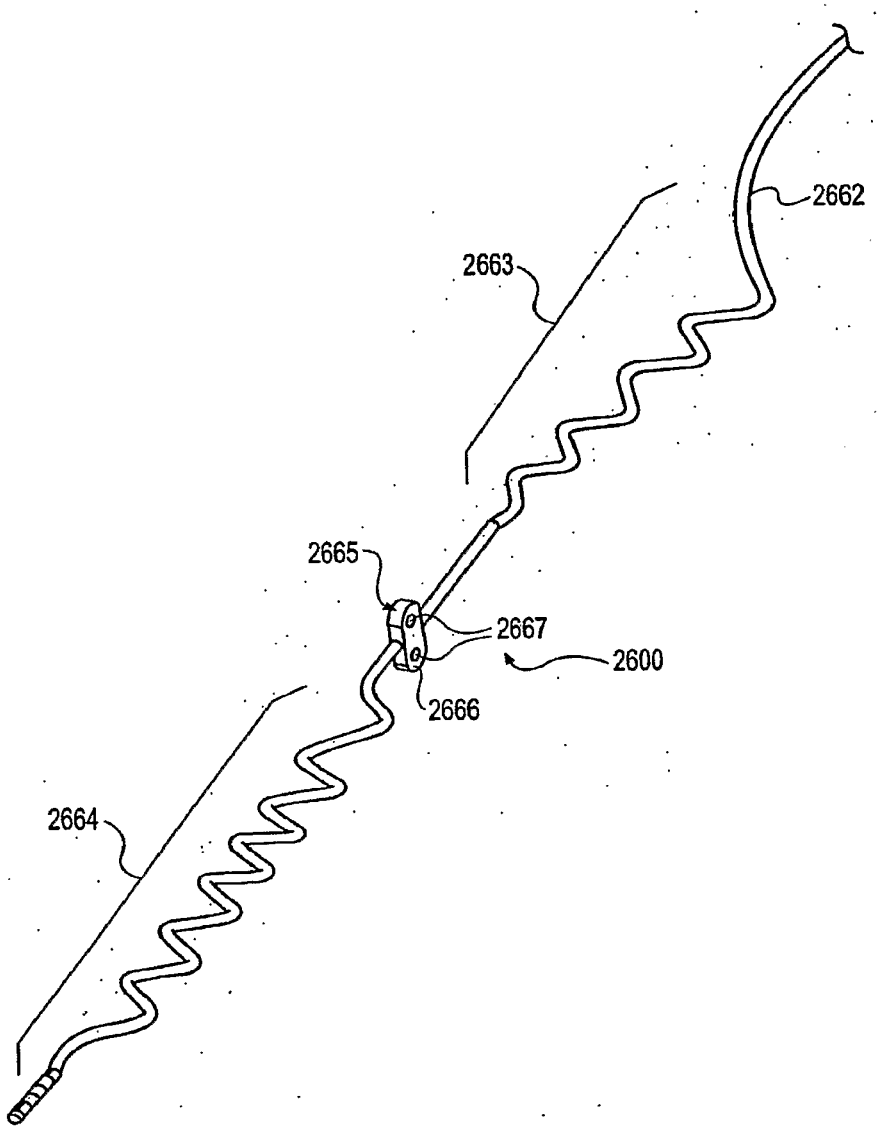


FIG. 26C

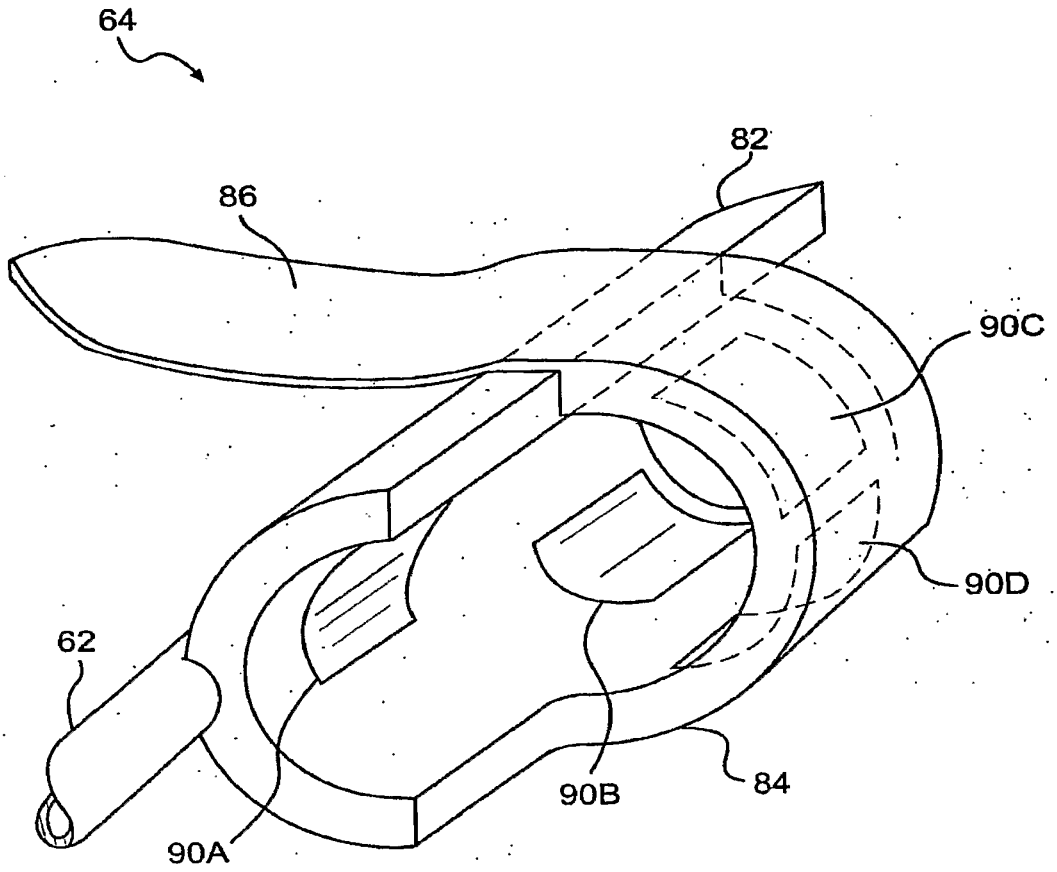


FIG. 27A

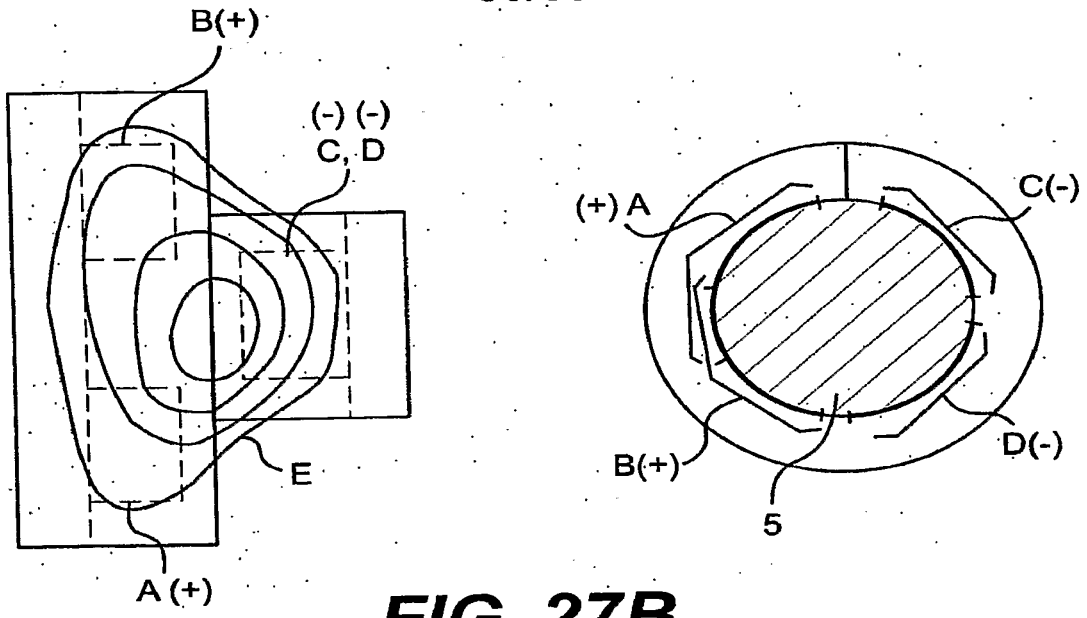


FIG. 27B

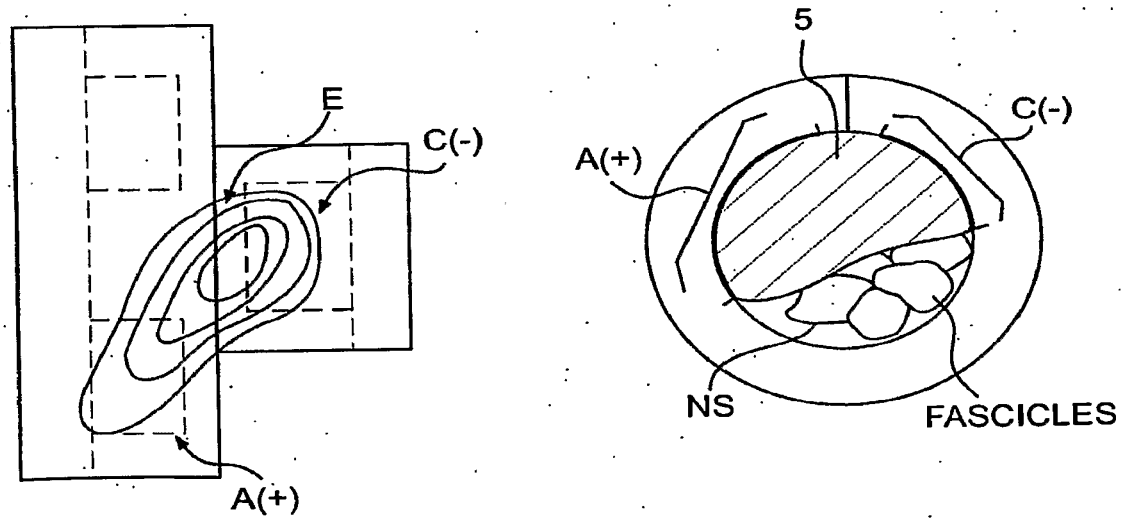


FIG. 27C

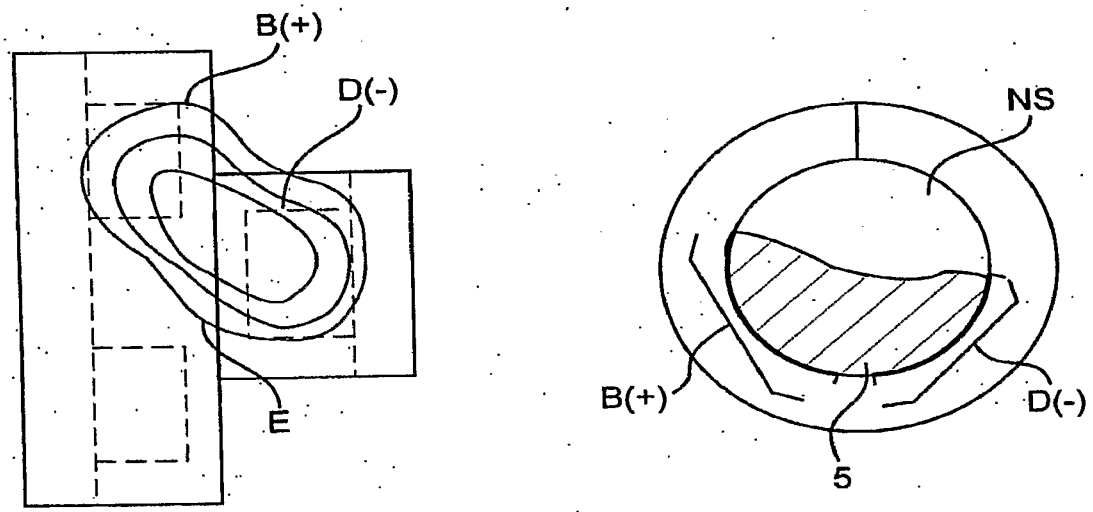


FIG. 27D

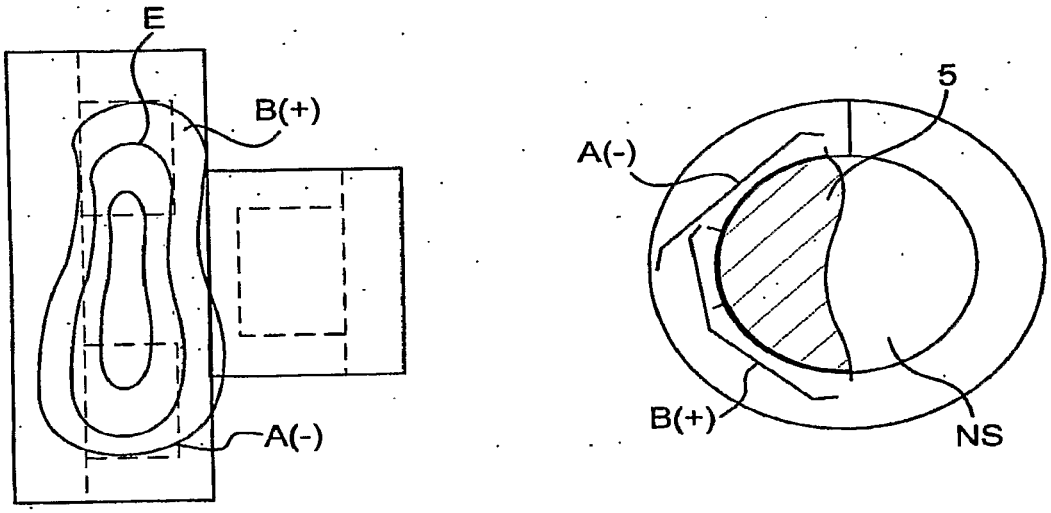


FIG. 27E

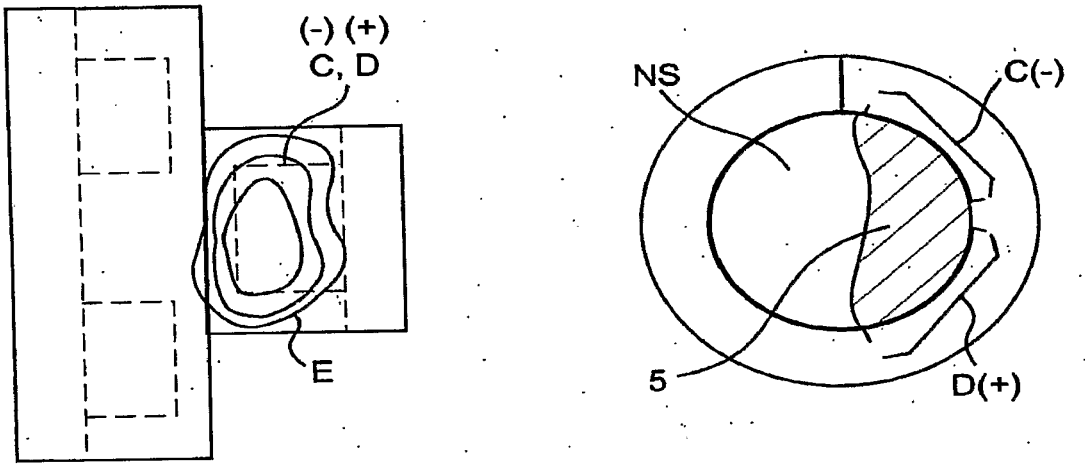


FIG. 27F

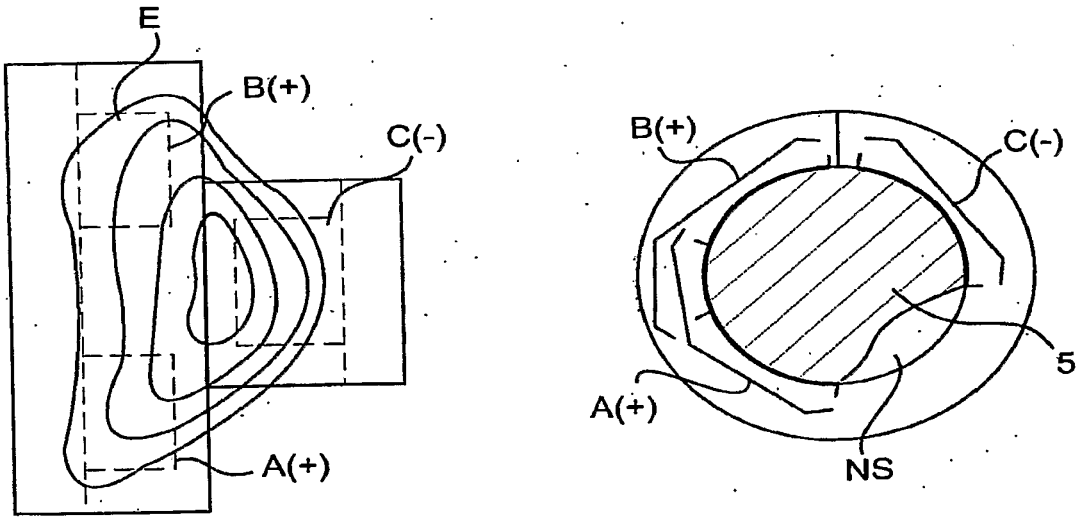


FIG. 27G

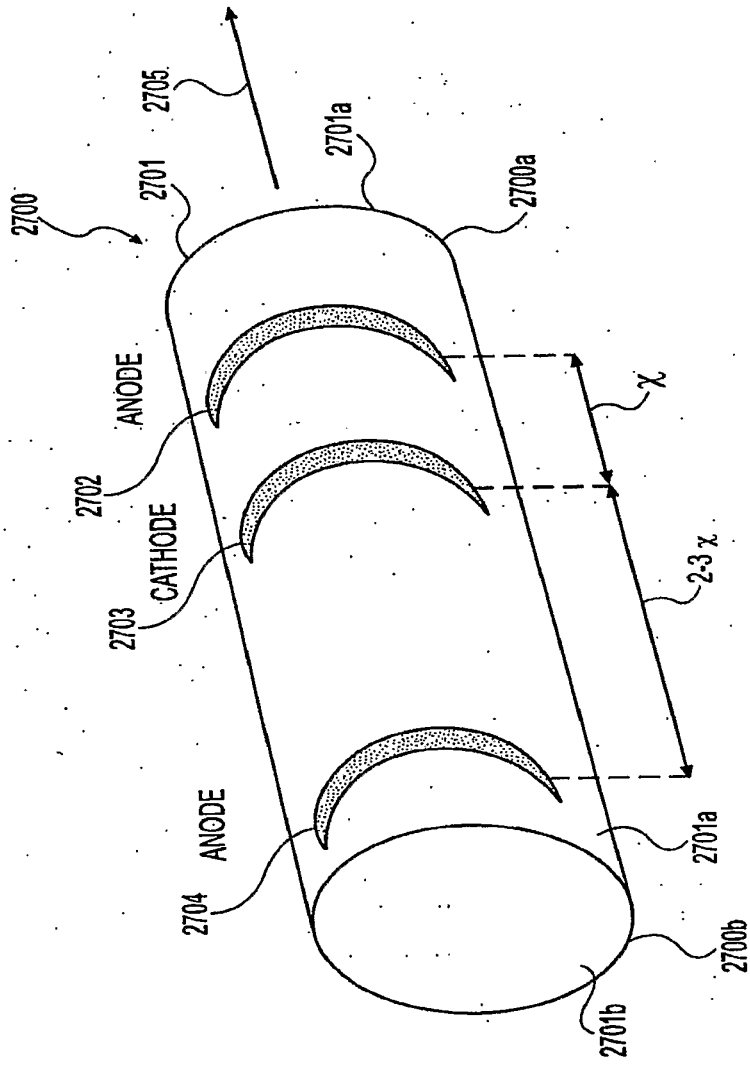

2705
2701a
2701
2700a
2700
ANODE
2702
CATHODE
2703
ANODE
2704
2701a
2700b
2701b
x
2-3 x

FIG. 27H

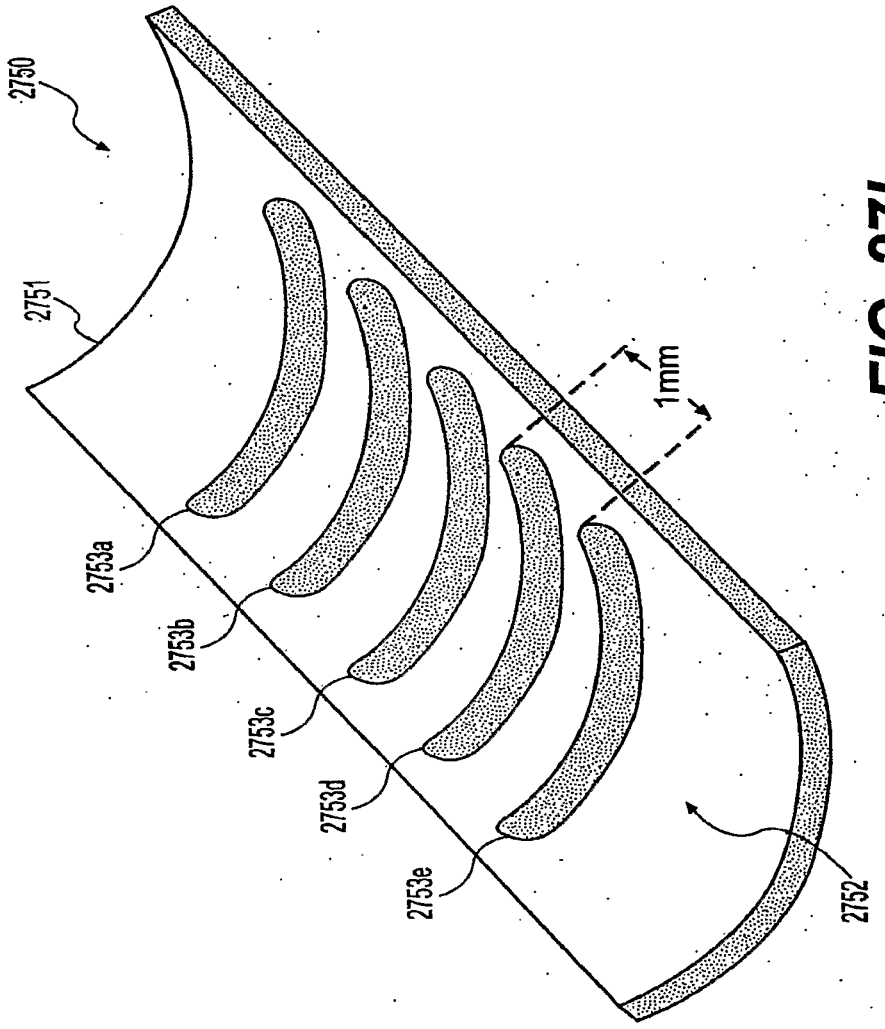


FIG. 27I

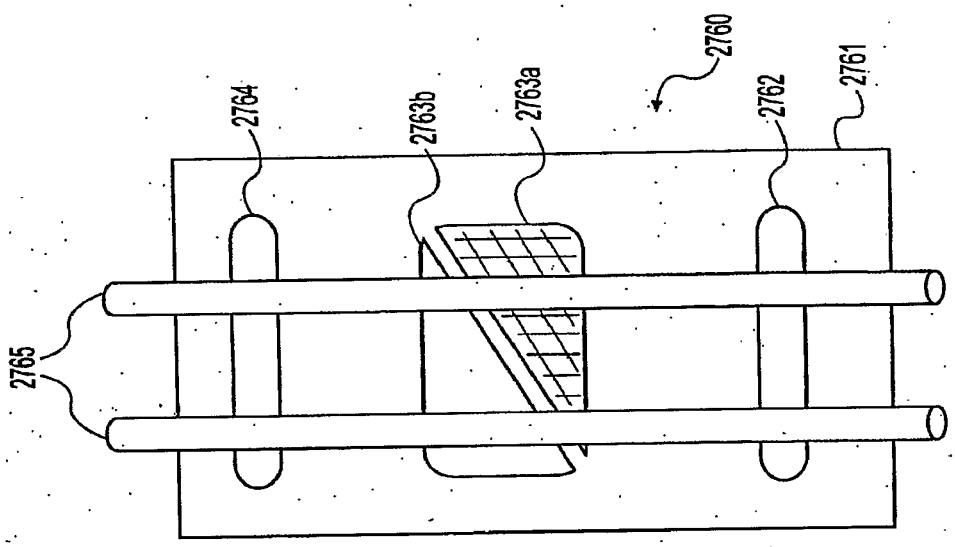


FIG. 27K

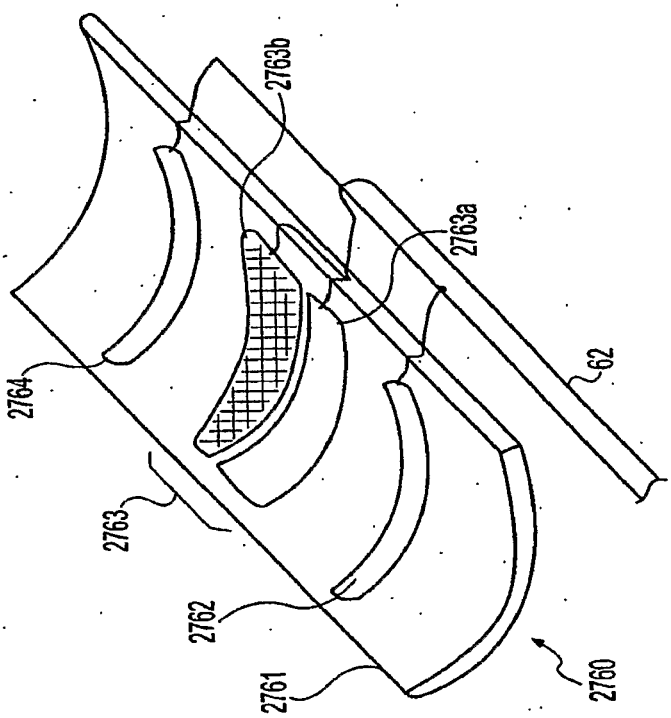


FIG. 27J

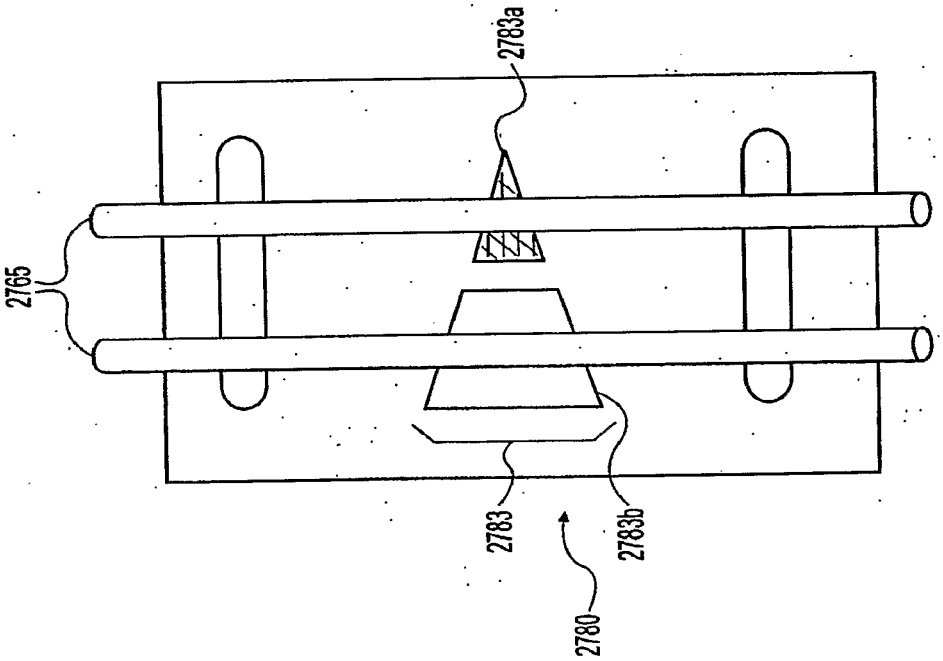


FIG. 27L

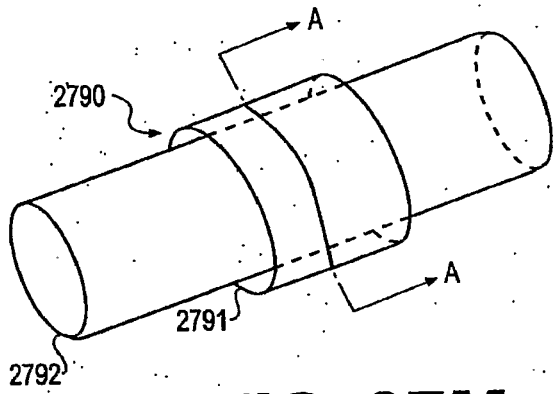


FIG. 27M

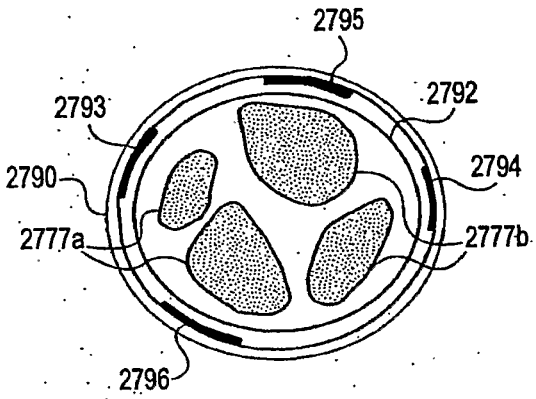


FIG. 27N

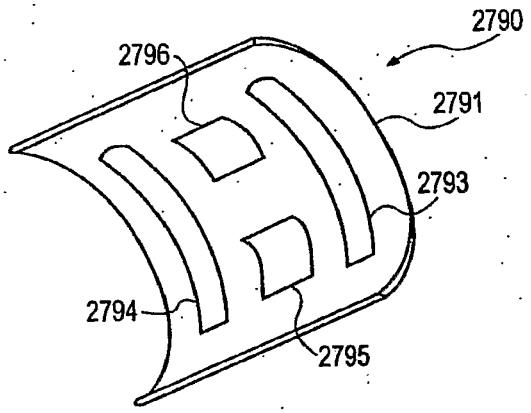


FIG. 27O

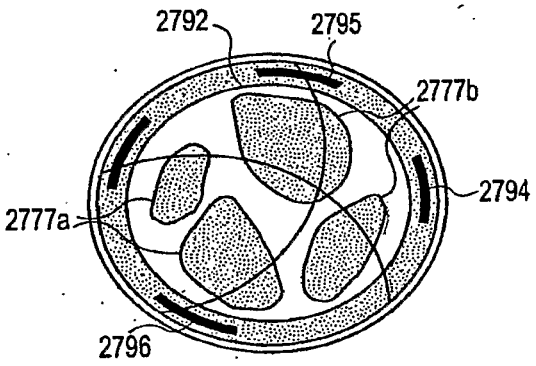


FIG. 27P

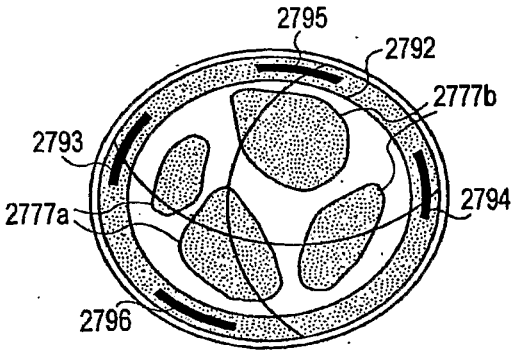


FIG. 27Q

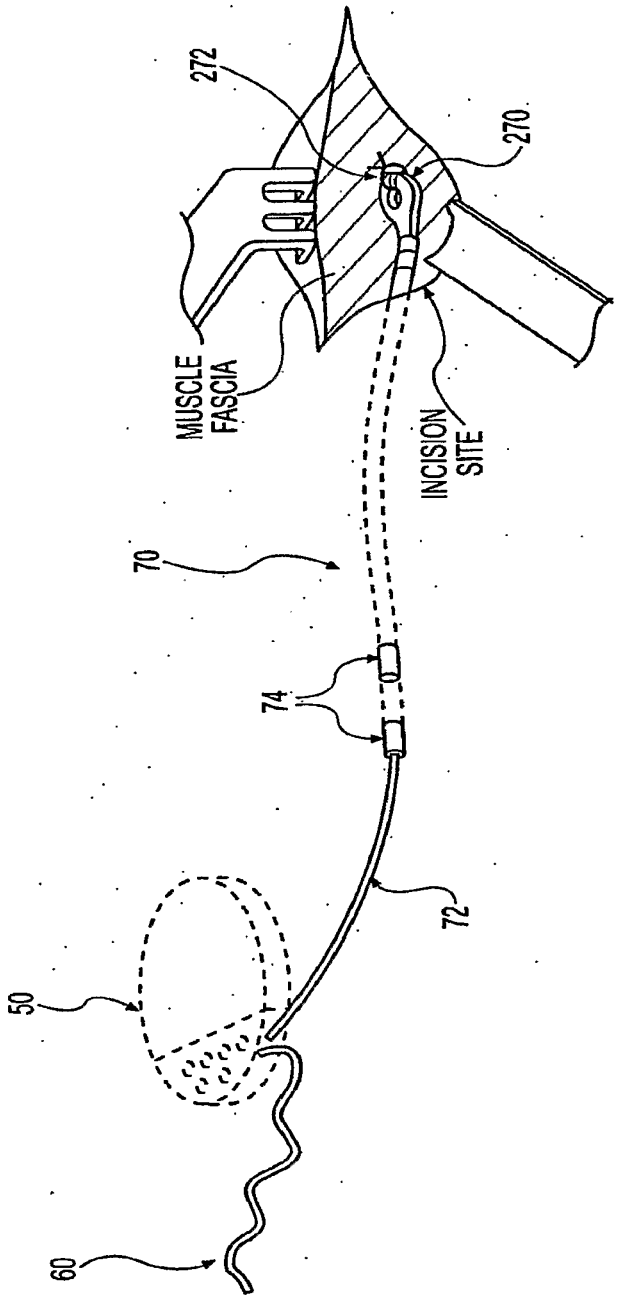


FIG. 28

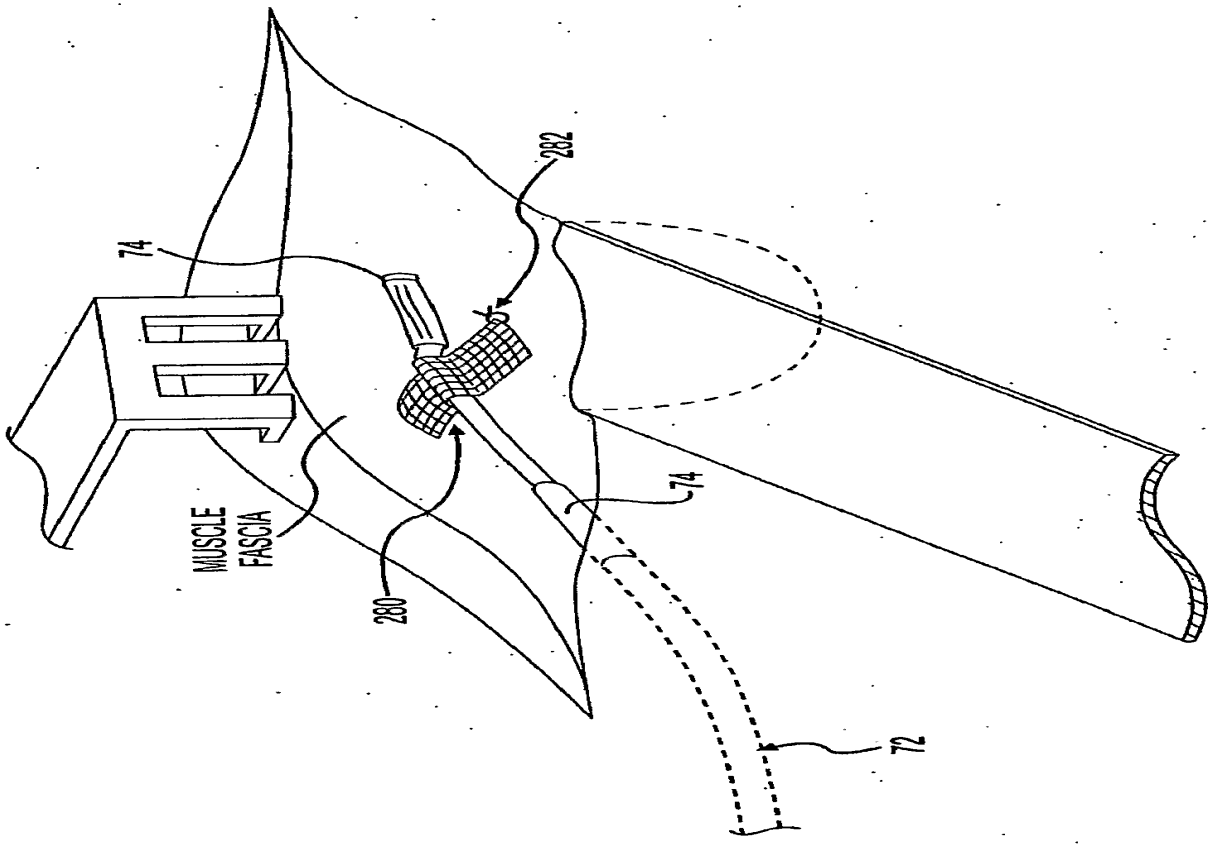


FIG. 29A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00857

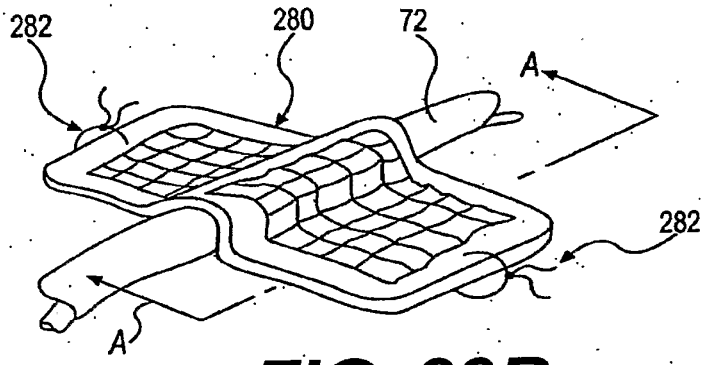


FIG. 29B

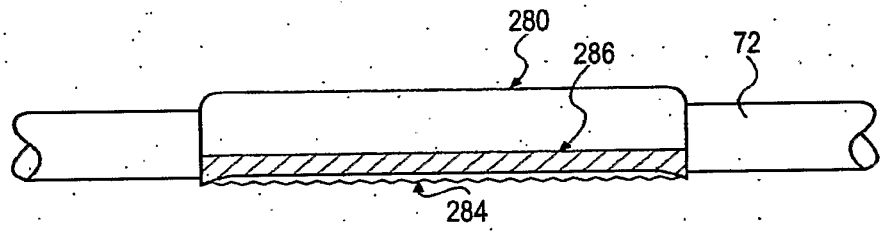


FIG. 29C

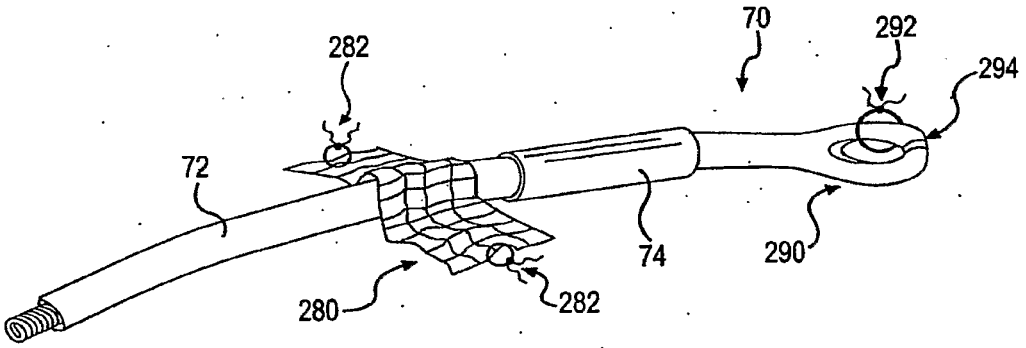


FIG. 30

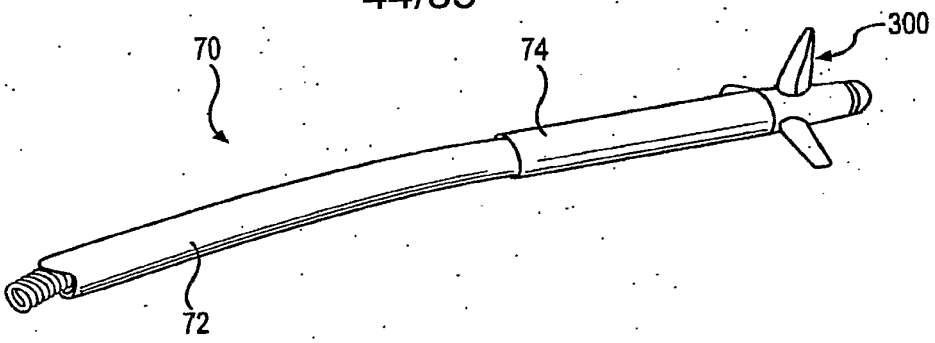


FIG. 31A

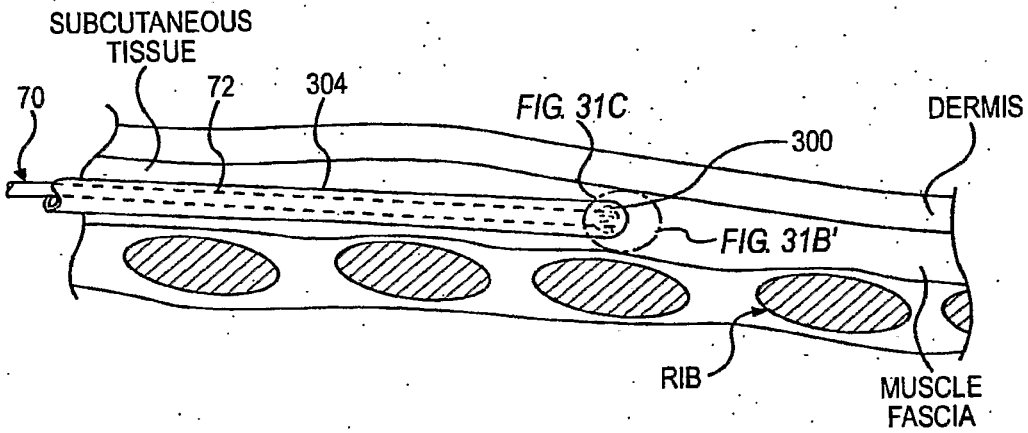


FIG. 31B

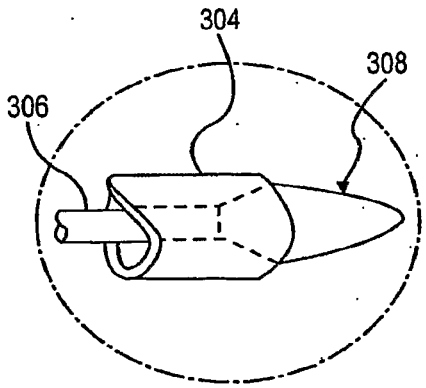


FIG. 31B'

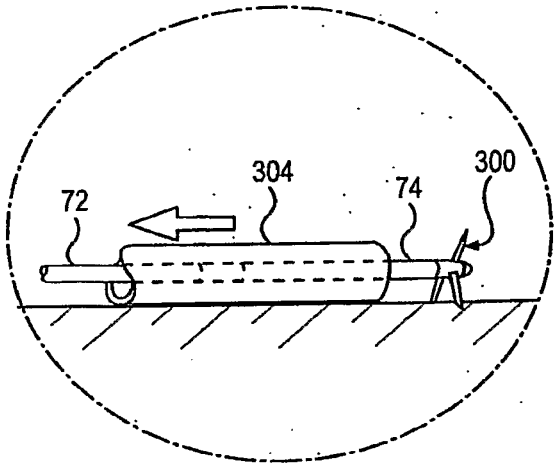


FIG. 31C

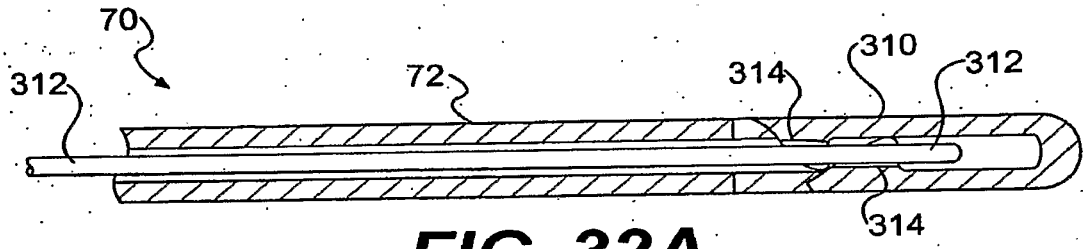


FIG. 32A

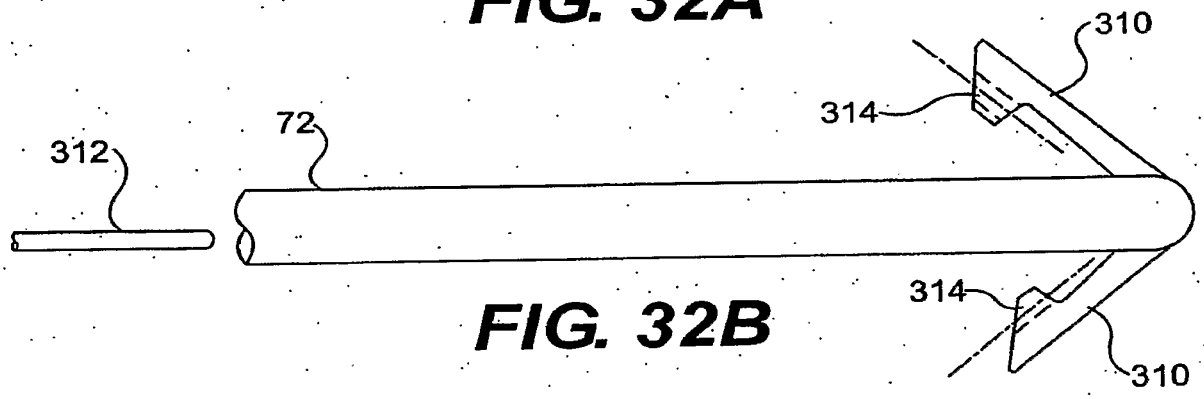


FIG. 32B

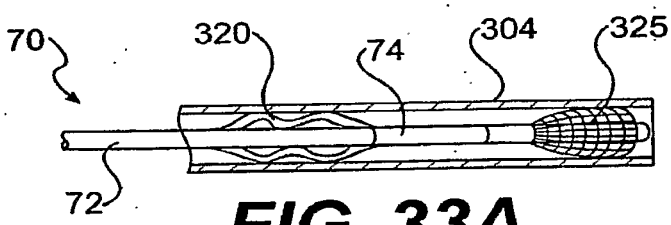


FIG. 33A

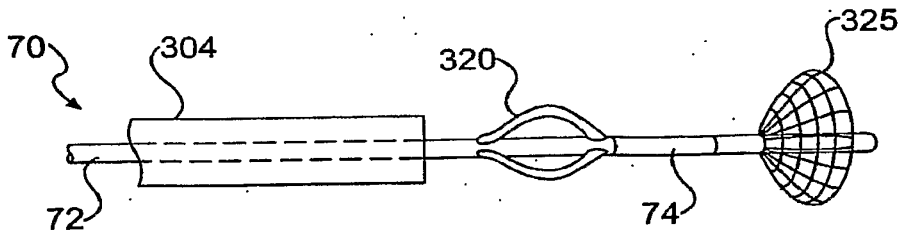


FIG. 33B

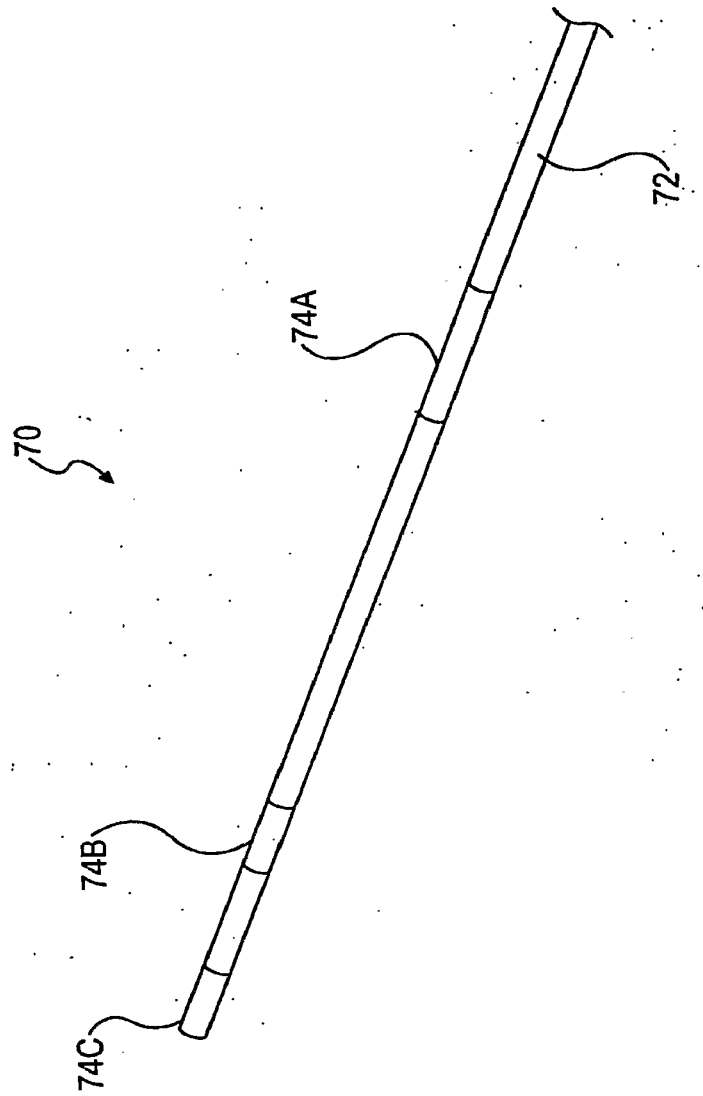


FIG. 34

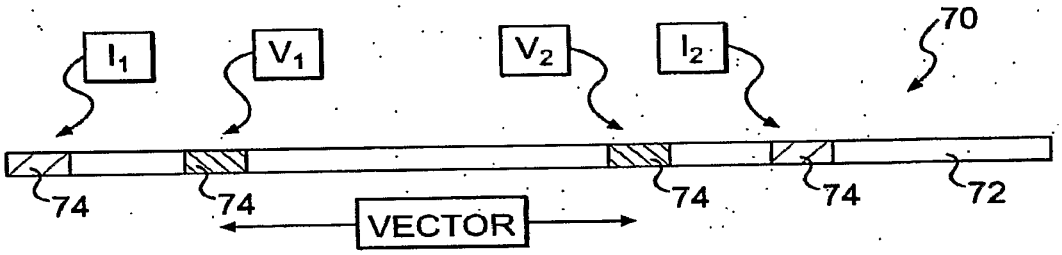


FIG. 35A

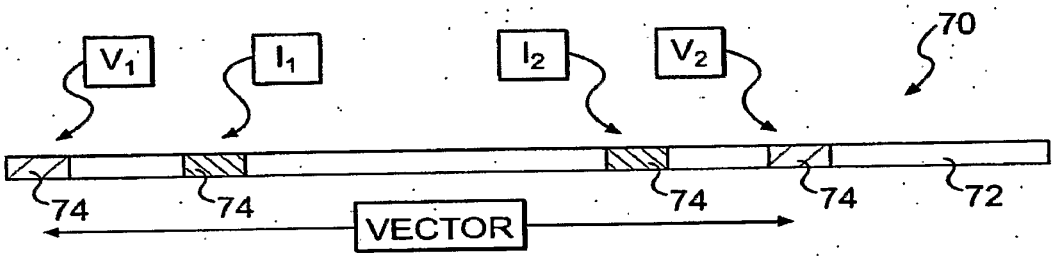


FIG. 35B

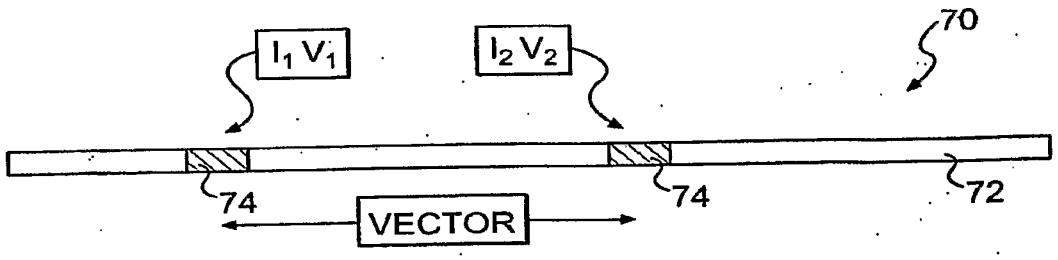


FIG. 35C

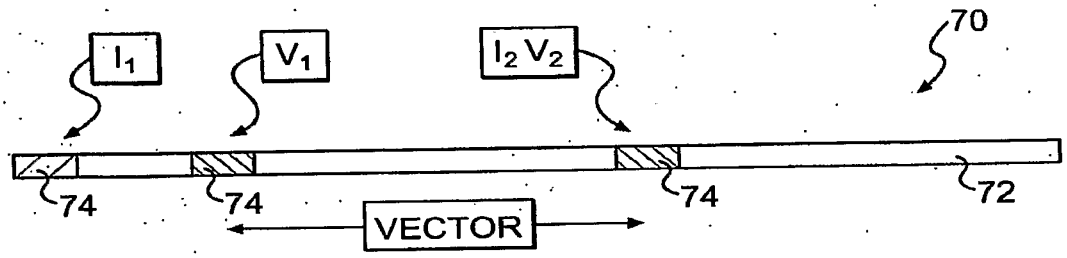


FIG. 35D

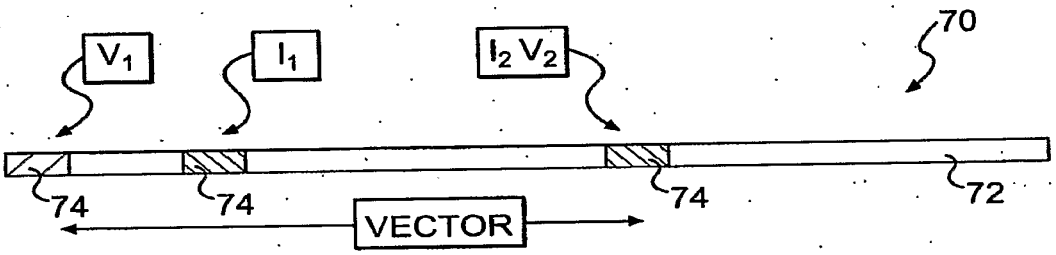


FIG. 35E

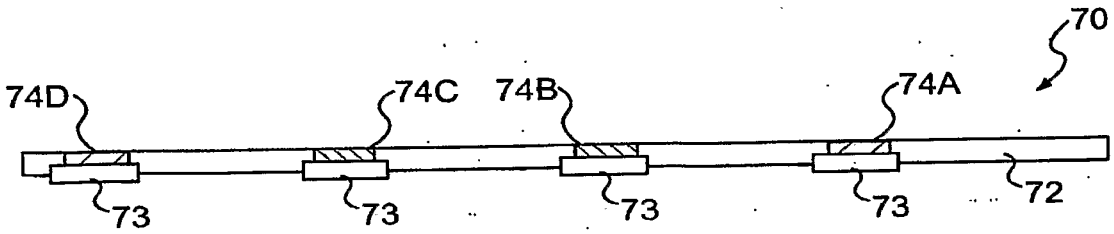


FIG. 36

PULSE GENERATOR LOCATION
PROXIMAL COMBINATION ELECTRODE
DISTAL VOLTAGE-SENSING ELECTRODE
DISTAL CURRENT-CARRYING ELECTRODE
PULSE GENERATOR LOCATION
DISTAL VOLTAGE-SENSING ELECTRODE
PROXIMAL COMBINATION ELECTRODE
DISTAL CURRENT-CARRYING ELECTRODE

FIG. 37

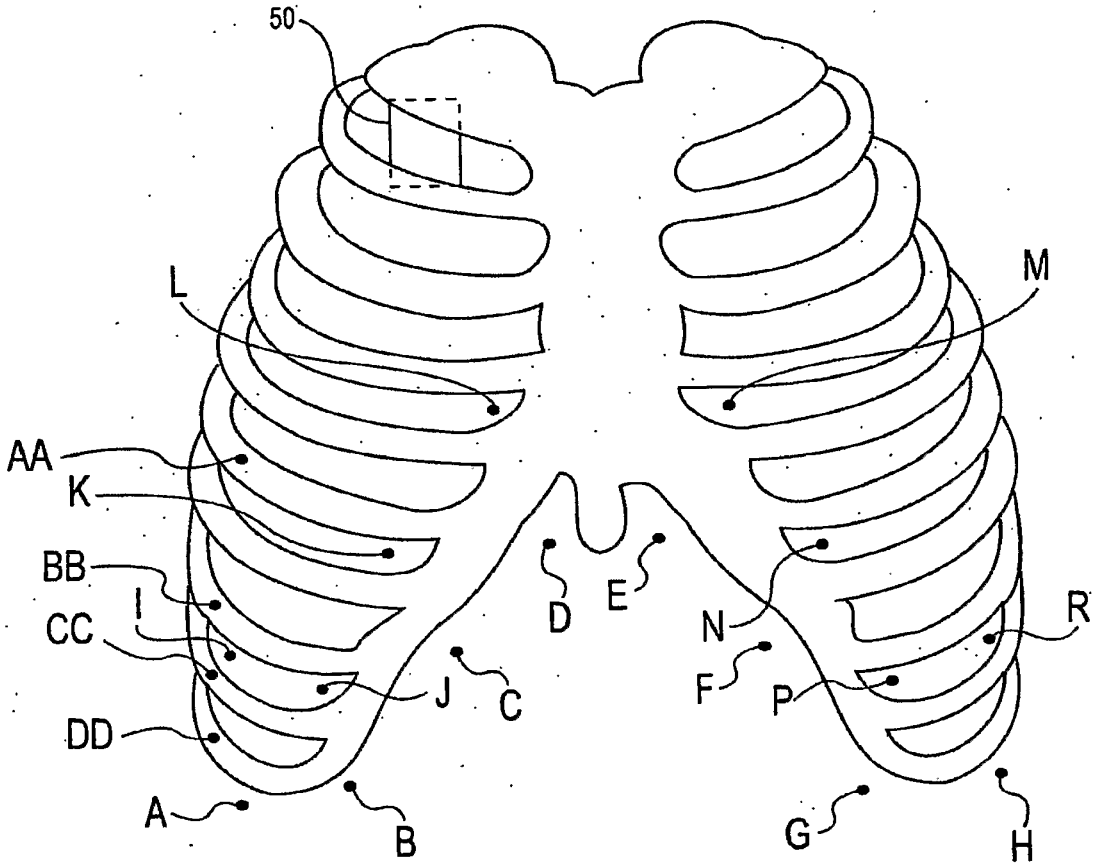


FIG. 37A

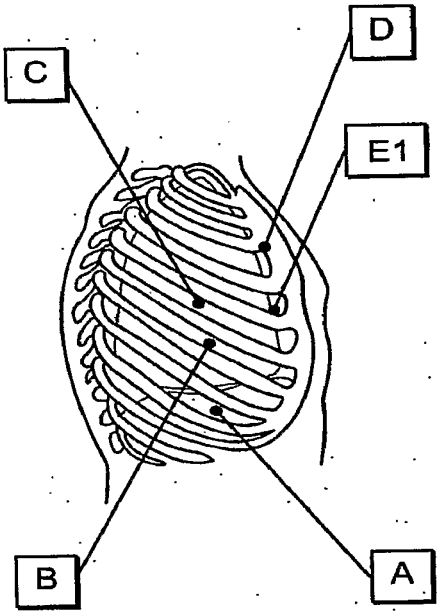


FIG. 37B

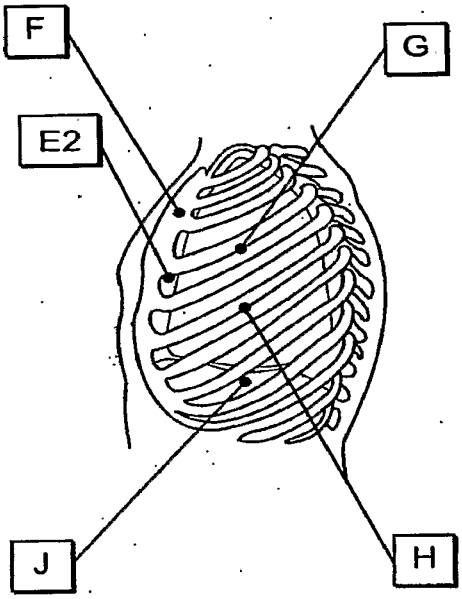


FIG. 37C

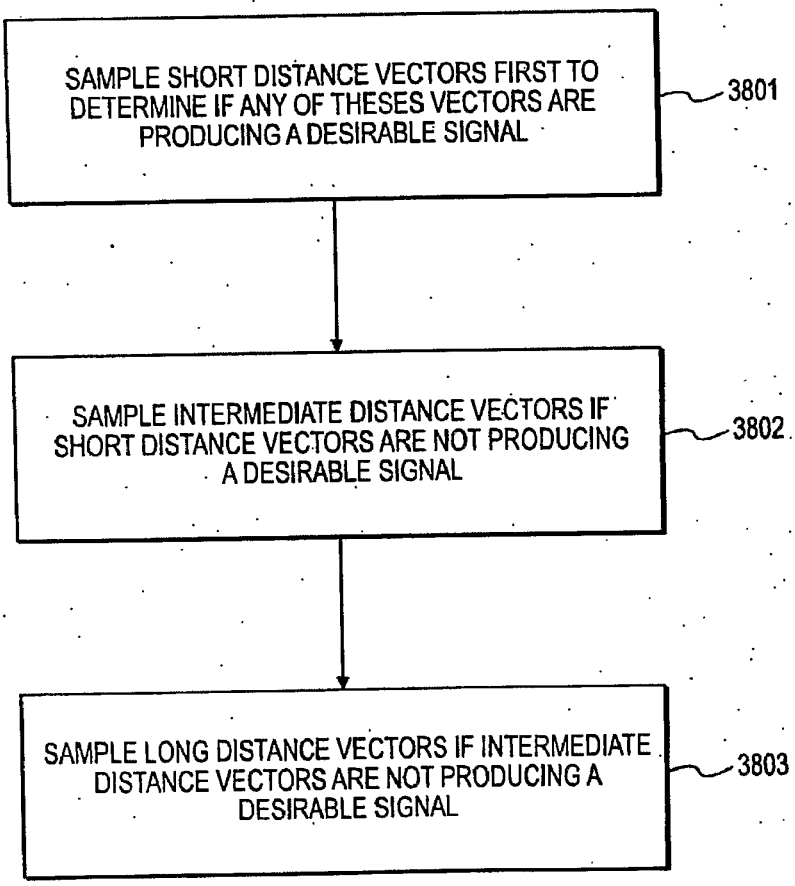

SAMPLE SHORT DISTANCE VECTORS FIRST TO DETERMINE IF ANY OF THESES VECTORS ARE PRODUCING A DESIRABLE SIGNAL
3801
SAMPLE INTERMEDIATE DISTANCE VECTORS IF SHORT DISTANCE VECTORS ARE NOT PRODUCING A DESIRABLE SIGNAL
3802
SAMPLE LONG DISTANCE VECTORS IF INTERMEDIATE DISTANCE VECTORS ARE NOT PRODUCING A DESIRABLE SIGNAL
3803

FIG. 38A

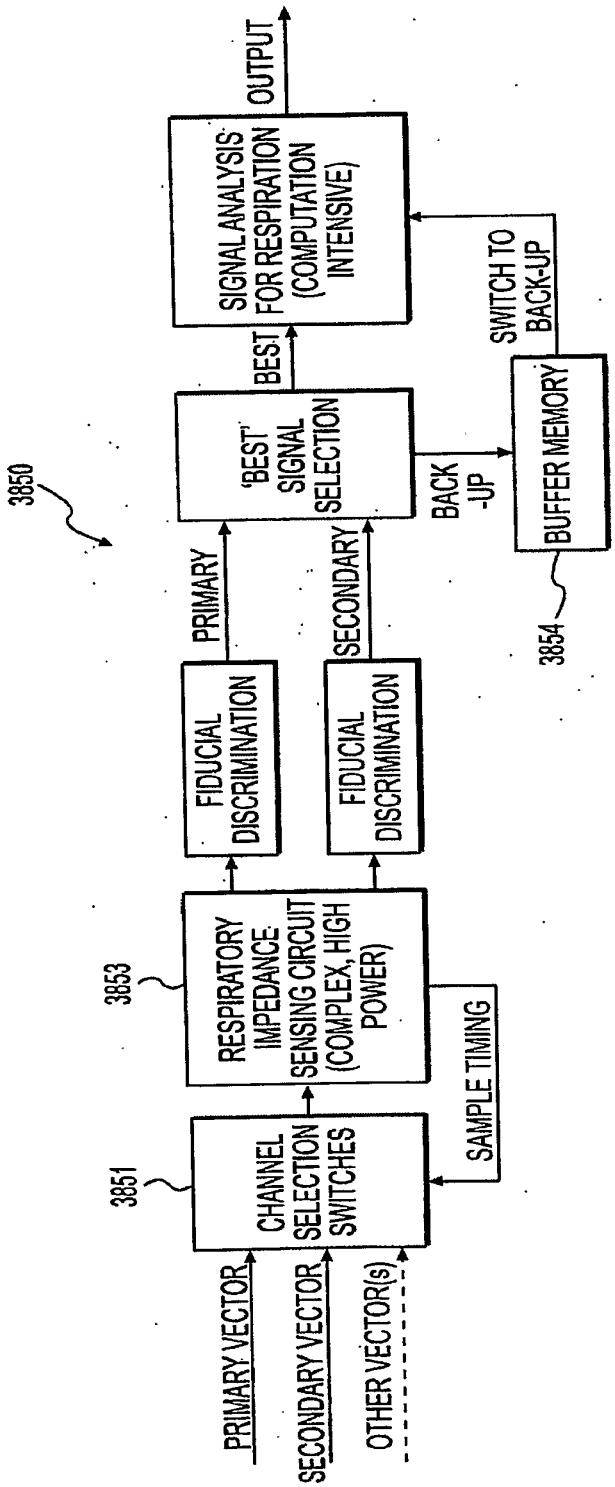


FIG. 38B

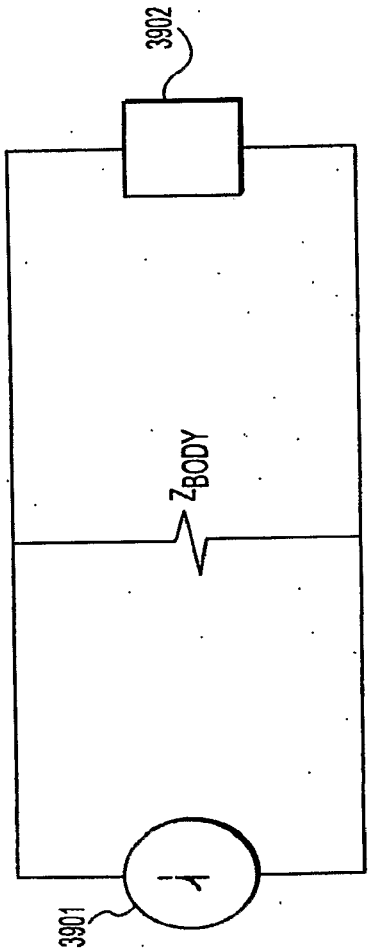


FIG. 38C

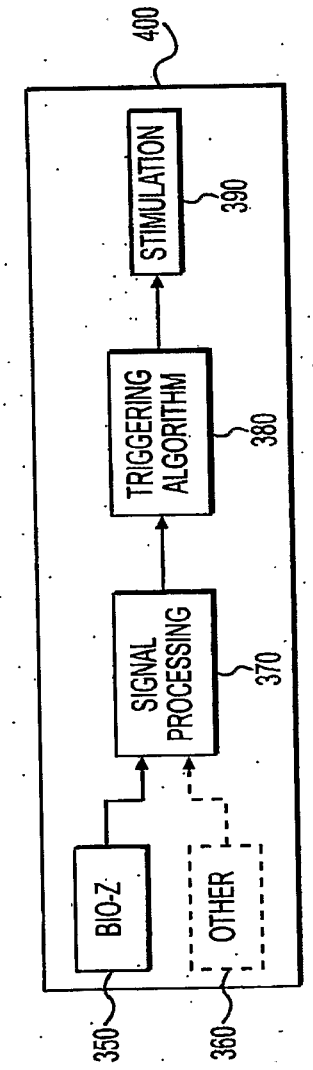

400
STIMULATION
390
TRIGGERING ALGORITHM
380
SIGNAL PROCESSING
370
BIO-Z
OTHER
350
360

FIG. 39

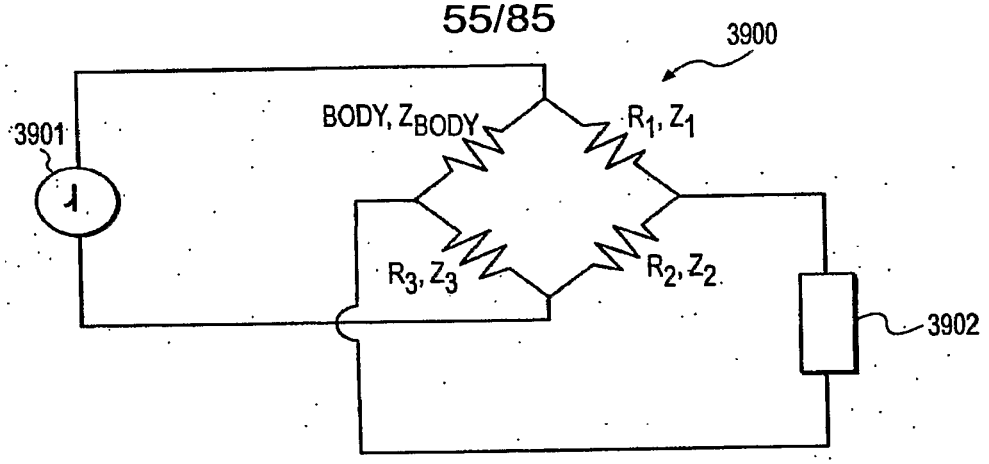


FIG. 39A

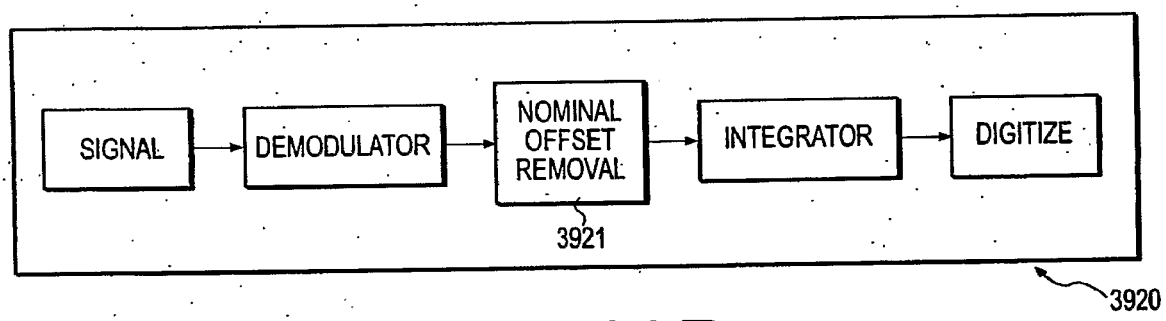


FIG. 39B

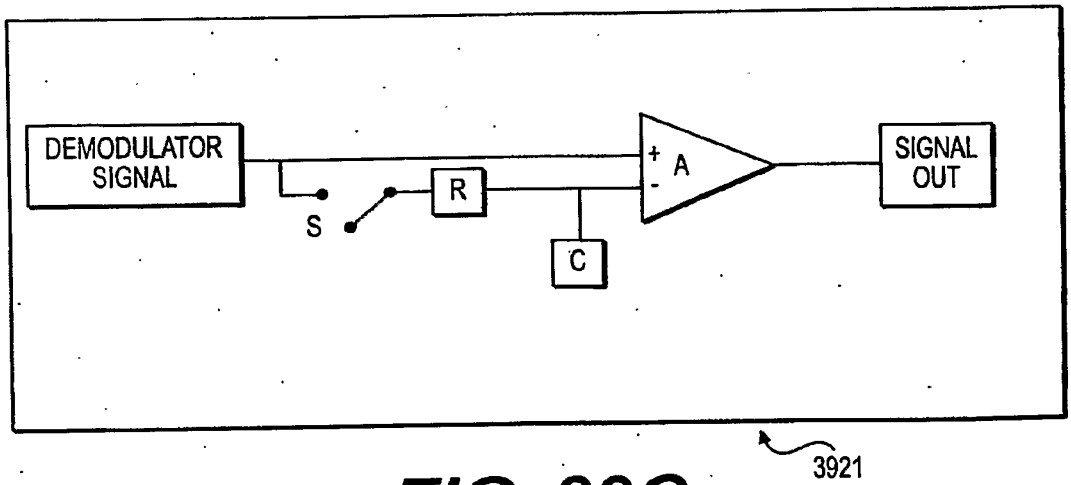


FIG. 39C

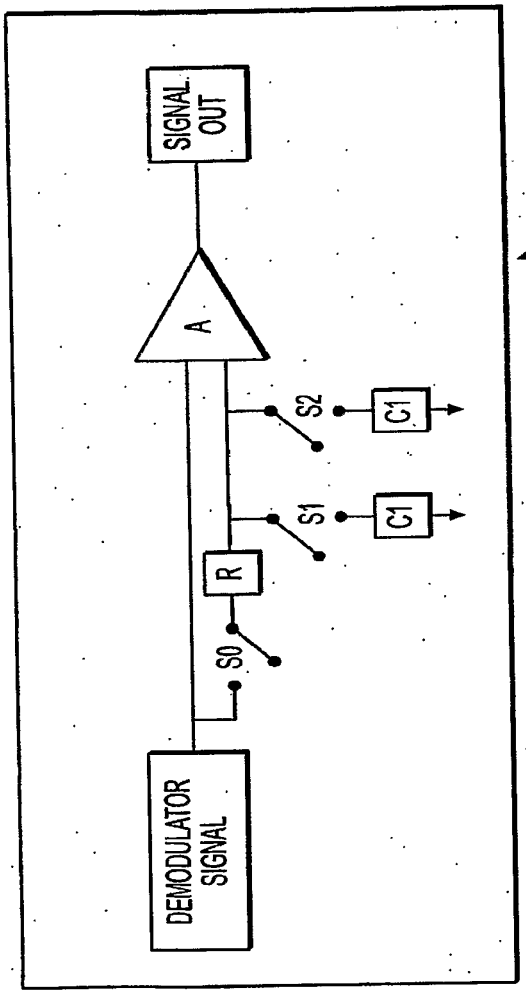


FIG. 39D

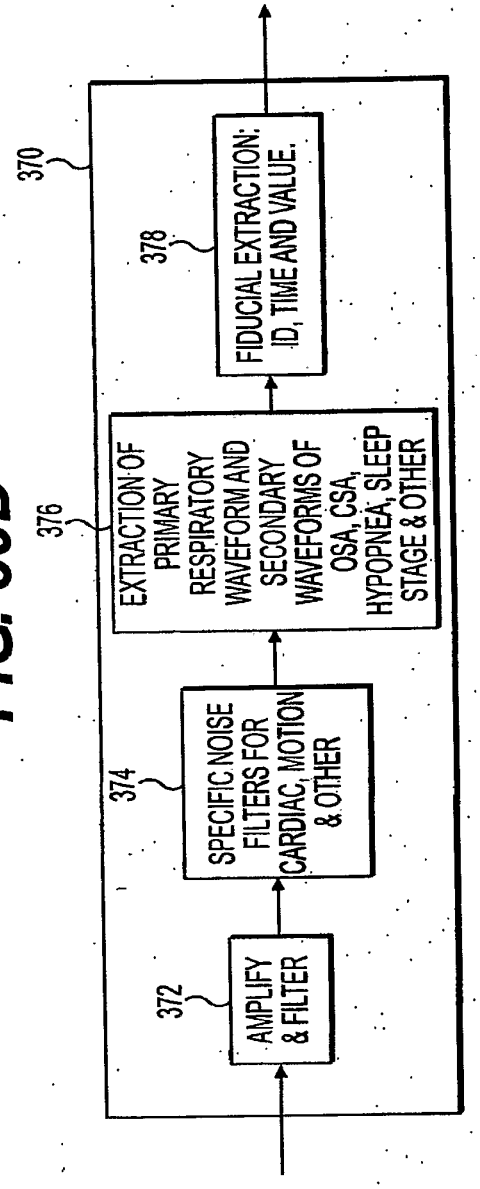


FIG. 40

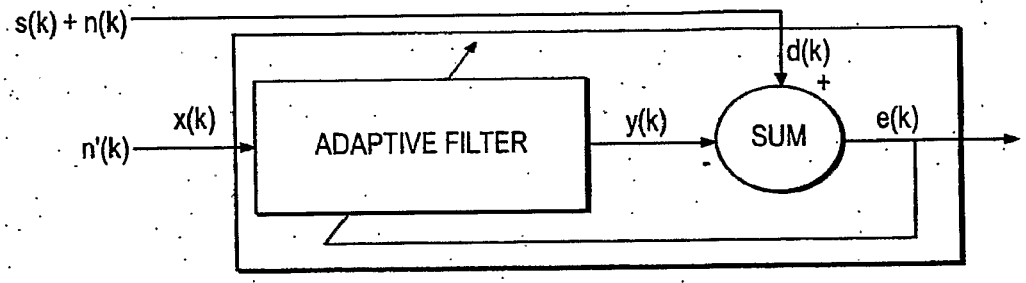


FIG. 41

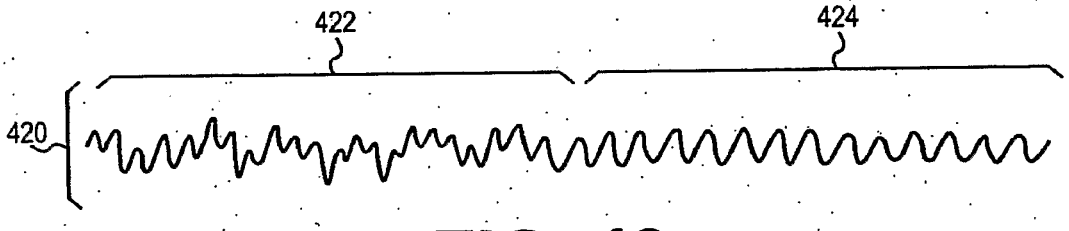


FIG. 42

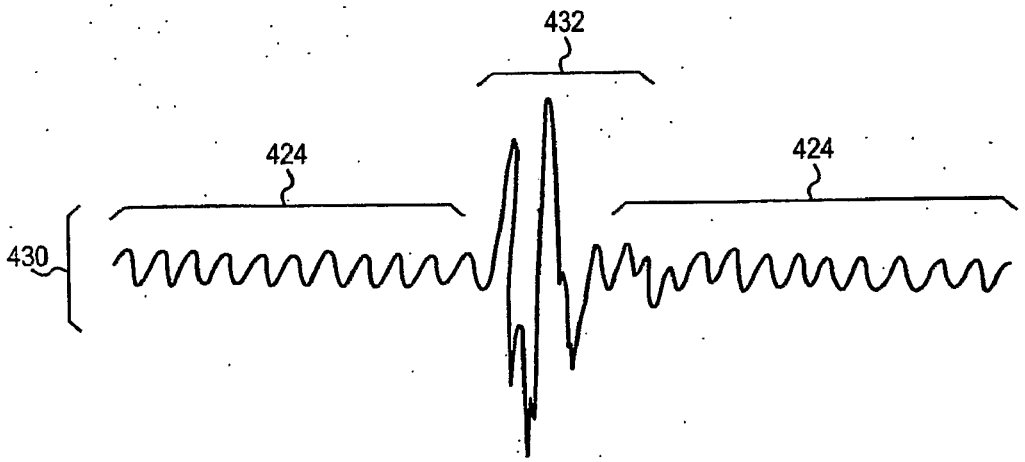


FIG. 43

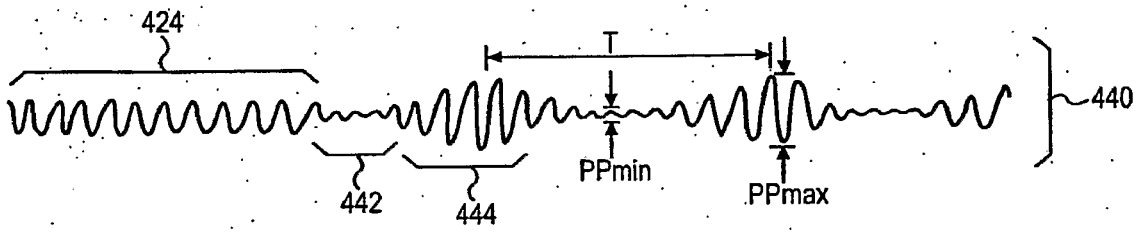


FIG. 44

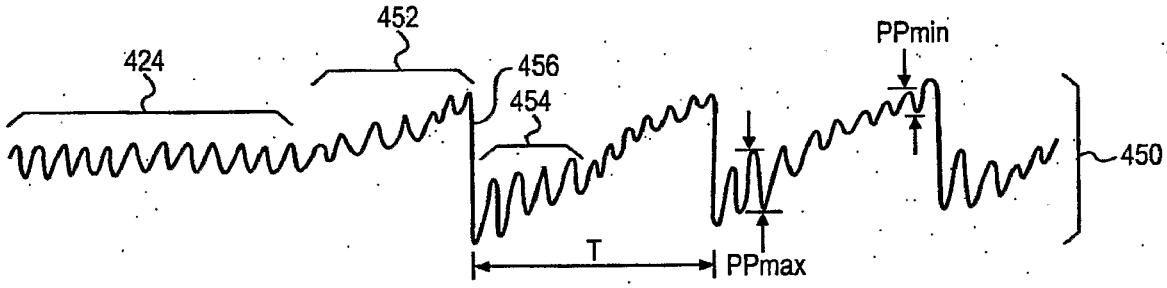


FIG. 45

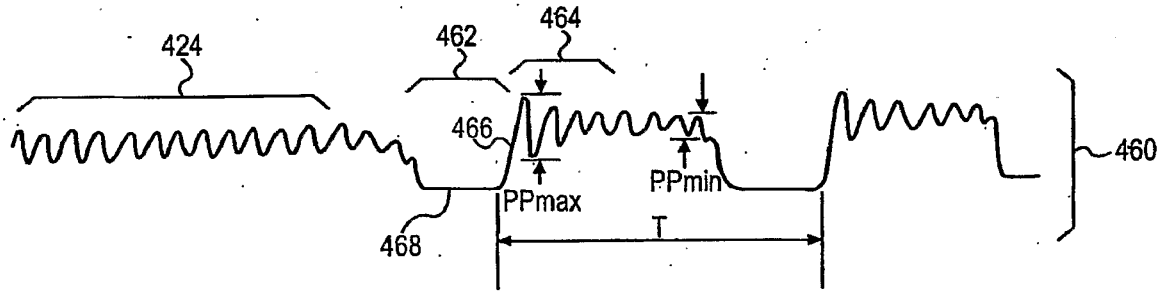


FIG. 46

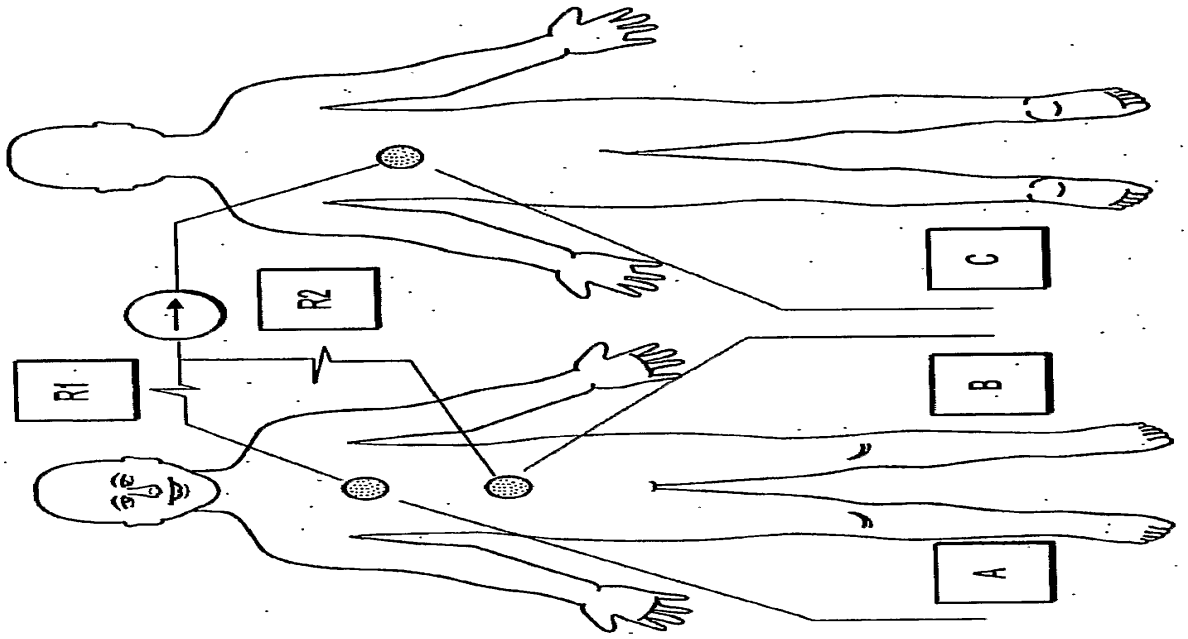


FIG. 47

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00874

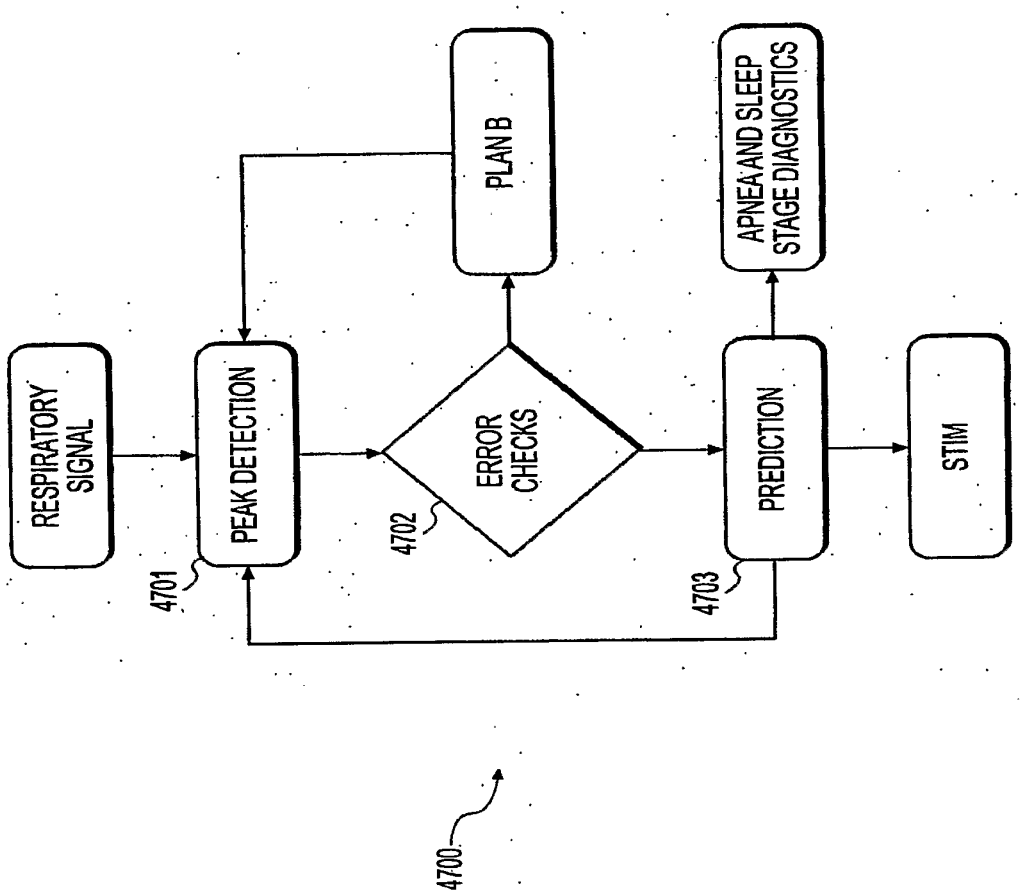

RESPIRATORY SIGNAL
PEAK DETECTION
4701
ERROR CHECKS
4702
PLAN B
PREDICTION
4703
APNEA AND SLEEP STAGE DIAGNOSTICS
STIM
4700

FIG. 47A

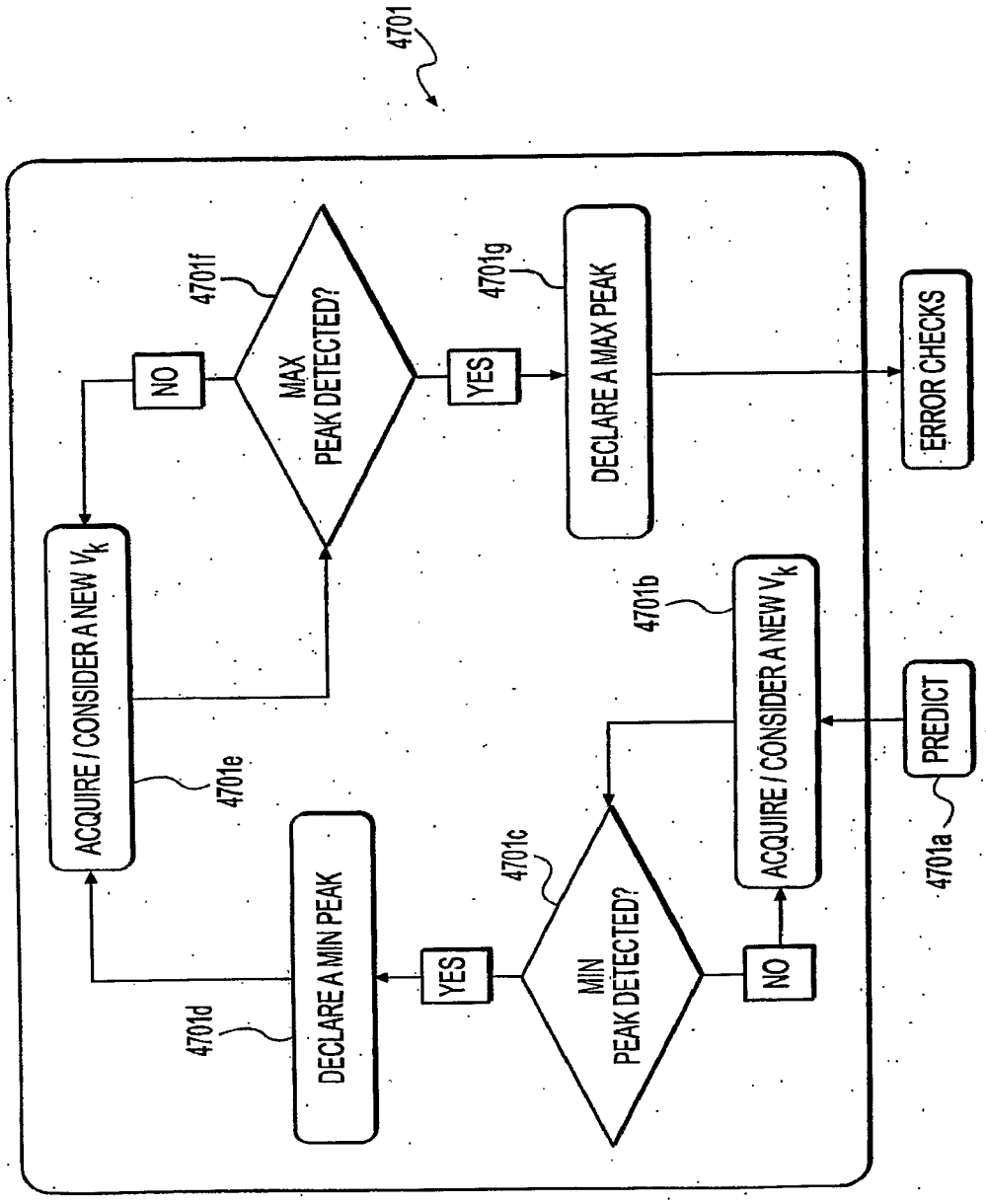

4701
4701a
PREDICT
4701b
ACQUIRE / CONSIDER A NEW V_k
4701c
MIN PEAK DETECTED?
NO
YES
4701d
DECLARE A MIN PEAK
4701e
ACQUIRE / CONSIDER A NEW V_k
4701f
MAX PEAK DETECTED?
NO
YES
4701g
DECLARE A MAX PEAK
ERROR CHECKS

FIG. 47B

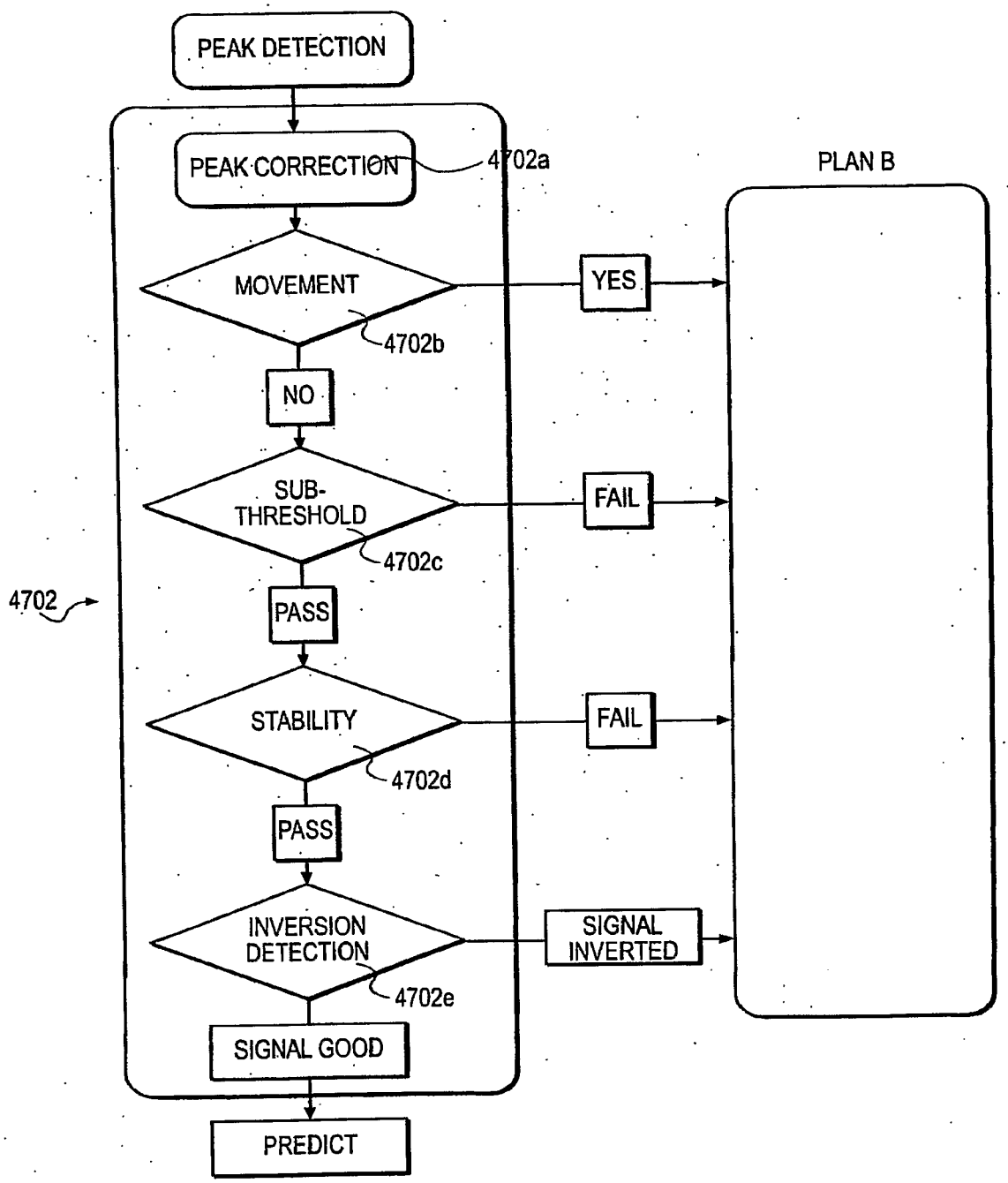

PEAK DETECTION
PEAK CORRECTION
4702a
MOVEMENT
4702b
YES
NO
SUB-THRESHOLD
4702c
FAIL
4702
PASS
STABILITY
4702d
FAIL
PASS
INVERSION DETECTION
4702e
SIGNAL INVERTED
SIGNAL GOOD
PREDICT
PLAN B

FIG. 47C

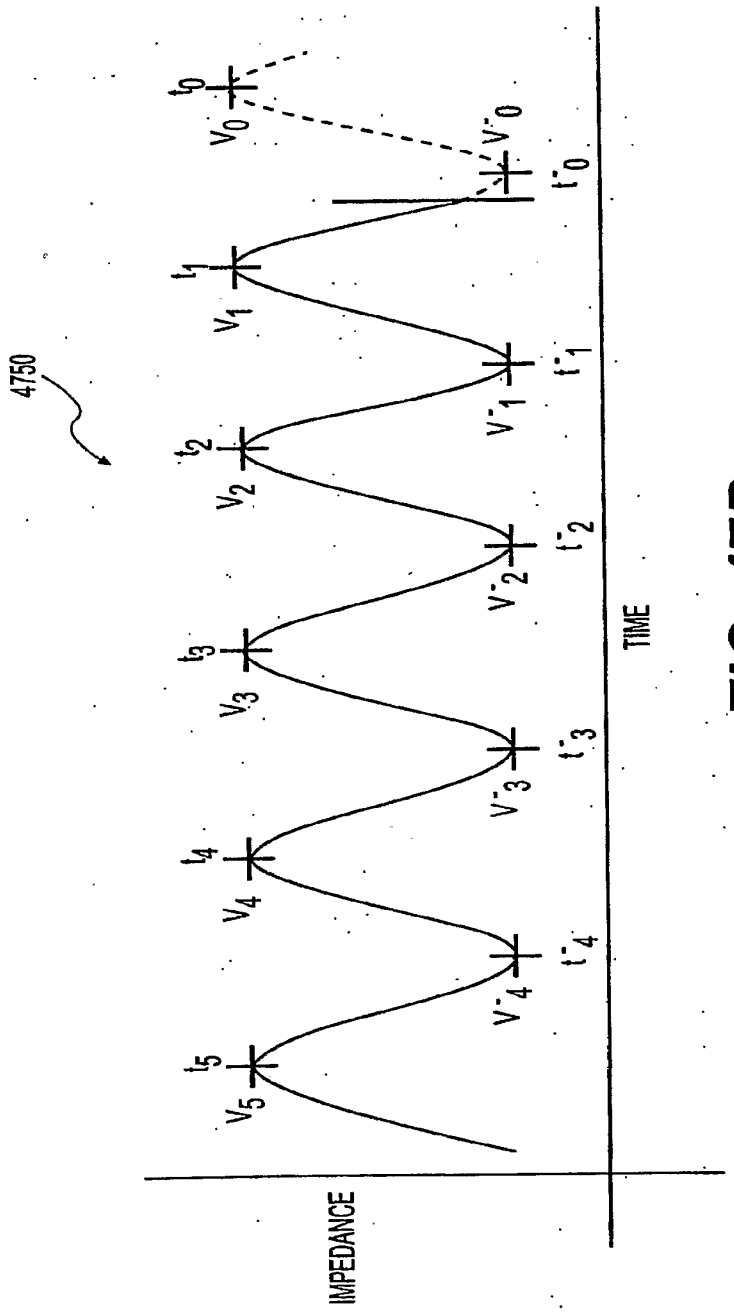

4750
IMPEDANCE
TIME
t0
t1
t2
t3
t4
t5
V0
V1
V2
V3
V4
V5
V'0
V'1
V'2
V'3
V'4
t'0
t'1
t'2
t'3
t'4

FIG. 47D

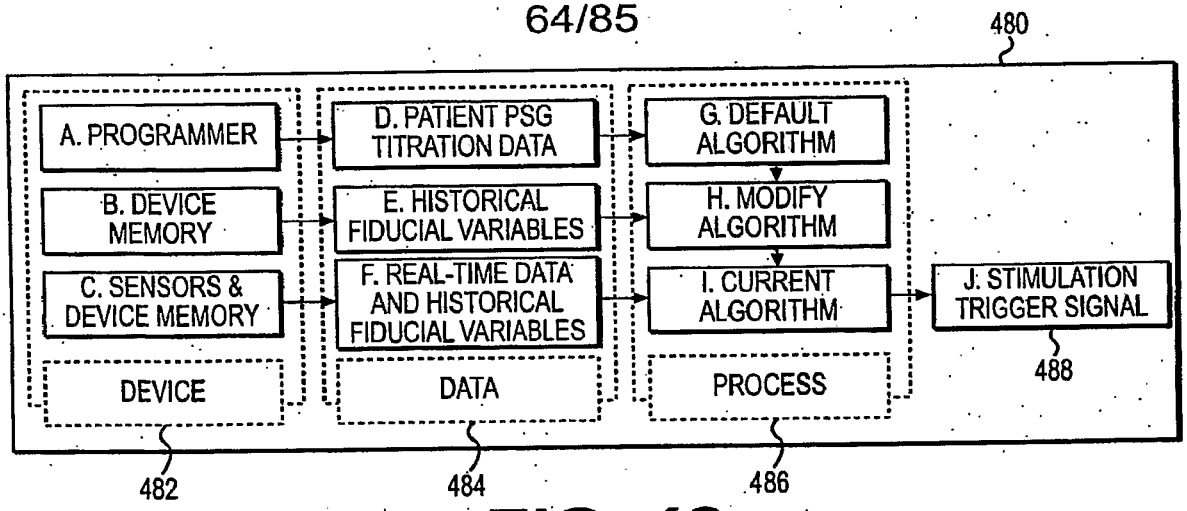


FIG. 48

REFERENCE MARKER ON GRAPH	VARIABLE NAME	VALUE & TIME OF EVENT
T	T	TIME OF ONSET OF INSPIRATION AS INDICATED BY PRESSURE SENSOR IN-LINE WITH AIRFLOW.
	T.est	ESTIMATED ONSET AS CALCULATED FROM HISTORICAL FIDUCIAL VARIABLES.
	T. pred	PREDICTED ONSET AS CALCULATED FROM REAL-TIME DATA AND HISTORICAL FIDUCIAL VARIABLES.
A	Vmax t.Vmax	POSITIVE PEAK OF PRIMARY SIGNAL
B	Vmin t.Vmin	MINIMUM OF PRIMARY SIGNAL BETWEEN SUCCESSIVE POSITIVE PEAKS
C	dV.in t.dV.in	MOST POSITIVE 1ST DERIVATIVE DURING EXPIRATION
D	dV.ex t.dV.ex	MOST NEGATIVE 1ST DERIVATIVE DURING EXPIRATION
E	D2V.in t.d2V.in	MOST POSITIVE 2ND DERIVATIVE DURING INSPIRATION. THIS TYPICALLY OCCURS SOON AFTER ONSET OF INSPIRATION.
F	d2V.pk t.d2V.pk	MOST NEGATIVE 2ND DERIVATIVE SLOPE. THIS OCCURS AT OR NEAR THE POSITIVE PEAK OF PRIMARY SIGNAL.
G	d2V.ex t.d2V.ex	MOST POSITIVE 2ND DERIVATIVE FOLLOWING INSPIRATION. THIS TYPICALLY OCCURS NEAR THE OFFSET OF EXPIRATION.
C2	V.in50 t.V.in50	THE POINT AT WHICH THE PRIMARY SIGNAL'S MAGNITUDE IS 50% BETWEEN POSITIVE PEAK AND PRECEEDING MINIMUM.
D2	V.ex50 t.V.ex50	THE POINT AT WHICH THE PRIMARY SIGNAL'S MAGNITUDE IS 50% BETWEEEN POSITIVE PEAK AND FOLLOWING MINIMUM.

FIG. 49

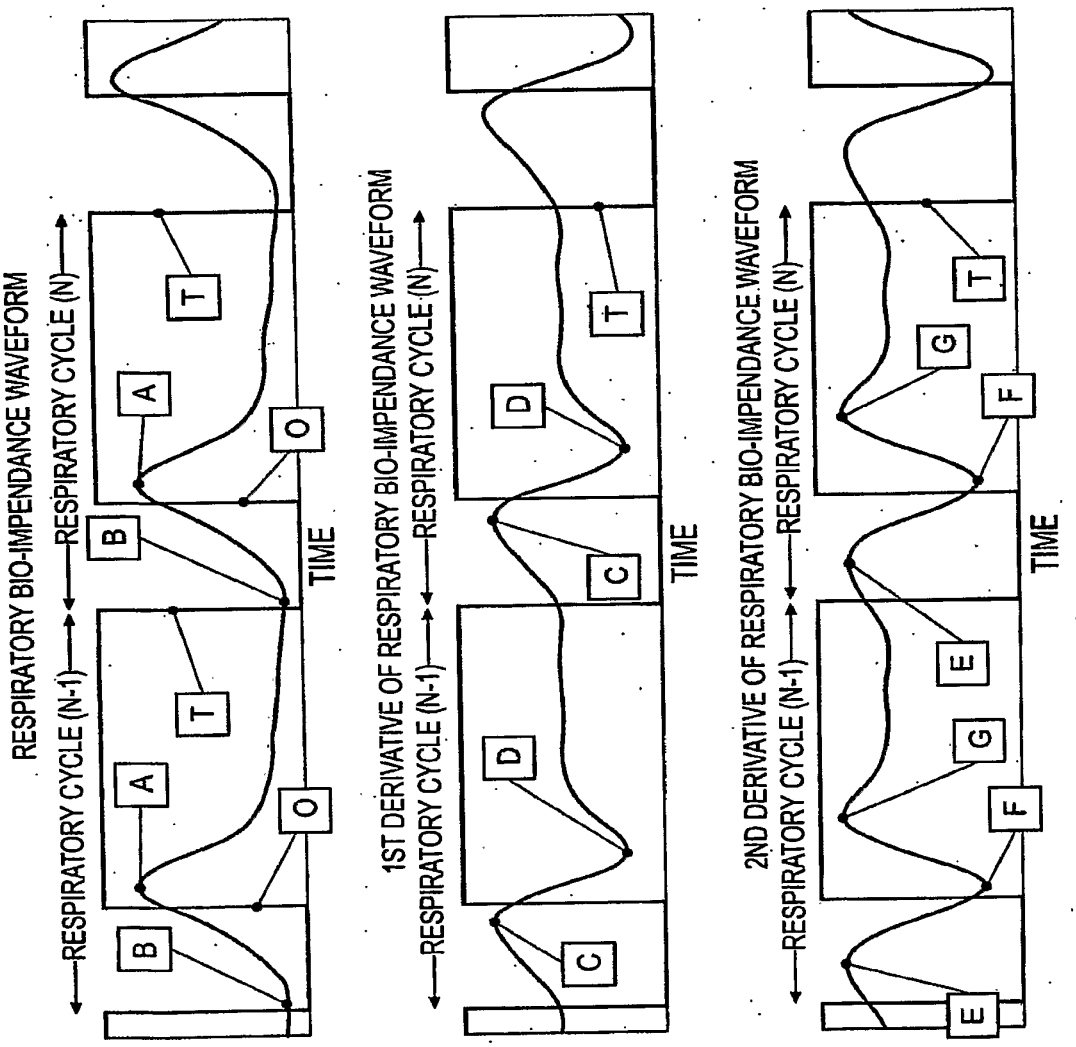

RESPIRATORY BIO-IMPENDANCE WAVEFORM
RESPIRATORY CYCLE (N-1)
RESPIRATORY CYCLE (N)
A
B
T
O
TIME
1ST DERIVATIVE OF RESPIRATORY BIO-IMPENDANCE WAVEFORM
RESPIRATORY CYCLE (N-1)
RESPIRATORY CYCLE (N)
C
D
T
TIME
2ND DERIVATIVE OF RESPIRATORY BIO-IMPENDANCE WAVEFORM
RESPIRATORY CYCLE (N-1)
RESPIRATORY CYCLE (N)
E
F
G
T
TIME

FIG. 50

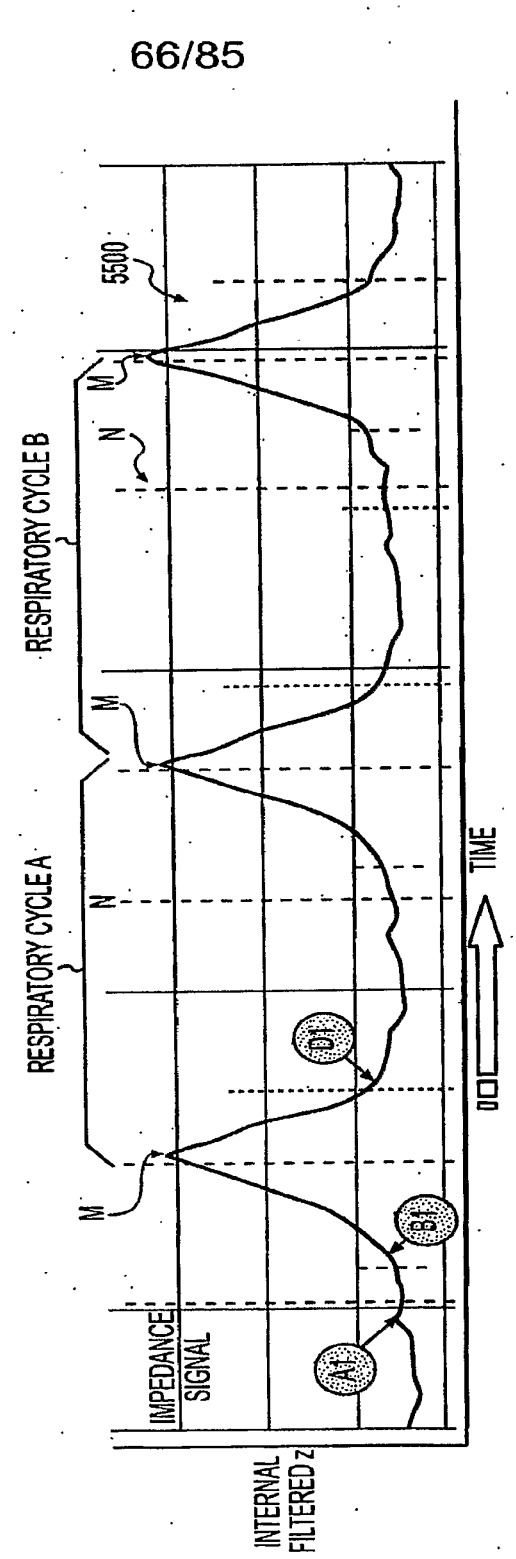

5500
M
N
M
N
M
RESPIRATORY CYCLE B
RESPIRATORY CYCLE A
D1
B1
A1
IMPEDANCE SIGNAL
INTERNAL FILTERED z
TIME

FIG. 50A

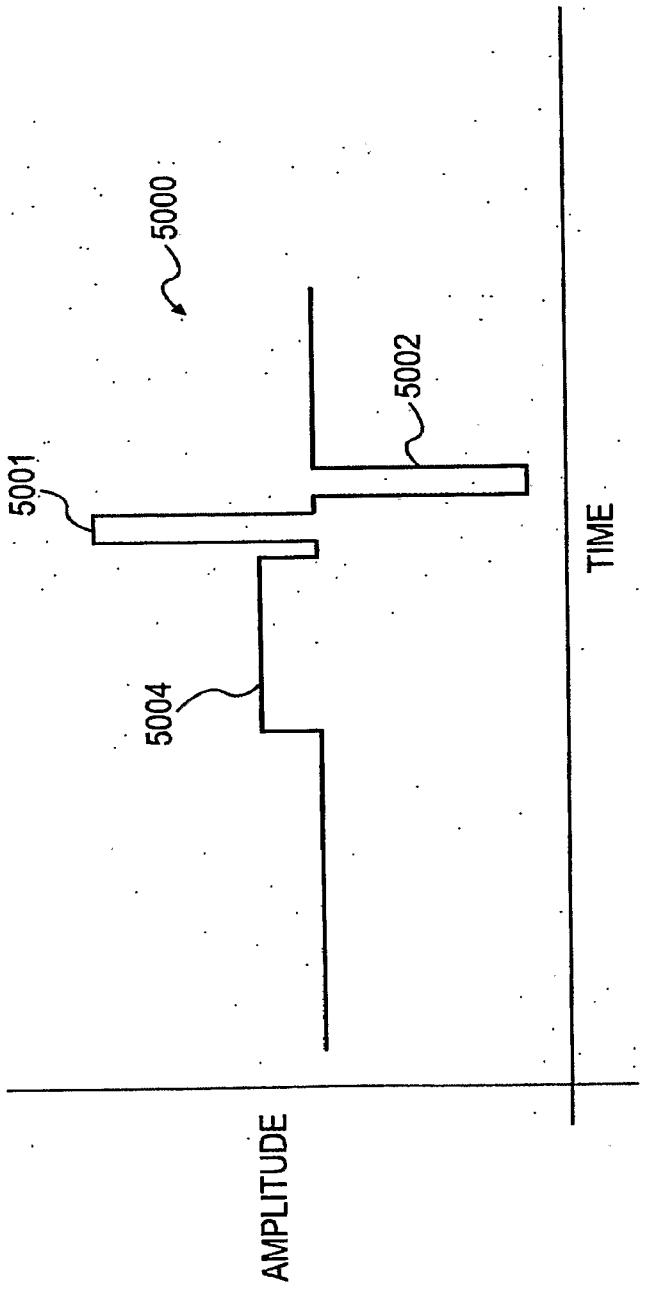


FIG. 50B

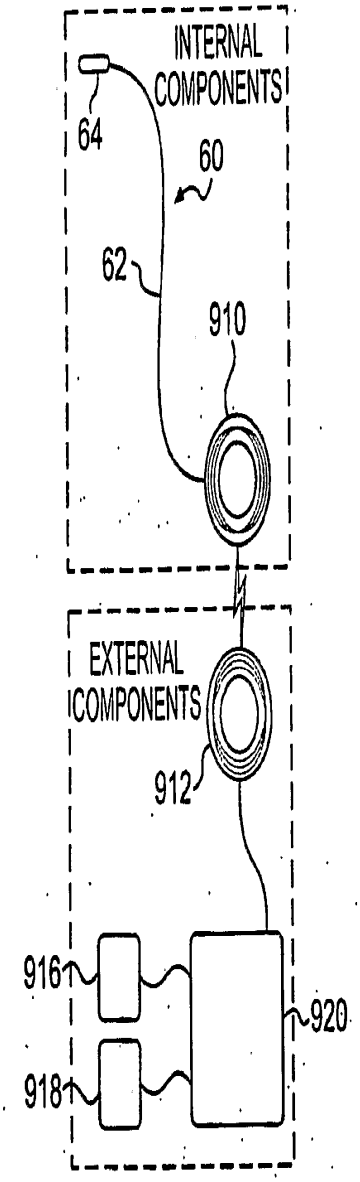


FIG. 51A

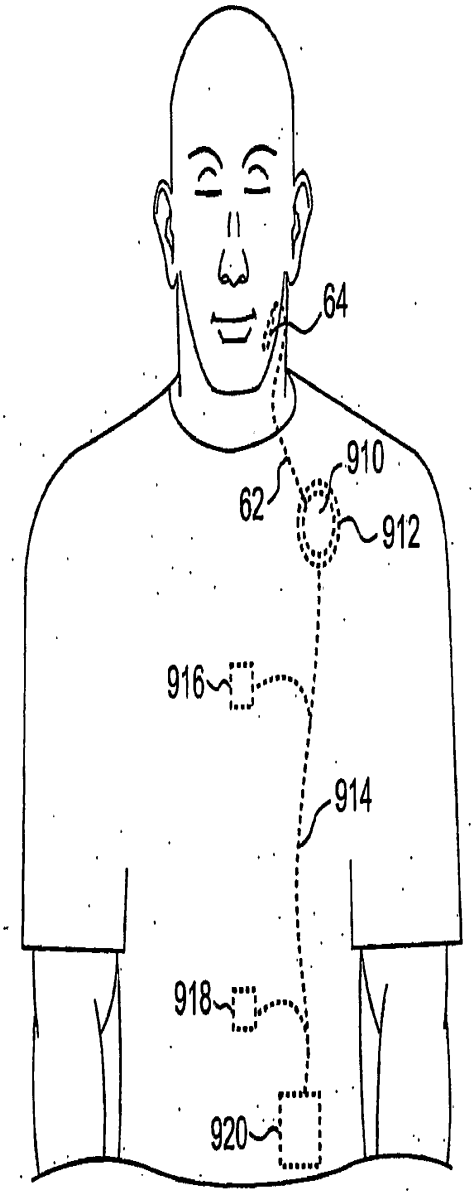


FIG. 51B

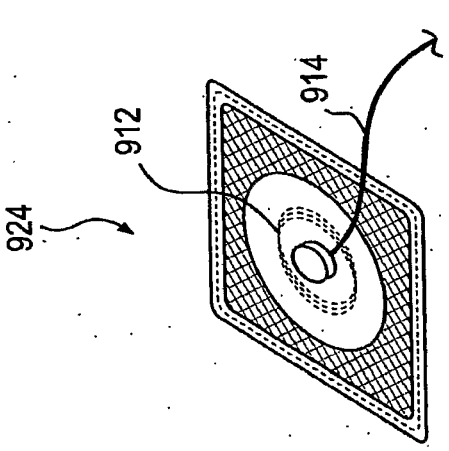


FIG. 51D

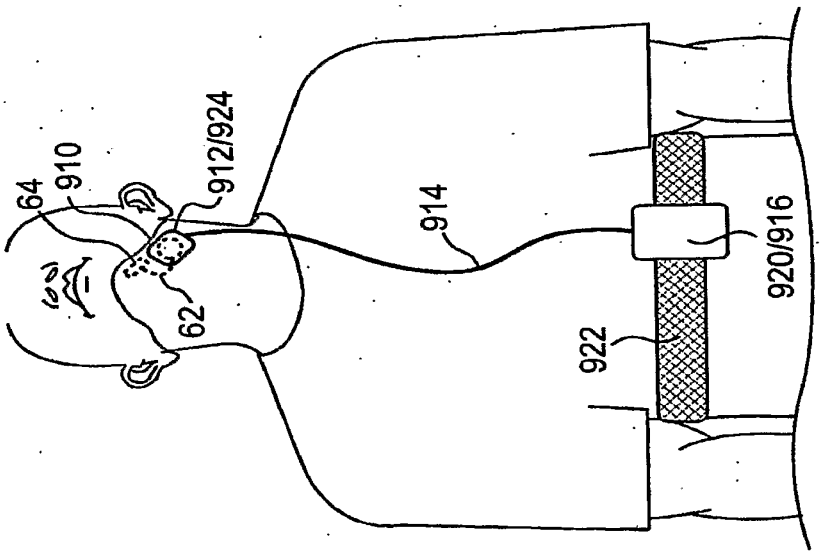


FIG. 51C

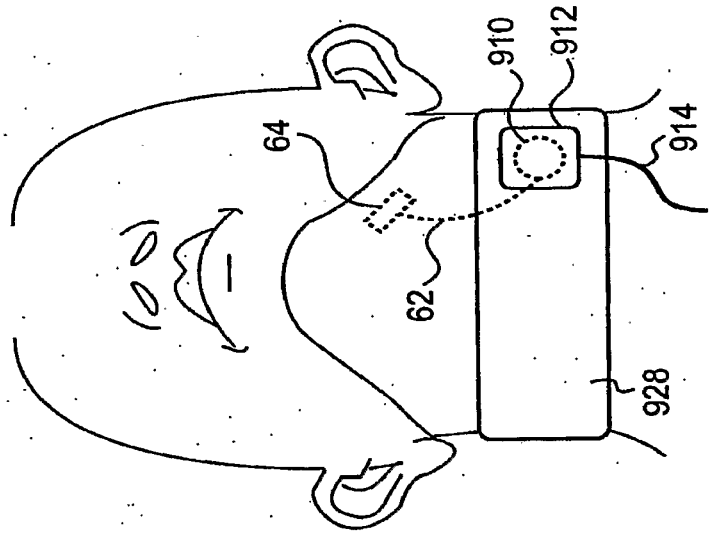


FIG. 51F

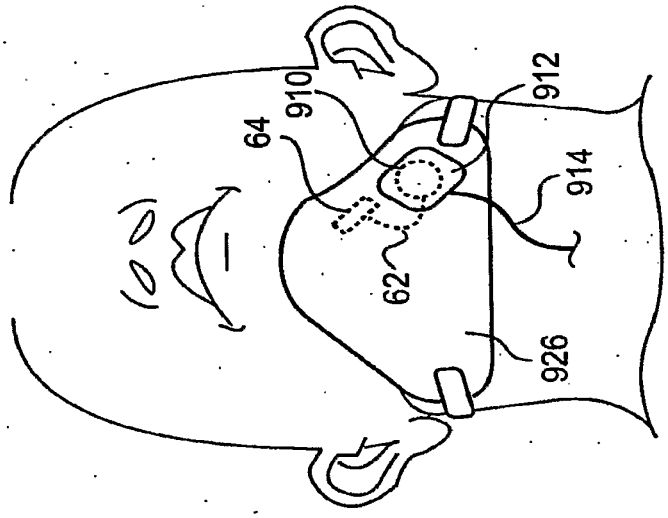


FIG. 51E

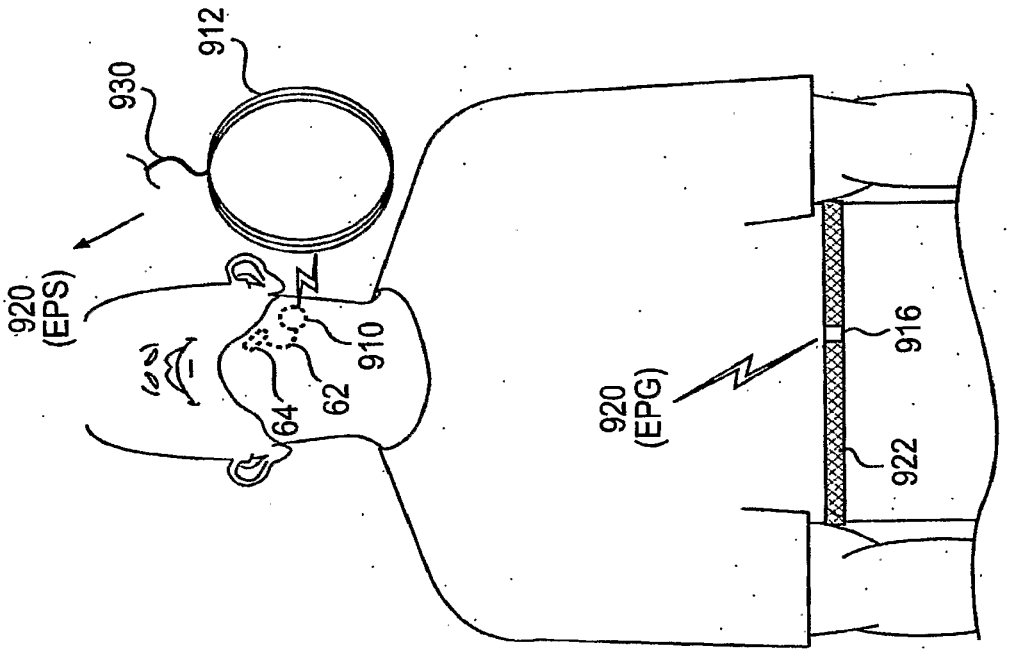


FIG. 51G

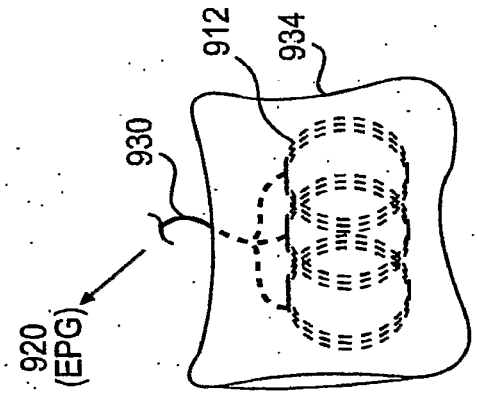


FIG. 51I

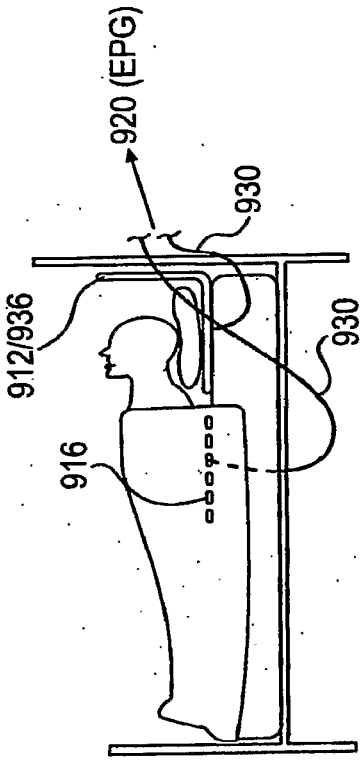


FIG. 51J

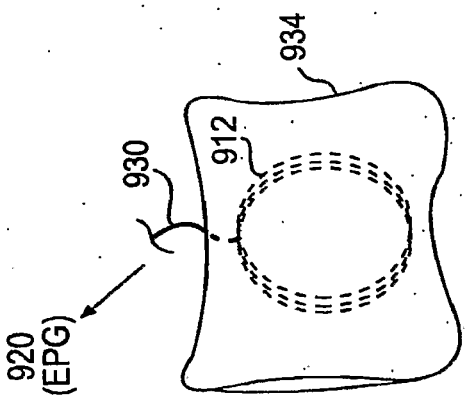


FIG. 51H

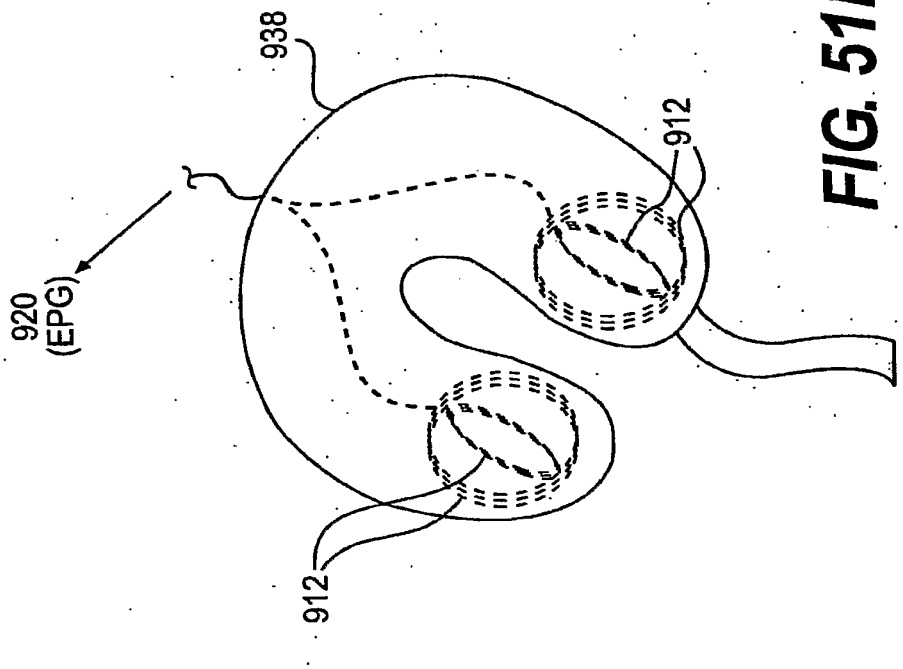


FIG. 51K

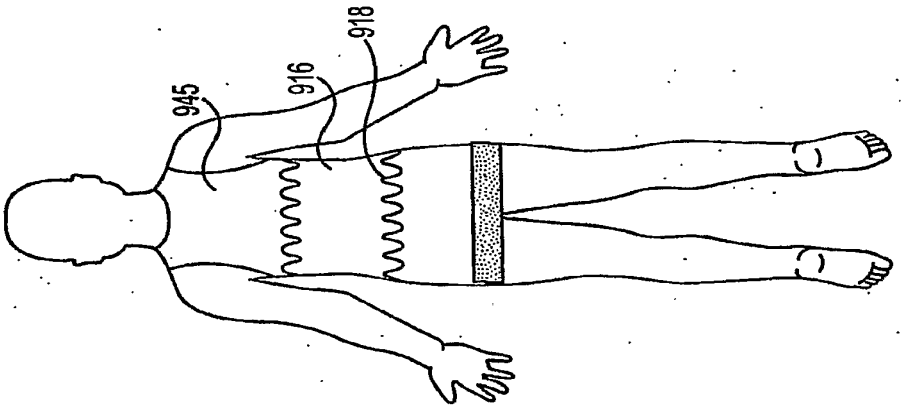


FIG. 51M

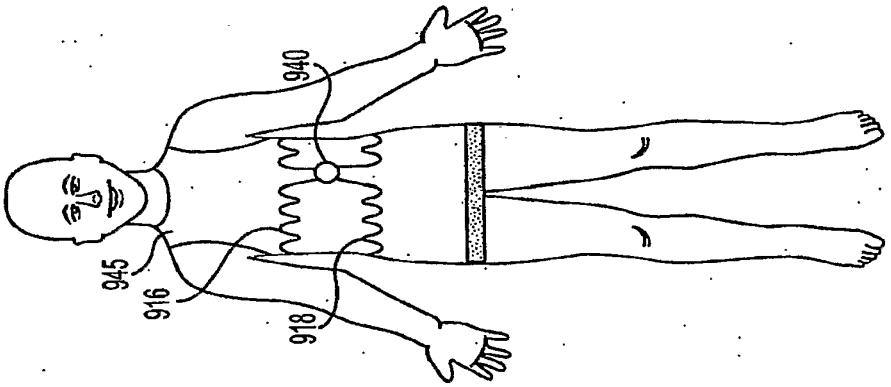


FIG. 51L

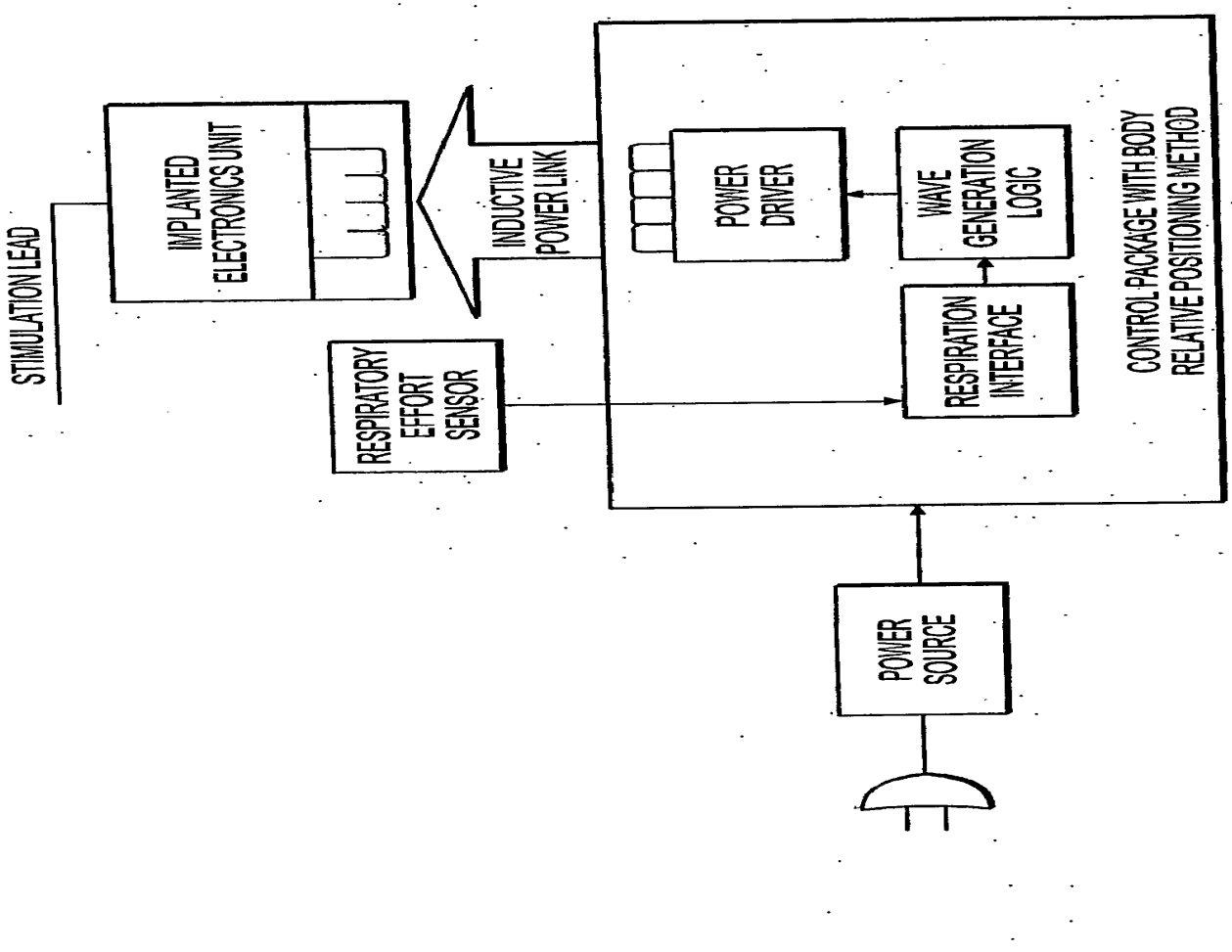


FIG. 52A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00890

WAVEFORMS - 1
MAXIMUM INSPIRATION
RESPIRATION
MAXIMUM EXPIRATION
MODULATION
TRANSMITTED SIGNAL
STIMULATOR OUTPUT
SEE WAVEFORMS - 2

FIG. 52B

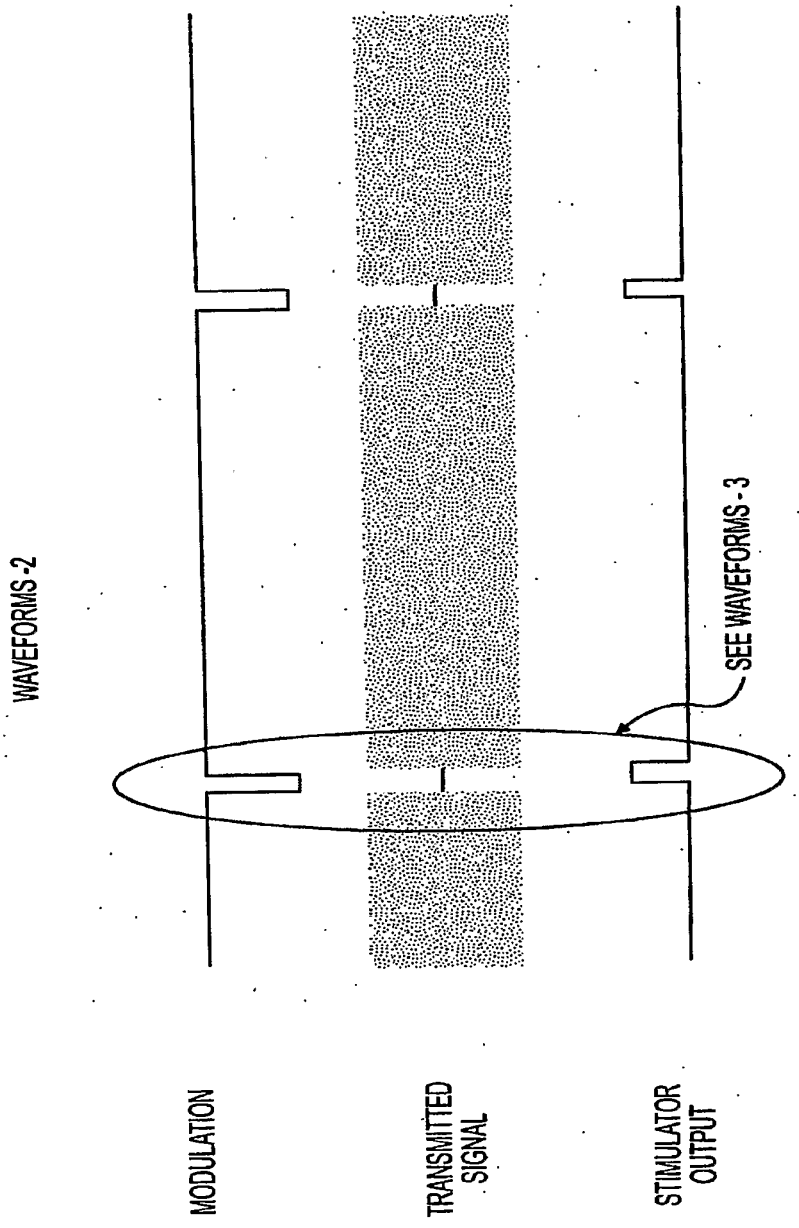

WAVEFORMS - 2
SEE WAVEFORMS - 3
MODULATION
TRANSMITTED SIGNAL
STIMULATOR OUTPUT

FIG. 52C

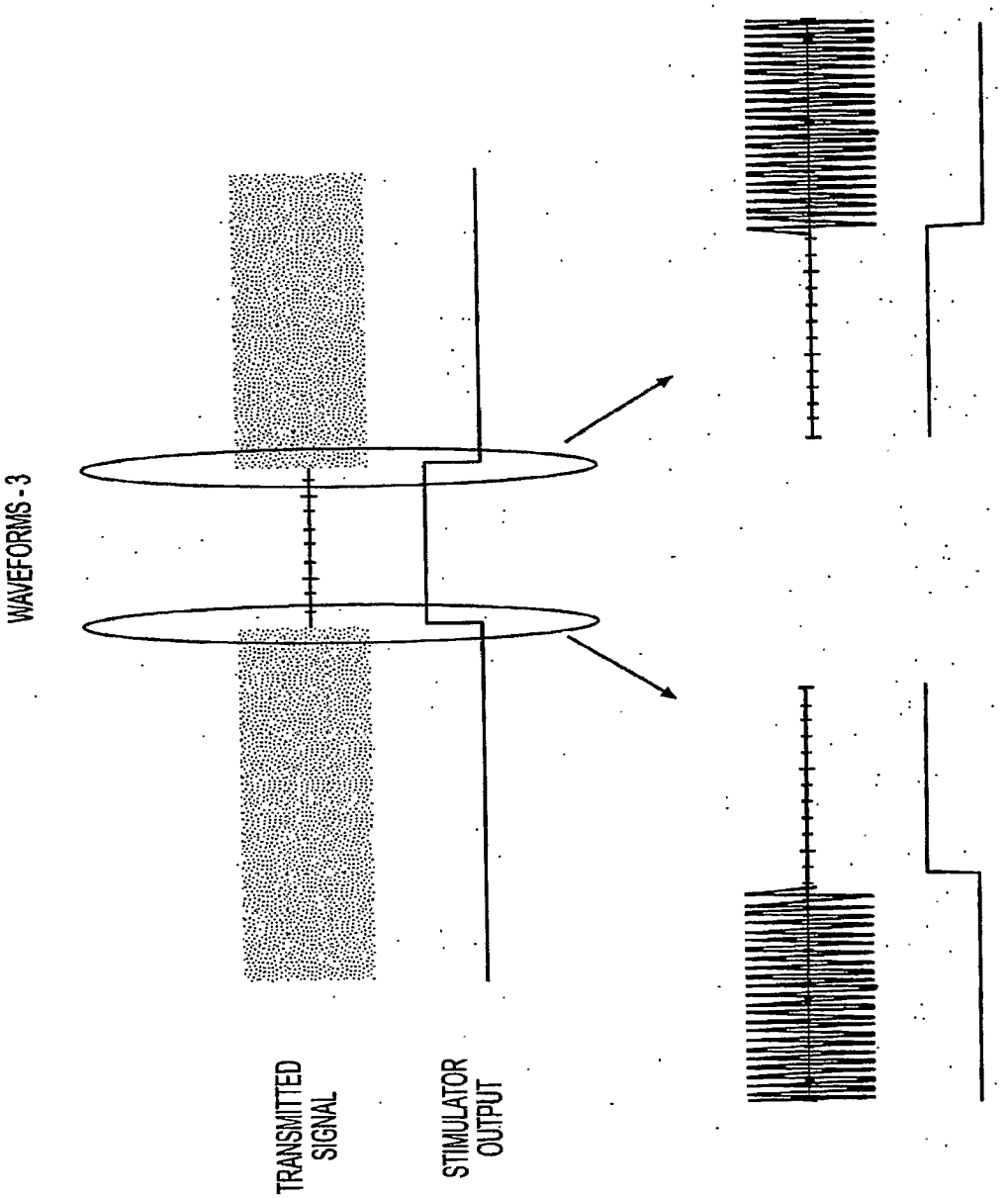


FIG. 52D

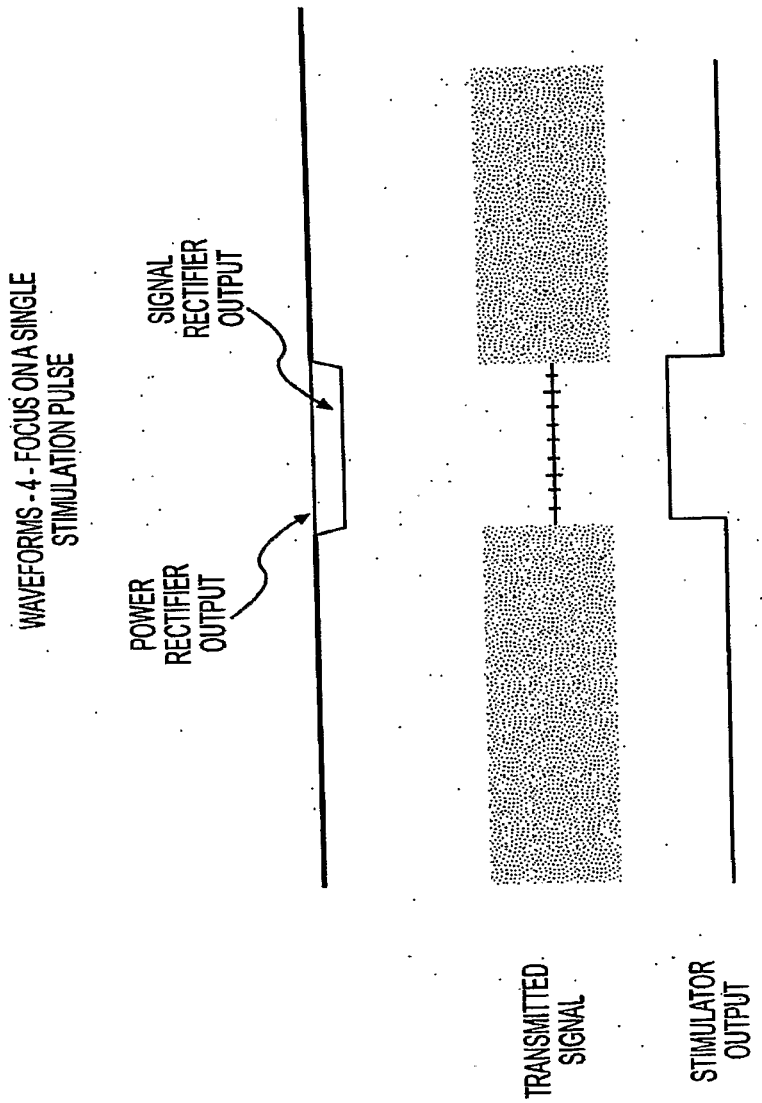

WAVEFORMS - 4 - FOCUS ON A SINGLE STIMULATION PULSE
SIGNAL RECTIFIER OUTPUT
POWER RECTIFIER OUTPUT
TRANSMITTED SIGNAL
STIMULATOR OUTPUT

FIG. 52E

FIG. 52F

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
00895

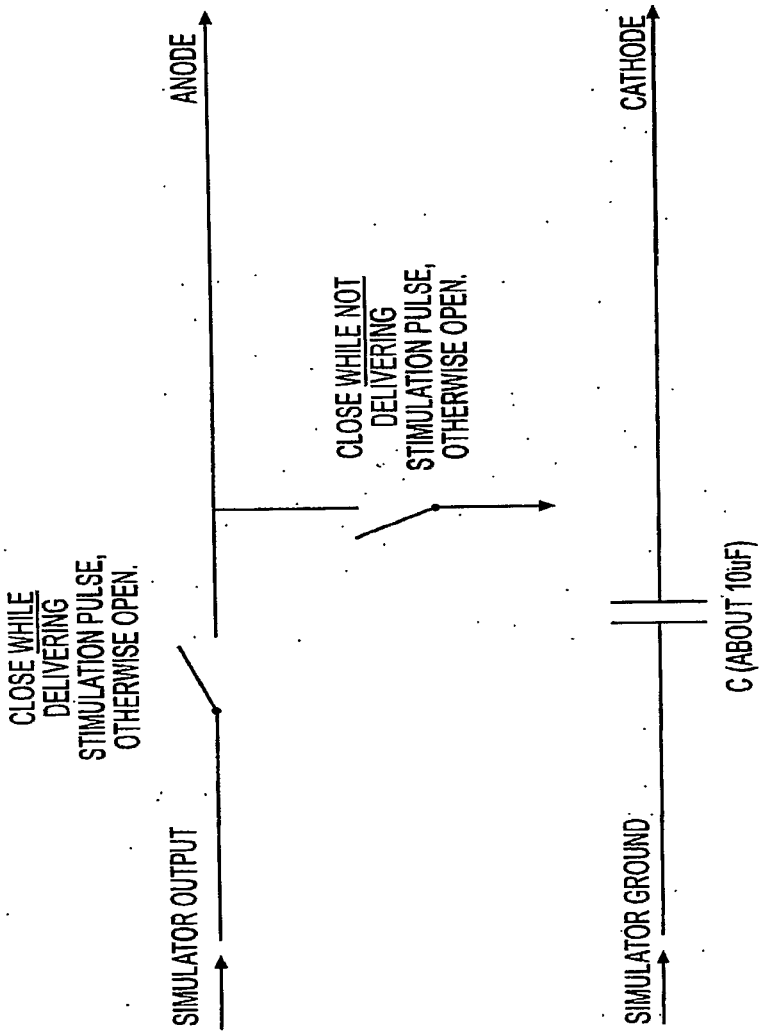

ANODE
CATHODE
CLOSE WHILE DELIVERING STIMULATION PULSE, OTHERWISE OPEN.
CLOSE WHILE NOT DELIVERING STIMULATION PULSE, OTHERWISE OPEN.
SIMULATOR OUTPUT
SIMULATOR GROUND
C (ABOUT 10uF)

FIG. 52G

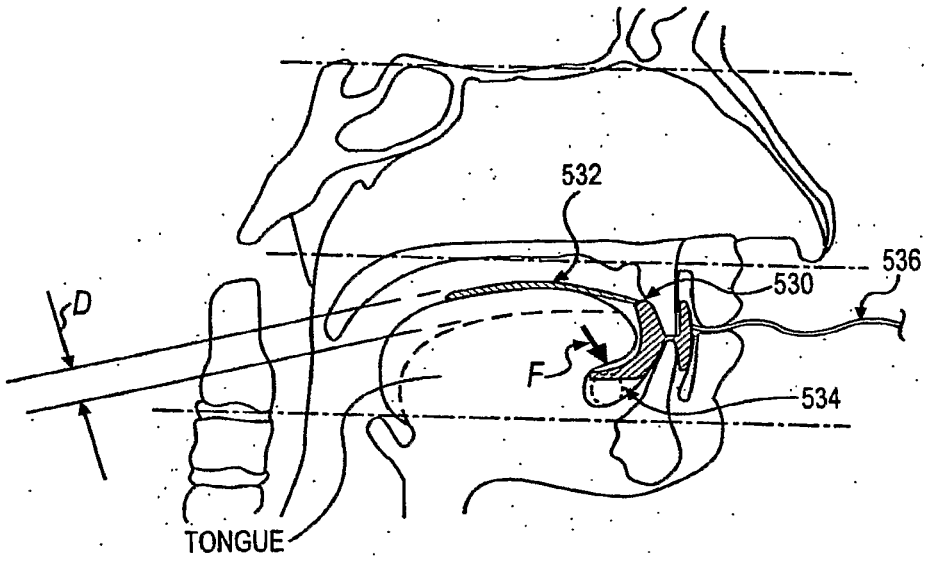


FIG. 53

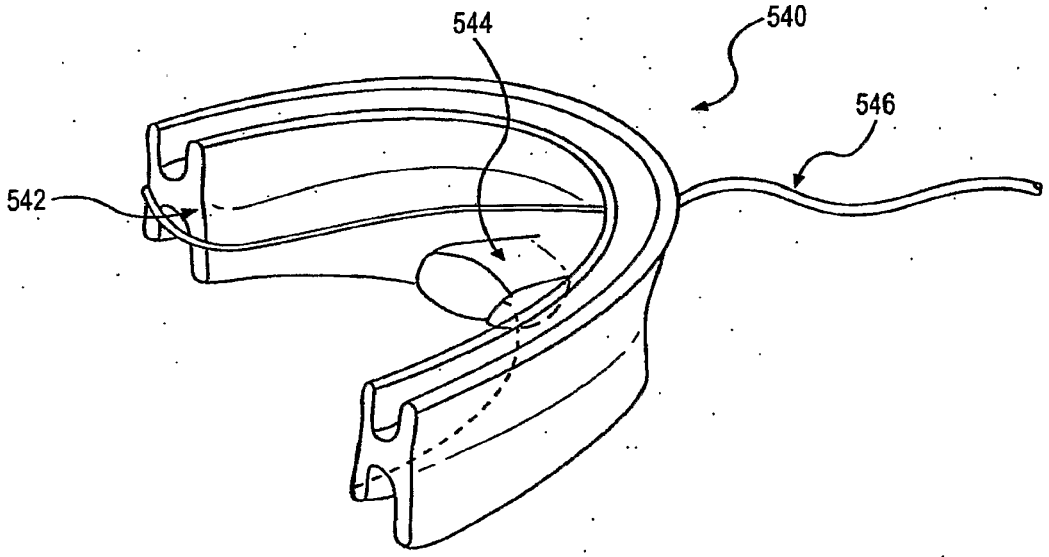


FIG. 54

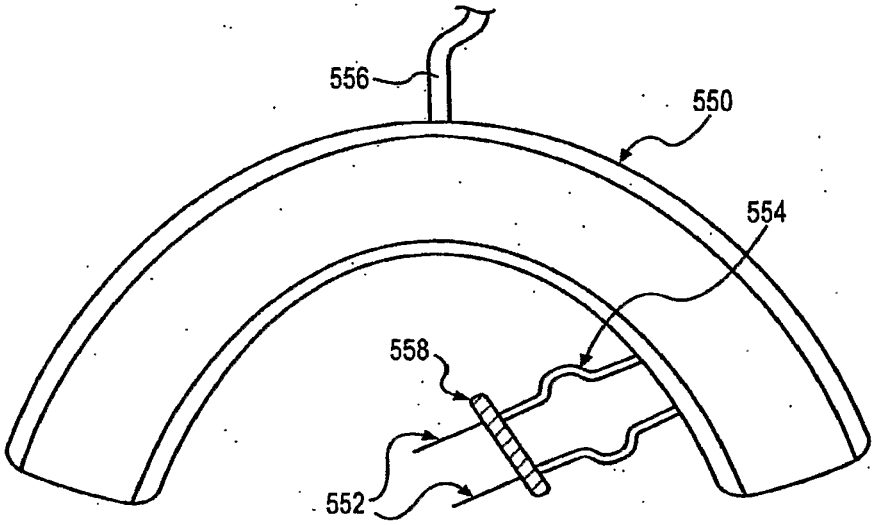


FIG. 55

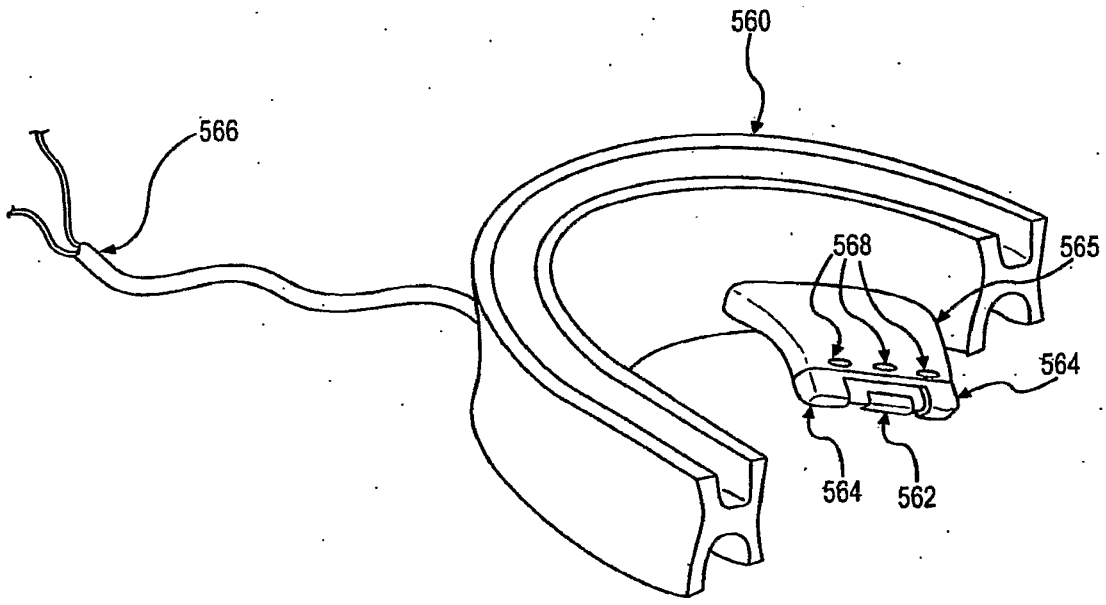


FIG. 56

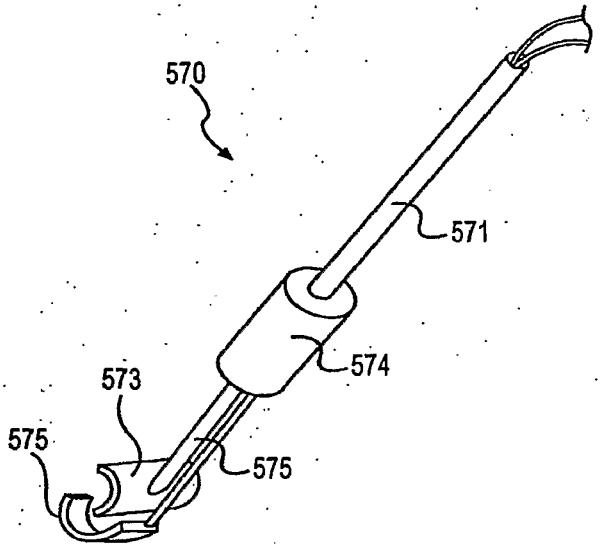


FIG. 57A

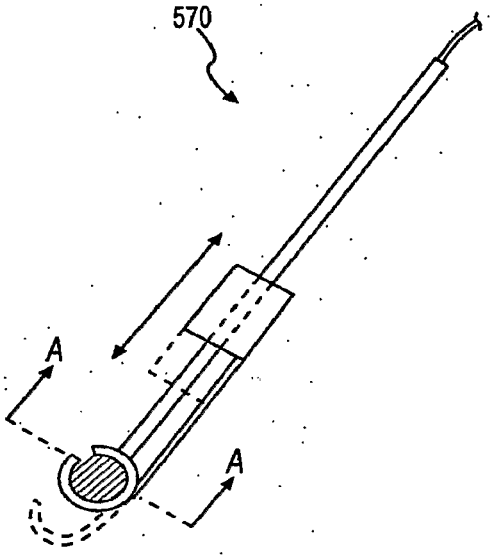


FIG. 57B

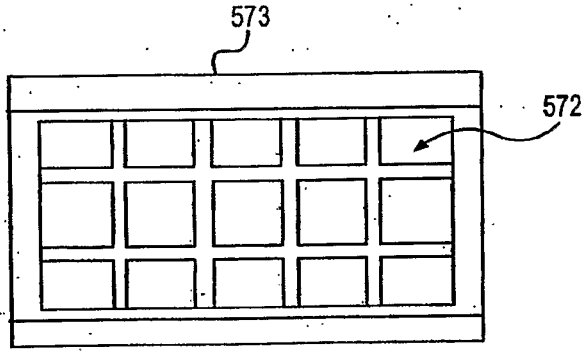


FIG. 57C

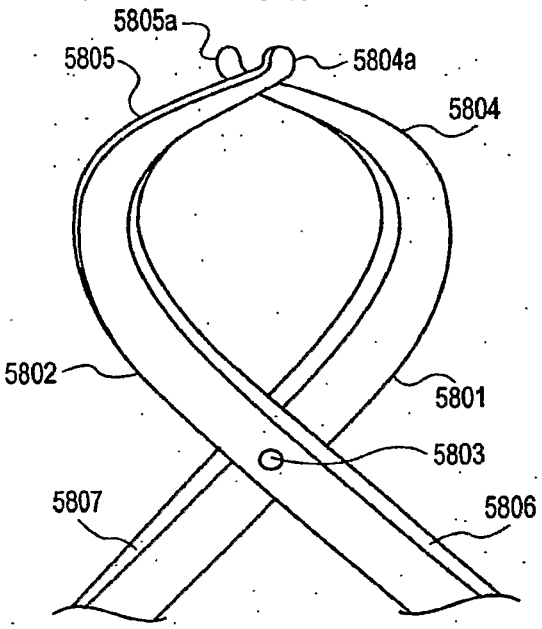


FIG. 58A

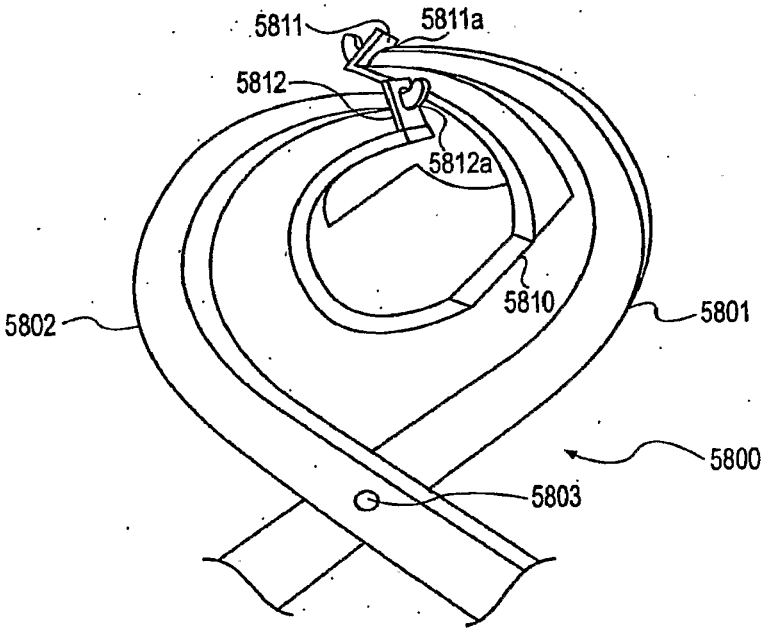


FIG. 58B

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 April 2009 (16.04.2009)

PCT

(10) International Publication Number
WO 2009/048580 A1

(51) International Patent Classification:
A61N 1/00 (2006.01)

(21) International Application Number:
PCT/US2008/011598

(22) International Filing Date: 9 October 2008 (09.10.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/978,519	9 October 2007 (09.10.2007)	US
61/017,614	29 December 2007 (29.12.2007)	US
61/136,102	12 August 2008 (12.08.2008)	US

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(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **MEADOWS, Paul, M.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US). **CRAIG, Stanley, R.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US). **LIMA, Marcelo, G.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US).

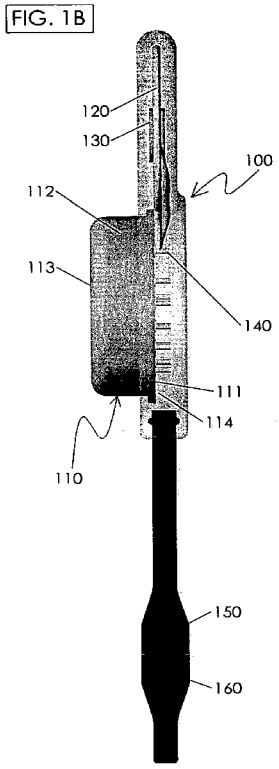
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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

[Continued on next page]

(54) Title: APPARATUS, SYSTEM, AND METHOD FOR SELECTIVE STIMULATION



(57) Abstract: An implantable neurostimulator system is disclosed, the neurostimulator system comprising a hollow cylindrical electronics enclosure having a top, a bottom, and a side; a coil extending from a first part of the electronics enclosure; and at least one electrode operatively connected to the electronics enclosure.

WO 2009/048580 A1

ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

TITLE

APPARATUS, SYSTEM, AND METHOD FOR SELECTIVE STIMULATION

STATEMENT OF RELATED APPLICATIONS

[0001] This application is related to International Patent Application No. [Docket No. 069737-5004-WO], and claims the benefit of United States Patent Application Nos. 60/978,519 and 61/017,614 and 61/136,102, filed on October 9, 2007 and December 29, 2007 and August 12, 2008 respectively, which are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

[0002] The present invention relates to an apparatus, system, and method for implantable therapeutic treatment of a patient.

BACKGROUND OF THE INVENTION

[0003] Acute and chronic conditions such as pain, arthritis, sleep apnea, seizure, incontinence, and migraine are physiological conditions affecting millions of people worldwide. For example, sleep apnea is described as an iterated failure to respire properly during sleep. Those affected by sleep apnea stop breathing during sleep numerous times during the night. There are two types of sleep apnea, generally described in medical literature as central and obstructive sleep apnea. Central sleep apnea is a failure of the nervous system to produce proper signals for excitation of the muscles involved with respiration. Obstructive sleep apnea (OSA) is caused by physical obstruction of the upper airway channel (UAW).

[0004] Current treatment options range from drug intervention, non-invasive approaches, to more invasive surgical procedures. In many of these instances, patient acceptance and therapy compliance is well below desired levels, rendering the current solutions ineffective as a long-term solution.

[0005] Implants are a promising alternative to these forms of treatment. For example, pharyngeal dilation via hypoglossal nerve (XII) stimulation has been shown to be an effective treatment method for OSA. The nerves are stimulated using an implanted electrode. In particular, the medial XII nerve branch (*i.e.*, in. genioglossus), has demonstrated significant reductions in UAW airflow resistance (*i.e.*, increased pharyngeal caliber).

[0006] Implants have been used to treat other conditions as well. For example, stimulation of the vagus nerve is thought to affect some areas in the brain prone to seizure activity; sacral

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nerve stimulation is an FDA-approved electronic stimulation therapy for reducing urge incontinence; and stimulation of peripheral nerves may help treat arthritis pain.

[0007] While electrical stimulation of nerves has been experimentally shown to remove or ameliorate certain conditions (*e.g.*, obstructions in the UAW), current implementation methods typically require accurate detection of a condition (*e.g.*, a muscular obstruction of an airway), selective stimulation of a muscle or nerve, and a coupling of the detection and stimulation components. Additionally, attempts at selective stimulation have focused on activating entire nerves or nerve bundles. A need therefore exists for an apparatus and method for selectively activating only the portion of the nerve responsible for activating the desired muscle or muscle groups while avoiding activation of unwanted muscles or muscle groups.

[0008] Accordingly, the present invention is directed to an apparatus, system, and method for selective stimulation that substantially obviates one or more problems due to limitations and disadvantages of the related art.

SUMMARY OF THE INVENTION

[0009] The present invention includes an implantable neurostimulator system with a hollow cylindrical electronics enclosure having a top, a bottom, and a side; a coil extending from a first part of the electronics enclosure; and at least one electrode operatively connected to the electronics enclosure.

[0010] In another embodiment, an implantable neurostimulator system includes a symmetrical chevron-shaped molded body having an apex, a first and second side, and a base; a coil at the apex of the molded body; an electronics enclosure at least partially integral with the molded body; and at least one electrode operatively connected to the electronics enclosure.

[0011] In a further embodiment, an implantable neurostimulator system includes an electronics enclosure; a coil; and at least one perforated cuff electrode operatively connected to the electronics enclosure.

[0012] In yet another embodiment, an implantable neurostimulator system includes an electronics enclosure; a coil; and at least one flat-bottomed open trough electrode operatively connected to the electronics enclosure.

[0013] Another embodiment of the invention includes an apparatus and method of neurostimulation, the method including the steps of at least partially encircling a nerve with a cuff having a first and second surface, the cuff having at least one contact on one of the first

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and second surfaces; connecting at least one stimulus generator to the at least one contact; and delivering a stimulus to the at least one contact.

[0014] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory, and are intended to provide further explanation of the claimed invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] The accompanying drawings, which are included to provide a further understanding of the invention and are incorporated in and constitute a part of this specification, illustrate embodiments of the invention, and together with the description serve to explain the principles of the invention. In the drawings:

[0016] **FIGS. 1A – 1F** show an exemplary embodiment of a mastoid bone implantable pulse generator (IPG) implant;

[0017] **FIGS. 2A – 2D** show an exemplary embodiment of a sub-mandibular implantable pulse generator (IPG) implant;

[0018] **FIGS. 3A – 3C** show exemplary embodiments of IPG cables and connectors;

[0019] **FIGS. 4A – 4D** show exemplary embodiments of IPG power systems;

[0020] **FIGS. 5A – 5D** show exemplary embodiments of IPG accessories;

[0021] **FIGS. 6A – 6G** show exemplary embodiments of IPG electrodes;

[0022] **FIGS. 7A** and **7B** show exemplary embodiments of monopole electrode configurations;

[0023] **FIG. 8** shows an exemplary embodiment of a bipolar electrode configuration;

[0024] **FIGS. 9A** and **9B** show exemplary embodiments of multipolar electrode configurations;

[0025] **FIGS. 10A** and **10B** show an example of a multiplexed system using force vectoring; and

[0026] **FIGS. 11A** and **11B** show exemplary embodiments of non-multiplexed waveform generators.

DETAILED DESCRIPTION OF THE INVENTION

[0027] Reference will now be made in detail to the embodiments of the present invention, examples of which are illustrated in the accompanying drawings. Wherever possible, like reference numbers are used for like elements.

[0028] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory and are intended to provide further

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explanation of the invention as claimed. Additional features and advantages of the invention will be set forth in the description that follows, and in part will be apparent from the description, or may be learned by practice of the invention. The objectives and other advantages of the invention will be realized and attained by the structure particularly pointed out in the written description and claims hereof as well as the appended drawings.

[0029] According to some embodiments, an implantable neurostimulator system of the present invention includes an implantable pulse generator system (IPG); and at least one electrode operatively connected to the IPG to generate accurate, selective nerve stimulation patterns. Exemplary components of various embodiments of the claimed invention are described hereafter.

[0030] I. Implantable Pulse Generator Systems (IPGs)

[0031] Implantable pulse generator systems (IPGs) include one or more of (1) an implant (*e.g.*, **FIGS. 1A – 2D**); (2) a power system (*e.g.*, **FIGS. 4A-4D**); and (3) an IPG accessory (*e.g.*, **FIGS. 5A-5D**). Examples of each are discussed below.

[0032] A. Exemplary IPG Implants

[0033] **FIGS. 1A – 2D** illustrate exemplary embodiments of IPG implants. Referring to **FIGS. 1A – 1F**, an embodiment of the IPG system includes a mastoid bone implant **100**. Referring to **FIGS. 2A – 2D**, another embodiment of the IPG system includes a sub-mandibular implant **200**.

[0034] 2. Mastoid Bone Implant

[0035] **FIGS. 1A – 1F** illustrate a mastoid bone implant embodiment of an IPG for treating obstructive sleep apnea. In the exemplary embodiment shown in **FIGS. 1A – 1F**, the mastoid bone implant **100** is implanted into the mastoid, which is a bony portion of the skull behind the ear. The mastoid bone bed is close to the HGN, and provides a stable well-protected location for the mastoid bone implant **100**.

[0036] **FIG. 1A** illustrates an exemplary embodiment of a unilateral mastoid bone implant 100 implantable pulse generator system. This area is a common location for cochlear implants. The mastoid bone implant **100** is placed into a well that is surgically excavated in the mastoid bone below the surface of the skull to secure the implant in place. Placing the mastoid bone implant **100** in a well protects the implant, reduces the amount it protrudes from the skull, and provides a lower device profile.

[0037] The embodiment shown can be implanted to stimulate the left, right, or both HGNs. In a unilateral procedure, the mastoid bone implant **100** is typically located on the same side of the head as the HGN being stimulated. In a bilateral procedure, a tunnel is formed in the

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patient's neck from the mastoid bone implant **100** side to the opposite side for the second HGN lead and electrode. While only one electrode (discussed later) is shown in **FIG. 1A**, multiple electrodes may be used without departing from the scope of the invention.

[0038] a. Physical Configuration

[0039] In the exemplary embodiment shown in **FIGS. 1A – 1F**, the mastoid bone implant **100** has a hollow cylindrical electronics enclosure **110** (also known as a case or a can) with a top **111**, a bottom **113**, and a side **112**. The case **110** houses the implant electronics and power source. The case **110** is typically made of a biocompatible material, and may be hermetically sealed. In the embodiment shown, a lip **114** encircles at least a portion of the side **112** of the enclosure **110**, and in certain embodiments has one or more holes to allow a surgeon to anchor the mastoid bone implant **100** in place with sutures.

[0040] In certain embodiments, silastic and/or silicone rubber (referred to generically as silastic) covers at least a portion of the electronics enclosure **110**. Other materials known to those skilled in the art may be used without departing from the scope of the invention. In embodiments with a lip **114**, the lip may be used to help secure the silastic to the enclosure **110**. In certain embodiments, some or all of the remaining case exterior not covered with silastic acts as an electrode. The electronics enclosure **110** in **FIGS. 1A – 1F** is exemplary only, and not limited to what is shown.

[0041] An internal coil **120** extends from a first part of the side **112** of the electronics enclosure **110**. In the exemplary embodiment shown, the internal coil **120** receives power, and supports bidirectional data and command telemetry. The internal coil **120** is encased in silastic, which may have an internal Dacron mesh or similar cloth for added tear resistance and durability. Similar materials known to those skilled in the art can be used without departing from the scope of the invention.

[0042] In certain embodiments, an internal magnet **130** helps align the internal coil **120** with an external coil **511** (**FIG. 5B**). The internal magnet **130** may be hermetically sealed, and in certain embodiments is embedded in the approximate center of the internal coil **120**. In certain embodiments, a second magnet (not shown) is located in the external controller coil **511**. The internal magnet **130** and external controller magnet (not shown) are oriented so that they are attracted to each other when the external controller coil is near the internal coil **120**. The attractive force of the two magnets brings the two coils close together, helping to maintain alignment between the coils. Aligning the coils helps optimize power and telemetry data transfer between the external controller and the mastoid bone implant **100**.

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[0043] The mastoid bone implant **100** may be implanted to stimulate the left, right, or both HGNs. In certain embodiments, the mastoid bone implant **100** orientation affects the internal magnet **130** orientation. Therefore, in certain embodiments the internal magnet **130** in the mastoid bone implant **100** is reversible. In other exemplary embodiments, the internal magnet **130** is removable, for procedures such as an MRI where the presence of a strong magnet in the patient might affect the images obtained or the forces generated and applied to the implanted internal magnet **130** by the static magnetic field of the MRI system might be unsafe for the patient. In still other embodiments, the internal magnet **130** and/or external controller magnet may be replaced with a material that is attracted to a magnet, either to eliminate the magnet on one side of the pair of devices, or to provide a lower profile to the corresponding coil assembly.

[0044] b. Internal Components

[0045] In the embodiment shown in **FIGS. 1A – 1F**, one or more glass-to-metal feedthrough leads **140** extend through the top of the electronics enclosure **110**. In the exemplary embodiment shown, the leads **140** are encased in silastic or similar material. The location of the feedthrough leads **140** is exemplary only, and not limited to what is shown. Feedthrough leads **140** at the top of the electronics enclosure **110** bring electrode and antenna connections from the enclosure **110** to the internal electronics. The feedthrough leads **140** shown are glass-to-metal feedthrough leads, but other non-conducting material known to those skilled in the art can be used in place of or in addition to glass to make the feedthrough leads **140**. Gold or nickel wires connect case feedthrough pins to internal circuitry inside the enclosure **110**. Stainless steel, platinum-iridium, gold or MP35N wires connect external portions of the feedthrough pins to connector, lead, or antenna connections external to the enclosure **110**.

[0046] The electronics design within the case **110** varies, often depending on the implant power source. For example, referring to **FIG. 4A**, in an exemplary embodiment of an RF implant (discussed later), the implant uses an external controller and power source. Since the power source and controller are external to the implant, the internal electronics are relatively simple. The implant need not have volume for a battery or ultracapacitor, and with the controller external to the implant, control and stimulation functions may be reduced to such a significant extent that a state-machine design could realistically be utilized. This has the added advantage of reducing power consumption and hybrid assembly real estate area as well, but has the disadvantage of being a more inflexible design with future product changes requiring a new application-specific integrated circuit (ASIC) state machine design.

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[0047] Other exemplary embodiments have their own power sources. These exemplary embodiments have means to charge and protect the internal power storage elements, and may have means to monitor these functions. Because of this added complexity, and because of the opportunity for independent operation without constant external supervision, the architecture of the IPG electronics may include a microcontroller along with the custom ASIC to generate the stimulus pulses and handle charging and telemetry functions. This has the added benefit of future functionality improvements along with field upgrade options for existing patients, as well as increased diagnostic functionality. In still other embodiments, the IPG electronics may include an acoustic pickup and sound processor to identify snoring. The snoring may be used as a trigger to initiate and/or modify stimulus patterns as the patient moves from one stage of sleep to another.

[0048] In still other embodiments, the mastoid bone implant **100** has an internal RF interface. In these embodiments, RF may be used to send power and/or control signals to the implant. The internal RF interface operates according to the principle of inductive coupling. The internal RF interface may also include a passive RFID transponder with a demodulator and a modulator. In certain embodiments, the RFID-based implant exploits the near-field characteristics of short wave carrier frequencies of approximately 13.56 MHz. In yet another embodiment, the RFID-based implant uses frequencies between 10 and 15 MHz. This carrier frequency may be further divided into at least one sub-carrier frequency.

[0049] The internal RF interface may also have a number of other characteristics. For example, the internal RF interface may include one or more of a transponder, internal antenna, modulator, demodulator, clock, and rectifier. The transponder may be passive or active. Furthermore, the transponder may have further separate channels for power delivery and data and control, and in some embodiments, the transponder may employ a secure full-duplex data protocol. The RF interface may further include an inductive coupler, an RF to DC converter, and an internal antenna, and the antenna may include a magnetic component. In other embodiments, the internal RF interface can send and/or receive control logic and/or power.

[0050] In some embodiments, the internal RF interface uses a sub-carrier frequency for communication with an external RF interface that may be located, for example, in an external controller. The sub-carrier frequency may be used for communication between the internal and external RF interfaces and is obtained by the binary division of the external RF interface carrier frequency. The transponder may use the sub-carrier frequency to modulate a signal back to the external RF interface.

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[0051] c. Connectors

[0052] As shown in **FIGS. 1B – 1F**, one or more multi-contact implant connectors **150** extending from a second part of the side **112** of the electronics enclosure **110** opposite the coil **120** connect electrode lead connectors **160** with cables having one or more electrode leads to the mastoid bone implant **100**. The type of connector, number of pins, and the location of the connectors are exemplary only, and not limited to what is shown.

[0053] In one embodiment, the implant connector **150** is a five to nine position female connector, which mates to corresponding lead pins in the electrode lead connector **160**. These electrode lead connections **160** extend from cables having one or more electrode leads that connect with electrode contact connections for four to eight cathodic contacts and a single or array of common anodes. This configuration allows stimulation to occur between any two or more independent contacts and/or the case **110**. The receptacles are made of a biocompatible material such as stainless steel, titanium, or MP35N, and arranged in a staggered row or other configuration to reduce space.

[0054] In certain embodiments, molded silicone rubber provides a detent feature to the female implant connector **150**, which helps hold the male portion of the electrode lead connector **160** in place. Male portions of the electrode lead connectors **160** optionally have a taper feature providing strain relief to the lead to prevent stress fracture failures in the lead wires. If a connector is unused, as, for example, in a unilateral implant for a single HGN, it is protected with a dummy plug (not shown) to prevent tissue ingrowth and isolate any unused contacts from bodily fluids.

[0055] Certain embodiments include suture holes on the connector areas. The suture holes help the surgeon lock the connectors together. If used, the sutures help tighten the connection between the male and female connectors. As a non-limiting example, the surgeon may suture around the shroud around the female and male assembled connection to tighten the connection between elements. Other methods known to those skilled in the art may be used without departing from the scope of the invention.

[0056] 2. Sub-Mandibular IPG Implant

[0057] **FIGS. 2A – 2D** illustrate an embodiment of a sub-mandibular IPG implant **200** for treating obstructive sleep apnea (OSA). In this embodiment, the sub-mandibular implant **200** stimulates the hypoglossal nerve (HGN), a peripheral nerve located below and behind the lower mandible. The HGN is typically 4 to 5 mm in diameter, with a typical epineurium thickness of less than 1 mm. In the embodiment shown, the sub-mandibular implant **200** may be placed within the sub-mandibular space. There is minimal nerve motion in this area

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during sleep. There, the sub-mandibular implant **200**, attached leads **342 (FIGS. 3B – 3C)** (discussed later), and electrodes **(FIGS. 6A – 6G)** (discussed later) are protected from jaw and neck movement relative to the tissues adjacent to the implanted elements. This helps secure the sub-mandibular implant **200** in place and prevent migration and drooping into the neck region. The sub-mandibular implant **200** is minimally invasive and easily implanted.

[0058] a. Physical Configuration

[0059] In the exemplary embodiment shown in **FIGS. 2A – 2D**, the sub-mandibular implant **200** is chevron-shaped, roughly triangular with the base **202** of the triangle pulled upwards toward the apex **201** of the triangle, with smooth corners **203** and a small surface area. The apex **201** and corners **203** of the sub-mandibular implant **200** are curved to eliminate sharp corners that may harm a patient. The chevron shape helps the sub-mandibular implant **200** fit within the sub-mandibular space. One or more holes **204** along each side of the chevron apex **201** optionally allow a surgeon to anchor the sub-mandibular implant **200** in place with sutures. If used, the sutures connect to the fascia attached to the bottom and inner surfaces of the mandible, to help secure the sub-mandibular implant **200** in place and prevent migration and drooping into the neck region. Because of its shape, the sub-mandibular implant **200** may be implanted to stimulate the left, right, or both HGNs. The sub-mandibular implant **200** orientation with respect to the target HGN is the same on either HGN, meaning that the sub-mandibular implant **200** cannot be incorrectly implanted with respect to its inside or outside surface, enabling efficient power and data transfer in any configuration.

[0060] In the embodiment shown, the bulk of the sub-mandibular implant **200** is silastic and/or silicone rubber (generically referred to as silastic) with an internal Dacron mesh or similar cloth to add tear resistance and durability to the package. These materials are exemplary only, and not limited to what is shown. Other materials known to those skilled in the art may be used without departing from the scope of the invention.

[0061] b. Internal Components

[0062] In the embodiment shown in **FIGS. 2A – 2D**, an internal coil **210** lies at the apex **201** of the sub-mandibular implant **200**. With the internal coil **210** located as shown, it is not sensitive to orientation. It functions equally well whether implanted on the right or left HGN. The internal coil **210** receives power, and supports bidirectional data and command telemetry. The internal coil **210** shown is made of gold or platinum wire, but may be made from other conductive materials known to those skilled in the art without departing from the scope of the invention.

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[0063] In certain embodiments, an internal magnet **220** helps align the internal coil **210** with an external coil **511** (**FIG. 5B**). The internal magnet **220** may be hermetically sealed, and in certain embodiments is embedded in the approximate center of the internal coil **210.** In certain embodiments, a second magnet (not shown) is located in the external controller coil **511**. The internal **220** and external **520** controller magnets are oriented so that they are attracted to each other when the external controller coil **511** is near the internal coil **210.** The attractive force of the two magnets brings the two coils close together, helping to maintain alignment between the coils. Aligning the coils helps optimize power and telemetry data transfer between the external controller and the sub-mandibular implant **200**.

[0064] As previously discussed, the sub-mandibular implant **200** may be implanted to stimulate the left, right, or both HGNs. In certain embodiments, sub-mandibular implant **200** orientation affects the internal magnet **220** orientation. Therefore, in certain embodiments the internal magnet **220** in the sub-mandibular implant **200** is reversible. In other exemplary embodiments, the internal magnet **220** is removable, for procedures such as an MRI where the presence of a strong magnet in the patient might affect the images obtained or the forces generated and applied to the implanted internal magnet **220** by the static magnetic field of the MRI system might be unsafe for the patient. In still other embodiments, the internal magnet **220** and/or external controller magnet (not shown) may be replaced with a material that is attracted to a magnet, either to eliminate the magnet on one side of the pair of devices, or to provide a lower profile to the corresponding coil assembly.

[0065] In one embodiment shown in **FIGS. 2A – 2D**, just below the internal coil **210**, at the base **202** of the chevron, lies an electronics enclosure (the case) **230** housing the implant electronics and power source. In the embodiment shown, silastic covers at least a portion of the case **230.** In certain embodiments, at least a portion of the case **230** surface is left exposed to act as an electrode. The case **230** location is exemplary only, as is the portion of the case **230** covered with silastic, and not limited to what is shown.

[0066] The case **230** is typically made of biocompatible metal, such as a 6-4 titanium alloy. A titanium alloy is chosen because of its high resistivity compared to commercially pure (CP) titanium. The higher resistivity helps minimize power losses due to eddy currents resulting from exposure to RF fields, such as a charging field. Other biocompatible materials may be used without departing from the scope of the invention. In certain embodiments, the electronics enclosure **230** is hermetically sealed. The enclosure **230** may be any hermetic enclosure known to those skilled in the art.

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[0067] Feedthrough leads **240** in the sides of the electronics enclosure **230** bring electrode and antenna connections from the enclosure **230** to the internal electronics. The feedthrough leads **240** shown are glass-to-metal feedthrough leads, but other non-conducting material known to those skilled in the art can be used in place of or in addition to glass to make the feedthrough leads **240**. Gold or nickel wires connect case feedthrough pins to internal circuitry inside the enclosure **230**. Stainless steel, platinum-iridium, gold or MP35N wires connect external portions of the feedthrough pins to connector, lead, or antenna connections external to the enclosure **230**. In certain embodiments, such as the embodiment shown in **FIG. 3A** (discussed later), at least one permanently attached electrode lead **341 (FIG. 3A)** connects the electrodes and antenna to the sub-mandibular implant **200**. Using permanently attached electrode leads **341** rather than connectors **350** increases system reliability.

[0068] The electronics design within the case **230** varies, often depending on the implant power source. Examples of how the electronics design varies with the power source are described in the sections discussing the mastoid bone implant **100** (above) and are not repeated here.

[0069] c. Connectors

[0070] **FIGS. 3A – 3C** show exemplary embodiments of IPG electrode leads **341**, **342** and multi-contact implant connectors **350**. Although shown with a sub-mandibular implant **200**, they may also be used with a mastoid bone implant **100**. The implant connectors **350** connect electrode leads **341**, **342** and electrodes to the sub-mandibular implant **200**. The electrode leads **341**, **342** and electrodes connect to the implant connectors **350** with lead wires having polyurethane, silicone rubber, or similar insulating material, and wiring made from stainless steel, MP35N, titanium, 90/10 Pt-Ir, gold, or other material with high conductivity, high fatigue resistance, and good tensile properties. The lead wires have high biocompatibility and high corrosion resistance in implanted stimulation conditions. In certain exemplary embodiments, the wire material is MP35N drawn-filled-tube (DFT) with a silver core. This material has excellent fatigue resistance and high tensile strength, and the silver core lowers its electrical resistance to more desirable levels.

[0071] In one embodiment, the implant connector **350** is a five to nine position female connector, which mates to corresponding lead pins in the electrode lead **341**, **342**. These electrode leads **341**, **342** connect with electrode contact connections for four to eight cathodic contacts and a single or array of common anodes. This configuration allows stimulation to occur between any two or more independent contacts and/or the case **230**. The receptacles are made of a biocompatible material such as stainless steel, titanium, or MP35N, and

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arranged in a staggered row or other configuration to reduce space. One or more multi-contact implant connectors **350** on at least one corner of the sub-mandibular implant **200** connect electrode leads **341**, **342** to the sub-mandibular implant **200**.

[0072] In the embodiment shown in **FIG. 3A**, at least one electrode lead **341** and electrode are permanently attached to the sub-mandibular implant **200** at one of its corners. Another feedthrough lead **240** with a female implant connector **350** is available for attachment of another electrode lead **342** and electrode. The embodiment shown in **FIG. 3A** is typically used for unilateral implant patients, where a single electrode lead **341** is sufficient to achieve the desired clinical results, but would still allow a second electrode lead **342** and electrode to be added for bilateral applications. In the embodiment shown in **FIG. 3C**, the electrode leads **342** shown attach to the sub-mandibular implant **200** through implant connectors **350** only.

[0073] B. Implant Power Systems

[0074] **FIGS. 4A – 4D** illustrate exemplary embodiments of IPG power systems. Each embodiment illustrates a different power system. The four power systems are (1) RF-powered and controlled (**FIG. 4A**), with continuous application of RF power for operation of the implanted system; (2) ultra-capacitor powered (**FIG. 4B**), with at least one short RF-powered charge period to supply sufficient power to the implant for operation for one sleep period; (3) secondary-battery-powered (**FIG. 4C**), with occasional RF-powered charging periods to supply sufficient power to the implant for operation for at least one sleep period a day for a week or more; and (4) a hybrid combination of ultracapacitor and secondary battery powered (**FIG. 4D**). In the absence of sufficient internal energy charge in the latter three embodiments, the system would allow operation to occur as in the first embodiment, that is, continuous application of RF power for the operation of the implanted system for the duration of the sleep period.

[0075] 1. RF-Powered IPG Implant

[0076] **FIG. 4A** shows an exemplary embodiment of an RF-powered IPG implant **400**. In the embodiment shown, the RF-powered IPG implant **400** has no internal power source. It receives power and commands, and exchanges data with an external controller via an inductively coupled RF power and data link. The link is a flat coil **401** attached via feedthrough pins to a coupling circuit **402** inside the IPG electronics enclosure. The coil **401** is AC coupled using one or more capacitors to prevent DC current leakage, which can damage tissue and cause failures in the hermetically sealed IPG feedthroughs.

[0077] The power and data signals are sinusoidal or similar waveforms at one or more frequencies that minimize energy losses but still support the bandwidth requirements for

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adequate data transfer rates. In certain embodiments, these signals are in the radio frequency (RF) range. In the embodiment shown, RF power and data are supplied externally with a matching coil, which may be held in position over the IPG coil **401** using a magnet, a strap, adhesive, or other method known to those skilled in the art. Limited coil misalignment is allowed and expected, including lateral displacement, vertical displacement, and out of plane angular displacement.

[0078] In other embodiments, the implant **400** operates according to the principle of RFID inductive coupling. The RF may be used to send power and/or control signals to the implant. In an embodiment, the implant **400** exploits the near-field characteristics of short wave carrier frequencies of approximately 13.56 MHz. This carrier frequency is further divided into at least one sub-carrier frequency. The sub-carrier frequency is obtained by the binary division of the carrier frequency. In certain embodiments, the implant **400** can use between 10 and 15 MHz. The implant **400** may further have two channels, Channel A and Channel B. Channel A is for power delivery and Channel B is for data and control.

[0079] In the embodiment shown in FIG. 4A, the received waveform is internally rectified and converted into one or more supply voltages within the RF-powered IPG implant **400** by coupling circuitry **402** and at least one circuit **404** used by the RF-powered IPG implant **400** in regular operations, including stimulation of the HGN. In certain exemplary embodiments, the circuit **440** may be an application specific integrated circuit (ASIC). The RF-powered IPG implant **400** uses its internal coil **401** to send a signal to the external devices, sometimes on a different carrier frequency, chosen to optimize its signal integrity and data transfer characteristics without interfering with the inbound signal transfer process. In certain embodiments, the RF-powered IPG implant **400** sends the signal from the internal coil **401** concurrently. The supply voltages are filtered and stored internally in capacitors. The capacitors are sized to power the RF-powered IPG implant **400** during temporary interruptions of the power link, but are not large enough to power the RF-powered IPG implant **400** for an entire sleep session.

[0080] 2. Ultracapacitor-Powered IPG Implant

[0081] **FIG. 4B** shows an exemplary embodiment of an ultracapacitor-powered IPG implant **410**. In the exemplary embodiment shown, the embodiment has the same elements described above, along with an ultracapacitor **413** that is large enough to store sufficient energy for a single sleep session, and receives power at very high rates with insignificant degradation of performance over time. In the ultracapacitor-powered IPG implant **410** embodiment, the external controller and associated coil are placed over the internal coil **411**

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just long enough to exchange data and charge up the ultracapacitor **413** power storage element. The rate at which the ultracapacitor **413** storage element charges is inversely related to the time required to bring it to full charge – the higher the charge rate, the shorter the charge time. Once the ultracapacitor **413** storage element is sufficiently charged, the patient may remove the external controller and external coil and begin a sleep session.

[0082] 3. Secondary-Battery-Powered IPG Implant

[0083] **FIG. 4C** shows an exemplary embodiment of an IPG implant **420** with a secondary battery **423**. The secondary-battery-powered IPG implant **420** is similar to the passive RF-powered IPG implant **400** (**FIG. 4A**), but with an internal battery **423** as a secondary source of power. The secondary battery **423** is large enough to store sufficient energy for at least a single sleep session and optimally for many more, and in certain embodiments is sufficient for at least a week of use. In this embodiment, the secondary-battery-powered IPG implant **420** receives its power for charging the secondary battery **423**, receives commands, and exchanges data with an external controller using an inductively coupled RF power and data link. The external controller and its associated coil are placed over the internal coil **421** long enough to exchange data and charge up the secondary battery **423**.

[0084] The rate at which the secondary battery **423** may be charged is typically longer than the charge times for ultracapacitor embodiments. Charge rates for secondary batteries such as lithium ion and lithium polymer are typically expressed as a percentage of charge capacity, typically from C/40 to C/1, where C is the charge capacity of the battery. For instance, a 200 milliamp-hour (mA-hr) battery could be charged at 50 mA for a C/4 rate. There is a trade-off for all battery chemistries in performance and longevity of the battery depending upon both the charge and discharge rates, as well as the depth of discharge prior to a charging session. High rates of charge and discharge are known to reduce the longevity of a secondary battery system, as well as deeply discharging a battery, whereas low rates of charge and discharge, and limited discharge durations with short periods of charge tend to enhance battery performance and longevity. This translates to a convenience factor for the patient in that to lengthen the time between surgical replacement for the IPG occurs the patient must frequently charge their implanted system, but if the patient desires to only charge when absolutely necessary it is more likely that the IPG will have a shorter implanted lifetime. These issues must be considered by the patient and the clinician as to how often and how long the device must be recharged.

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[0085] 4. Hybrid Powered IPG Implant

[0086] **FIG. 4D** shows an exemplary embodiment of hybrid-ultracapacitor and secondary-battery-powered IPG implant **430**. In this embodiment, the hybrid-ultracapacitor and secondary-battery-powered IPG implant **430** receives power for charging the internal ultracapacitor **433** and its secondary battery **434**, receives commands, and exchanges data with an external controller with an inductively coupled RF power and data link. Charge may be stored in the secondary battery **434**, allowing sleep sessions with no external hardware for up to a week at a time (except for initial IPG turn-on and final turn-off). The patient may also charge for just a few moments to fill the ultracapacitor **433**, or use the hybrid-ultracapacitor and secondary-battery-powered IPG implant **430** in only a fall-back operation of ultracapacitor operation only when the service life of the secondary battery **434** is exhausted, avoiding the need for surgical replacement.

[0087] Other forms of implanted power sources may also be used without departing from the scope of this invention, such as harvesters of kinetic energy, fuel cells, and even atomic sources.

[0088] C. Exemplary IPG Accessories

[0089] In certain embodiments, the IPG interfaces with other devices. **FIGS. 5A – 5D** show exemplary embodiments of IPG accessories. The other devices may include, for example: (1) an external controller with an integrated or attached coil (**FIG. 5A** and **5B**); (2) a charging station to replenish energy to the external controller (**FIG. 5D**); and (3) a remote control that communicates with the controller (**FIG. 5C**). In certain embodiments, the remote control also establishes the operating mode for the patient and/or monitors the performance of the implant and controller. These embodiments are described below.

[0090] 1. External Controller

[0091] **FIG. 5A** shows an exemplary embodiment of an external controller **500**. In this embodiment, the external controller **500** has a rechargeable power source such as a secondary battery system (lithium ion, etc.), electronics to power and communicate with the IPG, and a telemetry portion that communicates with the remote control. The telemetry portion as shown is a coil, but can be any item used by those skilled in the art to transmit and receive data. In the embodiment shown the coil as shown is integrated with the external controller **500**, but can be separate from the external controller **500** in other embodiments. In the embodiment shown, the telemetry portion between the external controller **500** and the remote control (**FIG. 5C**) uses Bluetooth or other wireless communication standard. Utilizing such a standard allows commonly available technologies to be utilized for the remote control and

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additionally allows communication with a computer programming system. The embodiment shown is exemplary only, and not limited to what is shown. In other embodiments, the external controller **500** communicates with the remote control or clinician's programmer (such as a computer or other electronic device) using a cable having a USB or other connection known to those skilled in the art. The cable can be in addition to or in place of the wireless telemetry.

[0092] The external controller **500** has user interface functions with an activity indicator, such as, for example, an LED indicating whether the device is operational. The interface may also have another indicator showing link and activity with the remote control. The external controller **500** interfaces with a recharging station (**FIG. 5D**), so that when the patient starts or ends a sleep session the controller **500** may be easily removed from or returned to the recharging station.

[0093] In the exemplary embodiment shown in **FIG. 5A**, the external controller **500** is mounted to a collar or neck strap **501** that allows simple fitting of the external controller **500** about the patient's neck and provides optimal alignment with the sub-mandibular IPG implant **200** (**FIGS. 2A – 2D**) for proper power and data transfer. The neck and sub-mandibular location of the external controller **500** and sub-mandibular IPG implant **200** are minimally affected by head and neck movement during sleep, with typical patient movement during sleep resulting in only minimal forces applied to the devices.

[0094] **FIG. 5B** shows another exemplary embodiment of an external controller **510**. In this exemplary embodiment, the controller **510** is worn behind the ear (BTE) and is similar in shape to a speech processor used with a cochlear implant. This shape gives the BTE controller **510** a low profile, which helps keep it from being dislodged during sleep. This shape is exemplary only, and not limited to what is shown. The controller operatively connects to a coil, which is placed near the mastoid bone implant **100** (**FIGS. 1A – 1F**) prior to sleeping. The controller coil optionally has a magnet to help align it with the internal coil **120**.

[0095] The BTE controller **510** has user interface functions with an activity indicator, such as, for example, a charge indicator LED **512** indicating whether the device is operational. The interface may also have another telemetry indicator LED **513** showing link and activity with the remote control. The BTE controller **510** interfaces with a recharging station (**FIG. 5D**), so that when the patient starts or ends a sleep session the BTE controller **510** may be easily removed from or returned to the recharging station.

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[0096] 2. Remote Control

[0097] **FIG. 5C** shows an exemplary embodiment of a remote control **530**. In the embodiment shown, the remote control **530** provides the patient with a simple and intuitive interface to the IPG system. The remote control **530** allows the patient to start and stop IPG operation, and interrogate the IPG system and external controller **500** (**FIG. 5**A) for proper function, status of the communication and power link to the IPG, and status of external controller **500** power. With the embodiment of the remote control **530** shown, the patient may also choose operating modes for the IPG, including but not limited to standard sleep mode, exercise mode, and alternative operating modes. If enabled by the clinician, the remote control **530** also allows the patient to adjust stimulation levels. The embodiment is exemplary only, and not limited to what is shown. For example, the remote control **530** may communicate with the external controller **500** using a cable having a USB or other connection known to those skilled in the art. The cable can be in addition to or in place of the wireless telemetry.

[0098] In certain embodiments, the remote control is incorporated into an Apple iPhone™ **520** or other wireless device. The iPhone™ **520** has an excellent user interface, Bluetooth telemetry capability, and is supported as a development platform for commercial applications. The iPhone™ **520** also allows the patient to transfer data to and from the Internet, enabling secure communications to the clinician and the manufacturer. Using a commercially available remote control also eliminates the need to manufacture the remote, simplifying the supply, support, and (potentially) the patient learning curve. Using a commercially available alternative also provides the opportunity to provide extensive help resources, such as context sensitive help screens, training videos, and live help from company and clinician support centers if required by the patient. In certain embodiments, one or more of the iPhone™ **520** commercial functions are disabled, with the iPhone™ **520** only acting as a remote control for the external controller **500**/IPG system. The iPhone™ **520** would enable the patient to operate the implant system and have access to help documents and videos that help the patient use the system. In other embodiments, one or more of the iPhone™ **520** commercial functions are enabled. Other embodiments of the iPhone™ **520**, or other forms of smart phones may also be used, and may be more readily available in certain markets around the world.

[0099] In certain embodiments, the external controller **500** interfaces with a computer. The interface may be wireless, or by a cable having a USB or other connection known to those skilled in the art. The cable can be in addition to or in place of the wireless telemetry. The

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computer may be a Windows™, UNIX ™, Linux™ or Macintosh™ based notebook or desktop computer having Bluetooth communication capability. Other telemetry known to those skilled in the art may also be utilized. Using telemetry known to those skilled in the art facilitates compatibility with industry standards and systems. Other wireless communication standards may be used without departing from the scope of the invention. The computer maintains a database to store all pertinent patient data, including stimulation settings, follow-up session changes, etc. The computer may also have an application with an intuitive method to test and program the IPG system so that the clinician can set IPG implant stimulation parameters for some or all of its operating modes.

[0100] 3. Recharging Station

[0101] **FIG. 5D** shows an exemplary embodiment of a recharging station **540**. In the embodiment shown, the recharging station **540** is a cradle-like device powered by a wall-wort power supply. The external controller **500** (**FIG. 5A**) is placed in its cradle for recharging during non-sleep periods. Recharging may be inductive, relying upon the orientation of the external controller **500** within the cradle for inductive coupling to the mating coils of the devices. Recharging may also utilize metal contacts **541** on the exterior surface of the controller for direct recharging to the external controller **500**, much like that of a standard cordless telephone handset. In certain embodiments, the wall-wort power supply is a commercially available recharger.

[0102] II. Electrodes

[0103] The IPG system delivers stimulation to targeted nerves or nerve fibers using implanted electrodes. In certain embodiments, the electrodes consist of biocompatible silicone rubber with a Dacron or similar woven material to lend tear resistance to the design. The electrode contacts are fabricated with 90 percent platinum and 10 percent iridium (90/10 Pt-Ir), known in the industry as highly biocompatible materials with excellent properties for neural excitation. Other materials known to those skilled in the art may also be used.

[0104] Researchers treating obstructive sleep apnea have discovered that the muscles of interest are activated by HGN nerve fibers lying interior to the HGN with respect to the outside of the patient (*i.e.*, the dorsal aspect of the HGN). **Figures 6A – 6G** (discussed below) show exemplary embodiments of IPG electrodes that take advantage of this neural organization. For example, in certain embodiments one or more electrode contacts lie preferentially on the inside surface of the cuff or trough on the interior portion. Some embodiments have at least four contacts, others as many as eight, which act as excitatory electrode contacts. Other embodiments have additional contacts located longitudinally distal

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to the excitatory contacts. In these exemplary embodiments, the additional contacts have a common electrical connection to the IPG case, or are multiplexed to at least one IPG output. This provides many ways of stimulating the HGN nerves, including contact to case indifferent, contact to array indifferent, contact to contact (bipolar or multipolar), and any combination of the above. These and other exemplary electrode embodiments are discussed below.

[0105] A. Electrode Designs

[0106] Electrodes can be designed in many different ways. Three possible designs include the fully encircling cuff (**FIGS. 6A – 6D**), the helical cuff (**FIG. 6E**), and the open trough (**FIGS. 6F – 6G**). Embodiments of each are discussed below. These embodiments are exemplary only, and not limited to what is shown.

[0107] 1. Fully-Encircling Cuff Electrodes

[0108] **FIGS. 6A – 6D** show exemplary embodiments of fully encircling cuff electrodes **600**. For example, **FIG. 6A** shows a non-perforated fully encircling cuff. Non-perforated fully encircling cuffs must be used with care, as connective tissue buildup in response to a foreign body can cause an increase of HGN **10** diameter and potential constriction of the HGN **10** after surgery. Some swelling of the HGN **10** is expected due to the surgical trauma the nerve endures when it is dissected and the electrode is installed. The swelling and increase in connective material may damage the nerve, due to the effect of pressure on the blood supply of the nerve trunk, and the increased pressure on the nerve axons of the trunk.

[0109] In other embodiments, the implantable neurostimulator system of the present invention includes a fully encircling perforated cuff electrode **605** (**FIGS. 6B – 6D**). In some embodiments, the perforated cuff electrode **605** is from about 4 mm to about 12 mm in diameter. In some embodiments, the perforated cuff electrode **605** is from about 6 mm to about 10 mm in diameter. In yet another embodiment, the perforated cuff electrode **605** is about 8 mm in diameter.

[0110] Alternatively, the diameter of the perforated cuff electrode **605** is expandable and increases or decreases in accordance with the diameter of the HGN **10**. In further embodiments, the perforations **607** and/or the plasticity of the material comprising the perforated cuff electrode **605** allows accommodation of the expected change in diameter and swelling response and prevents ischemic constriction of the HGN **10**. In some embodiments, the perforations **607** are about 2 mm in diameter. The perforated cuff electrode **605** may also be self-sizing. In some embodiments, the fully encircling perforated cuff electrode does not physically contact the entire circumference of the HGN **10**. In still other embodiments, the

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perforated cuff electrode **605** overlaps upon itself, thereby creating an empty space **606** into which a nerve may expand without ischemic constriction. In certain expandable cuff embodiments, the electrode diameter is expandable, with ranges extending from a diameter of approximately 2 mm to a diameter of approximately 12 mm. Other expansion ranges may be used without departing from the scope of the invention.

[0111] In some embodiments, the perforated cuff electrode **605** includes electrical contacts **608** on its inner surface facing a nerve. The perforated cuff electrode **605** may include any number and/or arrangement of contacts **608**. For example, the perforated cuff electrode **605** can include at least six contacts **608**. In other embodiments, the perforated cuff electrode **605** includes at least eight contacts **608**. In certain embodiments, the contacts **608** are axially aligned relative to the perforations **607** of the perforated cuff electrode **605 (FIG. 6B)**.

[0112] Alternatively, the contacts **608** can be axially staggered relative to the perforations **607 (FIGS. 6C– 6D)**. In some embodiments, the contacts **608** are about 1 mm in diameter. In still other embodiments, the distance between contacts **608** is about 1 mm. The contacts **608** need not circumscribe the entire circumference of the nerve. In certain embodiments, the flap of the electrode cuff overlaps an electrode lead (**FIGS. 6B – 6C**) and in others it does not (**FIG. 6D**). In further embodiments, the positions of the contacts **608** relative to a nerve changes as the diameter of the nerve increases or decreases. The contact size, number, location, and arrangement are exemplary only, and not limited to what is shown. Other combinations may be used without departing from the scope of the invention.

[0113] 2. Helical Cuff Electrodes

[0114] **FIG. 6E** shows an exemplary embodiment of a helical cuff electrode **610**. The helical cuff electrode **610** mitigates the problems of a fully encircling cuff electrode **600** (**FIG. 6A**). One example is a helical cuff electrode developed by the Huntington Medical Research Institute for stimulating the vagus nerve. In this example, the cuff electrode **610** winds around a nerve trunk, but does not overlap itself and is not sutured into a fixed diameter. In still other exemplary embodiments, the cuff electrode **610** is self-sizing. A self-sizing cuff encircles the nerve in its natural state. The cuff electrode **610** overlaps its ends but still allows some expansion of the cuff until the connective tissue overgrowth assumes its final state after surgical implantation.

[0115] 3. Open Trough Electrodes

[0116] **FIG. 6F** shows an exemplary embodiment of a round-bottomed open trough electrode **620**. In the exemplary embodiment shown, the contacts **621** reside on the inside of the trough. In certain round-bottomed open trough embodiments, contacts **621** are present on

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the innermost region of the interior of the trough, while the portion of the trough that covers the outer portion of the HGN **10** has no contacts.

[0117] The open trough electrode **620** addresses some of the problems associated with the fully encircling electrode **600** design by lying underneath the nerve trunk, rather than completely encircling or enclosing the nerve trunk. This allows tissue expansion and swelling, as well as the connective tissue buildup, while still allowing the nerve to expand away from the trough without constriction. The exemplary open trough electrode **620** embodiment shown slips underneath the HGN **10** with little dissection. The normal forces holding the tissues of the neck in place help keep the HGN **10** aligned with the open trough electrode **620**. The open trough electrode **620** may optionally be anchored to surrounding tissue to maintain its position with respect to the HGN **10** to prevent distension or other loading forces upon the HGN **10**.

[0118] In some embodiments of the present invention, it is desirable to place the contacts **621** of an open trough electrode **620** preferentially against one surface of the nerve bundle, and it is also desirable to avoid placing any forces against the nerve as it lies in the electrode **620** to force it into a new or different shape from its native shape. In some embodiments, the open trough electrode **620** maintains the position of the nerve within the electrode trough up until the point at which connective tissue growth has secured the nerve and electrode **620** interface.

[0119] **FIG. 6G** shows a flat-bottomed variant **625** of an open trough electrode. While the contemporary textbook view of the shape of peripheral nerves is that of rounded structures, they may in fact also assume oval or flattened shapes depending upon their internal structure and where they lie in respect to other tissue structures such as muscles, bones, and fascial planes. One of the internal structure determinants of cross-sectional shape may be the absence or presence of fascicular organization. The design of a flat-bottomed open trough electrode **625** advantageously allows a flattened nerve to lie against a series of contacts on a flattened surface, thereby also allowing a lower profile between the tissue structures where the peripheral nerve occurs.

[0120] In some embodiments of the present invention, an implantable neurostimulator system includes at least one flat-bottomed open trough electrode **625**. In some embodiments, an absorbable suture material **627** is placed between the flaps **626** of the electrode **625** to prevent the nerve from moving out of the trough during the connective tissue growth period after initial implantation. In some embodiments, the suture material **627** has a finite lifetime before dissolving. This limits the potential for long-term damage that might result from a

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permanent compressive or retentive mechanism such as a hard flap or fixed diameter cuff. In some embodiments, the flat-bottomed open trough electrode **625** provides a means of selective activation that only temporarily constrains the nerve within the electrode, and presents a lower profile for the same cross sectional nerve area than a comparable rounded trough electrode.

[0121] B. Electrode Configurations

[0122] The fully encircling cuff, helical cuff, and open trough electrodes can be configured as monopolar, bipolar or multipolar electrodes. For example, electrodes may be composed of at least one pair of platinum/iridium cathode and anode contacts arranged in a helical pattern on a substrate of heat shaped, biocompatible polystyrene strip material. The contact pairs are oriented transversely to the HGN to drive stimulus into internal nerve fibers. In another embodiment the electrode design is a helix. In another embodiment, the electrode design is a cuff with fingers, and in another embodiment, the electrode design is an electrode that penetrates the nerve itself. **FIGS. 7A – 9B** show selected exemplary embodiments of these electrode configurations. The number and arrangement of the contacts shown in each of these figures are exemplary only, and not limited to what is shown.

[0123] 1. Monopole Electrode Configuration

[0124] **FIGS. 7A** and **7B** show exemplary embodiments of monopole electrode configurations. Monopolar stimulation typically results in lowered stimulation thresholds since there is no shunting of current between contacts before it is free to enter the nerve bundle. **FIG. 7A** shows an exemplary embodiment of a monopolar, single cathodal contact, IPG case return electrode **700**. In the configuration shown, a stimulation electrode contact **702** acts as the excitatory cathodic contact, with the IPG case **701** providing the complementary current return path. **FIG. 7B** shows an exemplary embodiment of a monopolar, single cathodal contact, indifferent array return electrode **710**. In the embodiment shown in **FIG. 7B**, a stimulation electrode contact **711** acts as the excitatory cathodic contact, with another array of contacts (an indifferent array) **713** furnishing the complementary current return. The indifferent array **713** has one or more contacts, with the indifferent array contacts **713** typically having a larger surface area than the excitatory contact.

[0125] In monopolar or bipolar stimulation, the waveform is often asymmetrical biphasic, since it is sometimes undesirable to have a final excitatory phase of cathodic stimulation on the case electrode. Those skilled in the art of electrical stimulation understand that symmetrical biphasic pulses may result in excitatory cathodic phases of stimulation at each of

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the necessary contacts of a stimulation electrode. By utilizing asymmetrical waveforms the first cathodic phase is of an amplitude and phase duration adequate to achieve excitation of the nerve, but the later anodic phase is both longer and of lower amplitude, which at the return or second electrode contact, results in a cathodic phase which is not of sufficient amplitude to cause nerve excitation. The common practice of using a large indifferent or case electrode at a location away from the nerve electrode acts to reduce current density at the indifferent electrode at a site away from the nerve, which also minimizes the likelihood of excitation at that electrode.

[0126] 2. Bipolar Electrode Configuration

[0127] **FIG. 8** shows an exemplary embodiment of a bipolar electrode configuration **800**. Bipolar electrode configurations **800** have two contacts with approximately the same geometric surface area stimulating as a pair. One electrode is the excitatory contact **801** and the other electrode is the return (indifferent) contact **803**. The charge delivered and recovered by both contacts is approximately equal. Therefore, the return (indifferent) contact **803** can cause nerve **802** excitation during the last phase of the waveform if the waveform is symmetrical, and can cause anodic phase excitation depending upon the orientation and other features of the nerve **802** within the vicinity of the second contact **803**. If the waveform utilized in bipolar stimulation is symmetrical then it is likely that excitation will occur at each electrode contact. If the waveform is asymmetrical, it is likely that excitation will only occur at the primary cathodic contact **801**.

[0128] 3. Multipolar Electrode Configuration

[0129] Multipolar configurations allocate three or more contacts to stimulate as an array. **FIGS. 9A** and **9B** show exemplary embodiments of multipolar electrode configurations. **FIG. 9A** shows an exemplary embodiment of a multipolar, two cathodal contact, IPG case return multipolar electrode array **900**. The cathodal contacts **902, 905** typically function as the excitatory contacts. Although only two cathodal contacts **902, 905** are shown, each with their own source, additional cathodal contacts (with either independent or shared sources), may be used without departing from the scope of the invention. In the embodiment shown, the IPG case **901** provides the complementary current return. This embodiment is exemplary only, and not limited to what is shown.

[0130] **FIG. 9B** shows an exemplary embodiment of a multipolar, two cathodal contact, indifferent contact return multipolar electrode array **910**. The cathodal contacts **913, 914** typically function as the excitatory contacts. Although only two cathodal contacts **913, 914** are shown, each with their own source, additional cathodal contacts (with either independent

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or shared sources), may be used without departing from the scope of the invention. In the embodiment shown, another array of contacts (the indifferent array) **911** provides the complementary current return. This embodiment is exemplary only, and not limited to what is shown.

[0131] In multipolar configurations, current fields may be manipulated in different or multiple directions, thereby changing neural recruitment patterns, and may do so without adversely spilling over or recruiting undesired neural populations. This mode of operation is best served by current sources for each electrode contact that can be activated concurrently, *i.e.*, by a single timing generator. Alternatively, multiple timing generators may be used with multiple contacts to recruit different populations of neurons offset in time that result in approximately simultaneous activation of the motor units with which they associate. This occurs because of the relatively long time constant of muscle activation with respect to motor nerve recruitment but is not to be confused with concurrent stimulation as described previously, which can result in neural recruitment patterns unsupportable by single current source multiplexed stimulation alone or summated in time for motor unit recruitment.

[0132] C. Electrode Waveforms

[0133] These electrodes generate excitatory contact waveforms and complementary contact waveforms to stimulate targeted nerves or nerve fibers. Stimulation frequency is adjustable from approximately 1 Hertz (Hz) to approximately 100 Hz or higher. Typical frequencies for producing a tetanic contraction range from approximately 15 Hz to approximately 60 Hz. Lowering the frequency to the lowest required for a smooth, tetanic, and comfortable contraction reduces device power consumption and reduces muscle fatigue elicited by electrical stimulation. These stimulation patterns are exemplary only, and not limited to what is described. While only excitatory contact waveforms and complementary contact waveforms are explained below, other stimulation waveforms of other stimulation frequencies may be used without departing from the scope of the invention.

[0134] 1. Excitatory Contact Waveforms

[0135] Excitatory electrode contact waveforms may be symmetrical or asymmetrical biphasic, cathodic phase first, followed by a short interphase interval, followed by an anodic (charge recovery) phase. The first cathodic phase ranges from approximately 10 to approximately 1000 microseconds long. The interphase interval can be as short as approximately 10 microseconds and as long as approximately 250 microseconds, and is set to 50 microseconds by default. The interphase interval is set to be long enough to allow the first cathodic phase to achieve its full recruitment function before the charge recovery phase

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occurs. Shortening the interphase interval to less than the recruitment time would diminish the effect of the cathodic phase and waste a portion of the energy supplied during recruitment. The anodic phase duration and amplitude are approximately identical to the cathodic phase for a symmetrical biphasic waveform, and the anodic phase of an asymmetrical waveform is approximately six times the duration of the cathodic phase in certain embodiments, with a concomitant phase amplitude approximately one-sixth the amplitude of the cathodic phase.

[0136] In the symmetrical and asymmetrical waveforms, the charge delivered during the cathodic phase is approximately equal to the charge recovered in the anodic phase. In certain embodiments, ceramic coupling capacitors in series with the output circuitry to each electrode contact help maintain the charge balance and prevent the passage of direct current, known to be harmful to tissue and which may increase the likelihood of failure in feedthroughs of the electronics enclosure. The coupling capacitors must be large enough to pass current phases without significant droop.

[0137] 2. Complementary Contact Waveforms

[0138] Complementary electrode contact waveforms have the opposite polarity as excitatory electrode contact waveforms, but similar amplitude and phase duration characteristics. If the waveform is symmetrical biphasic, the third phase of the waveform at the complementary contact is cathodic, and could excite nerves in its vicinity. If the waveform is asymmetrical, the third phase of the waveform would be cathodic as well, but its amplitude would be roughly one sixth of the excitatory contact amplitude, and would be unlikely to excite any nerves.

[0139] D. Electrode Power

[0140] In the embodiments discussed above, independent current sources power each electrode contact. Each contact is driven by its own current generator, which sources or sinks up to approximately 12.7 mA in 0.1 mA steps. The compliance voltage is the voltage that the current generator utilizes for constant current generation for each current source, and in the exemplary embodiment shown is approximately 18 volts. In other embodiments, compliance voltage ranges from approximately 15 to approximately 20 volts. The expected bipolar electrode to tissue impedance is approximately 500 to 1500 ohms. Assuming an electrode-to-tissue impedance of 1000 ohms, it would take roughly 1 volt of compliance voltage to drive 1 mA of current through the electrode contact, and roughly 12.7 volts to drive 12.7 mA of current through the electrode contact for the initial access voltage portion of the pulse, and higher voltages as the current is maintained through the coupling capacitor. Since the outputs

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are capacitively coupled, the compliance voltage should be greater than this initial access voltage to maintain the current for the duration of the pulse phase. Compliance voltage is chosen based on factors such as maximum current desired, maximum phase duration desired, coupling capacitor size, and expense of providing high voltage power supplies to maintain constant current for the duration of the pulse phase.

[0141] Total current delivered to all contacts typically does not exceed the steady state output of the IPG power supply. Current in this exemplary embodiment is limited to approximately a 20 mA concurrent output. Overall current consumption depends on many factors, including, for example, phase duration, phase amplitude, and pulse frequency. Taking these factors into account, the total current output in the exemplary embodiment is approximately 2 mA. The current and voltage levels in these embodiments are exemplary only however. Other power levels may be used without departing from the scope of the invention.

[0142] III. IPG Nerve Stimulation

[0143] The embodiments described above allow for accurate, selective nerve stimulation, including for example, the HGN. By accurately and selectively stimulating the HGN with multiple independent current sources and site-specific multiple contact electrodes, often in combination with patient specific stimulus programming, only the portions of the HGN responsible for non-timing dependent activation are recruited and activated, enabling accurate open-loop stimulation. These exemplary embodiments incorporate independent and concurrent stimulation, enabling optimal selective stimulation of only the desired portions of the HGN.

[0144] This independent and concurrent stimulation produces the desired tongue movement without needing to sense breathing related events to achieve desired results. Other embodiments of the IPG can include timed stimulation. Timed stimulation allows for triggered open loop or fully closed loop stimulation. Various examples of stimulation are discussed in United States Patent Application Nos. 60/978,519 and 61/017,614 filed on October 9, 2007 and December 29, 2007 respectively, which are incorporated herein by reference. The sections below describe how nerves are recruited, and include examples of stimulation patterns generated with these exemplary embodiments. These patterns are exemplary only, and not limited to those discussed below.

[0145] A. Nerve Structure, Activation, and Recruitment

[0146] One of the contributors to nerve activation threshold is nerve fiber diameter. Due to the electrical cable properties of the nerve fibers, large diameter nerve fibers have a lower

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excitation threshold than smaller diameter fibers, and are more easily excited by electrical stimulation. Thus, nerve fibers are more likely to be recruited by an electrical stimulation pulse if they are closer to the activating electrode, and/or have a larger diameter than other fibers.

[0147] B. Force Vectoring and Field Steering

[0148] Multiple contact electrodes may be used in conjunction with multiplexed stimulator systems to co-activate multiple muscle groups to achieve a desired muscle response. In activating the muscles of the tongue, hand, or forearm, for instance, several contacts may be sequentially energized to deliver interlaced pulses to first one contact and then another, to activate two or more muscle groups that when added result in a force vector in the desired direction. This is force vectoring.

[0149] **FIGS. 10A** and **10B** show an example of a multiplexed system using force vectoring. Even using force vectoring, multiplexed or single-source electrodes have limitations in the stimulation patterns they could deliver. For example, with a single cathodic phase current from a single contact, the nerve fibers closest to the contact are the first to be recruited or activated (assuming uniform distribution of fiber diameters, etc). As shown in **FIG. 10A**, even if the source were multiplexed to multiple contacts however, the waveform generator **1000** would connect to each contact **1005-1008** via a switching network **1001-1004**. **FIG. 10B** illustrates this with an example. As shown in **FIG. 10B**, only a single waveform can be sent at any given time. First, channel 1 is enabled (*i.e.*, switched on) and a waveform is generated for channel 1 by a single waveform source. When the channel 1 waveform is complete, channel 1 is disabled (*i.e.*, switched off). Once channel 1 is disabled, channel 2 is enabled, and a waveform is generated for channel 2 using the same waveform source. Simultaneous transmission of multiple waveforms is not possible with this design.

[0150] **FIGS. 11A** and **11B** show exemplary embodiments of non-multiplexed waveform generators **1100**. These embodiments are used for field steering. Field steering solves the limitations of force vectoring. Field steering uses independent current sources and multiple electrode contacts together to define a volume of activated nerve fibers. Field steering uses multiple independent current sources to generate highly selective patient-specific activating current volumes.

[0151] Field steering is more selective than simple force vectoring. Field steering (also known as current steering) enables activation of a particular region or volume of nerve fibers near two or more electrode contacts by controlling the cathodic phase amplitude generated by each of the contacts independently. For example, using two cathodic contacts **1101** and **1102**

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with equal phase amplitudes (for example by connecting two contacts to a single current source or by setting independent current sources to the same amplitude), applying a stimulus to the contacts defines a neural activation volume constrained to a region approximately equidistant between the two contacts. In this configuration, a sub-threshold phase current on each of the contacts **1101** and **1102** could be delivered, which combine to form an overlapping current field with supra-threshold current field. As previously discussed, with two electrodes of equal current the central volume between the electrodes is the activated nerve region.

[0152] Field steering allows the ability to change the activation area by changing the proportion of cathodic phase current from a 50-50 split (requiring independent multiple current sources), thereby shifting the current volume from the midline to a region closer to the higher phase current source electrode contact. In field steering, independent current sources are connected to individual electrodes and energized approximately simultaneously to define a volume where nerve fibers will be activated. In order to activate a selected pool of neurons located somewhere between two contacts, a stimulator delivers coincident stimulation pulses. They are delivered simultaneously rather than sequentially multiplexed. In the example shown in **FIG. 11A**, sub-threshold currents are delivered to each contact **1101-1104** so that the fields around the individual contacts are below the recruitment threshold. As shown in **FIG. 11B**, the currents need not be identical. The pulse phase durations are approximately equal, but amplitudes may differ because they are generated by independent current sources. The fields combine in the targeted nerve area to create pulses sufficient to stimulate the targeted nerve or nerves. Thus, nerve populations other than those lying directly under a stimulation electrode contact can be preferentially and selectively activated to achieve a desired stimulus pattern. This is important because the desired region of activation might not be positioned directly under a stimulation contact due to the surgical approach or a lack of a priori understanding of nerve fiber organization prior to the application of stimulation, but which allows for the later adjustment of this stimulation field to achieve the desired result.

[0153] IV. Stimulation Triggering and Measurement

[0154] The apparatus, system, and methods described above may use open loop stimulation, triggered open loop stimulation, and closed loop stimulation, either separately or in combination, to control stimulation. Closed loop can use sensors and signals to initiate stimulation and to regulate its output so that a desired output function is obtained. Triggered open loop stimulation uses one or more measurements as triggers for initiating stimulation.

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These triggers may be obtained using one or more internal sensors, external sensors, or a combination of both. Internal sensors can be included in the IPG implant, while external sensors would transmit trigger information to the IPG implant. The triggers can be transmitted to the IPG implant wirelessly (for example by RF, Bluetooth, or other wireless means known to those skilled in the art), or by operatively connecting the external sensor to the IPG implant.

[0155] Examples of triggers include, but are not limited to, snoring, airflow, actigraphy, hypoxia, tongue position, and tongue protrusion. In certain exemplary embodiments, snoring could be detected internally using a vibration sensor in the IPG implant. In other embodiments, snoring could be detected internally using an acoustic sensor and sound processor. In still other embodiments, snoring could be detected externally using, for example, a nasal canula or a microphone placed in the ear. Airflow could be measured externally using a nasal canula or thermistor and used as a trigger or as a closed loop feedback signal. Actigraphy could be measured using, for example, an accelerometer, which could be located internally or externally. Hypoxia could be measured internally using, for example, an infrared source and sensor in the IPG implant, or externally using an earlobe-monitoring unit. Tongue position could also be used as a trigger using, for example, a proximity sensor, while tongue protrusion could be used as a trigger using, for example, an accelerometer. These triggers could be used at any time, including initial placement, programming, and/or IPG implant calibration.

[0156] V. Auto Titration

[0157] Any combination of parameters measured in open loop, triggered open loop, and closed loop stimulation can be used to program and/or control stimulation. In certain embodiments, one or more measured parameters are used to alter stimulation programming automatically in real time in response to changes in user condition. This is auto titration.

[0158] Auto titration may be performed during initial implantation and programming, during normal IPG system operation, or both. For example, auto titration may be used to optimize IPG implant settings while the patient is in a medical facility, such as a clinic or hospital, a physician's office, a sleep laboratory, or while the patient is at home (home titration). Small changes to stimulation parameters and configurations are made while observing their effect on one or more indicators such as airway diameter, airway resistance, airflow, snoring, or other generally accepted measurements used to evaluate obstructive sleep apnea.

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[0159] Clinician input and other related events may also be entered to associate these indicators with patient sleep phases, including EEG and manual selection/confirmation of phase identification. Since sleep phases greatly affect the range of sleep disordered breathing (SDB) measurements, and since there may be significant delays in effects resulting from changes in stimulation parameter and configuration changes, computers may be used to assist with data analysis and confirmation of clinician assessments in a semi-automated system. In certain titration embodiments, the titration system has an automated programming capability (*i.e.*, an auto titration system). For example, certain exemplary titration embodiments use predetermined algorithms to alter stimulus in response to detection of apnea indicators. In certain exemplary embodiments, the auto titration system is portable.

[0160] Auto titration may also be used during normal IPG implant operation. For example, in certain embodiments a sensor, which may be in the IPG implant or the external patient controller, monitors a respiration indicator like air flow, for example. When the indicator drops, for example if flow decreases by 10% below average unobstructed sleeping patient flow, or snoring is detected, the IPG implant or external controller slowly increases stimulus to cause an improvement in the monitored indicator (*e.g.*, an increase in airflow and/or a decrease in snoring). If the sensor is connected to the IPG implant, the IPG implant changes stimulation parameters. If the sensor is connected to an external controller, the controller changes simulation parameters, or it triggers a preprogrammed increase in the IPG implant. The indicators are exemplary only. Other indicators known to those skilled in the art may be used without departing from the scope of the invention.

[0161] It will be apparent to those skilled in the art that various modifications and variations can be made in the Apparatus, System, and Method for Selective Stimulation without departing form the spirit or scope of the invention. Thus, it is intended that the present invention cover the modifications and variations of this invention provided they come within the scope of the appended claims and their equivalents.

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CLAIMS

What is claimed is:

1. An implantable neurostimulator system, comprising:
a hollow cylindrical electronics enclosure having a top, a bottom, and a side;
a coil extending from a first part of the electronics enclosure; and
at least one electrode operatively connected to the electronics enclosure.

2. The implantable neurostimulator of claim 1, wherein the coil is at least partially integral with the molded body.

3. The implantable neurostimulator of claim 1, further comprising a magnet.

4. The implantable neurostimulator of claim 1, wherein the electronics enclosure is hermetically sealed.

5. The implantable neurostimulator of claim 1, wherein the electronics enclosure contains a microcontroller and custom ASIC.

6. The implantable neurostimulator system of claim 1, further comprising at least one feedthrough lead extending through the electronics enclosure.

7. The implantable neurostimulator of claim 1, wherein the electronics enclosure operatively connects to an antenna and at least one electrode.

8. The implantable neurostimulator of claim 7, wherein the electronics enclosure operative connection is at least one feedthrough.

9. The implantable neurostimulator of claim 7, wherein the electronics enclosure operative connection is a permanently attached lead.

10. The implantable neurostimulator of claim 1, further comprising at least one power source.

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11. The implantable neurostimulator of claim 10, wherein the at least one power source is an RF device.

12. The implantable neurostimulator of claim 10, wherein the at least one power source is an ultracapacitor.

12. The implantable neurostimulator of claim 10, wherein the at least one power source is a battery.

14. The implantable neurostimulator of claim 1, further comprising an ultracapacitor and a battery.

15. The implantable neurostimulator of claim 1, wherein the neurostimulator receives power and telemetry commands from at least one external source.

16. An implantable neurostimulator system, comprising:

a symmetrical chevron-shaped molded body having an apex, a first and a second side, and a base;

a coil at the apex of the molded body;

an electronics enclosure at least partially integral with the molded body; and

at least one electrode operatively connected to the electronics enclosure.

17. The implantable neurostimulator of claim 15, wherein the implant has at least one hole along at least one of the first and second sides of the molded body.

18. A neurostimulator electrode, comprising:

a cuff having a first and a second surface;

at least one contact on one of the first and second surfaces; and

means for delivering a stimulus to the at least one contact.

19. The neurostimulator electrode of claim 18, wherein the cuff is biocompatible.

20. The neurostimulator electrode of claim 18, wherein the cuff is expandable.

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21. The neurostimulator electrode of claim 18, wherein the cuff has at least one perforation.

22. The neurostimulator electrode of claim 21, wherein the perforation penetrates through the first and second cuff surfaces.

23. The neurostimulator electrode of claim 18, wherein the cuff is helically shaped.

24. The neurostimulator electrode of claim 18, wherein the cuff is at least partially circular.

25. The neurostimulator electrode of claim 24, wherein the cuff is expandable from a diameter of approximately 2 mm to a diameter of approximately 12 mm.

26. The neurostimulator electrode of claim 24, wherein the cuff is self-sizing.

27. The neurostimulator electrode of claim 18, wherein the cuff overlaps at least a portion of itself to form an empty space defined by the second cuff surface.

28. The neurostimulator electrode of claim 18, wherein the cuff forms an open trough.

29. The neurostimulator electrode of claim 28, wherein the open trough has a round bottom.

30. The neurostimulator electrode of claim 28, wherein the open trough has a flat bottom.

31. The neurostimulator electrode of claim 18, further comprising at least one stimulation source.

32. The neurostimulator electrode of claim 18, further comprising at least two contacts.

33. The neurostimulator electrode of claim 18, further comprising at least three contacts.

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34. The neurostimulator electrode of claim 32 or 33, wherein each contact individually connects to a stimulation source.

35. The neurostimulator electrode of claim 18, further comprising a first and second contact array.

36. The neurostimulator electrode of claim 35, wherein the surface area of the second contact array is larger than the surface area of the first contact array.

37. An implantable neurostimulator system, comprising:
an electronics enclosure;
a coil; and
at least one perforated cuff electrode operatively connected to the electronics enclosure.

38. An implantable neurostimulator system, comprising:
an electronics enclosure;
a coil; and
at least one flat-bottomed open trough electrode operatively connected to the electronics enclosure.

39. A method of neurostimulation, comprising the steps of:
at least partially encircling a nerve with a cuff having a first and a second surface, the cuff having at least one contact on one of the first and second surfaces;
connecting at least one stimulus generator to the at least one contact; and
delivering a stimulus to the at least one contact.

40. The neurostimulation method of claim 39, wherein the stimulus is a controlled current.

41. The neurostimulation method of claim 39, further comprising the step of defining a neural activation volume by applying at least two stimuli to at least two contacts.

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42. The neurostimulation method of claim 41, wherein the at least two stimuli are delivered approximately simultaneously.

43. The neurostimulation method of claim 41, wherein at least one of the applied stimuli is an asymmetric pulse.

44. The neurostimulation method of claim 39, wherein the stimulus is pulse train having a frequency between approximately 1 and approximately 100 Hertz.

45. The neurostimulation method of claim 39, further comprising the step of detecting a trigger.

46. The neurostimulation method of claim 39, further comprising the step of changing the stimulus in response to a respiration indicator.

47. The neurostimulation method of claim 39, further comprising the step of initiating a preprogrammed stimulus in response to a respiration indicator.

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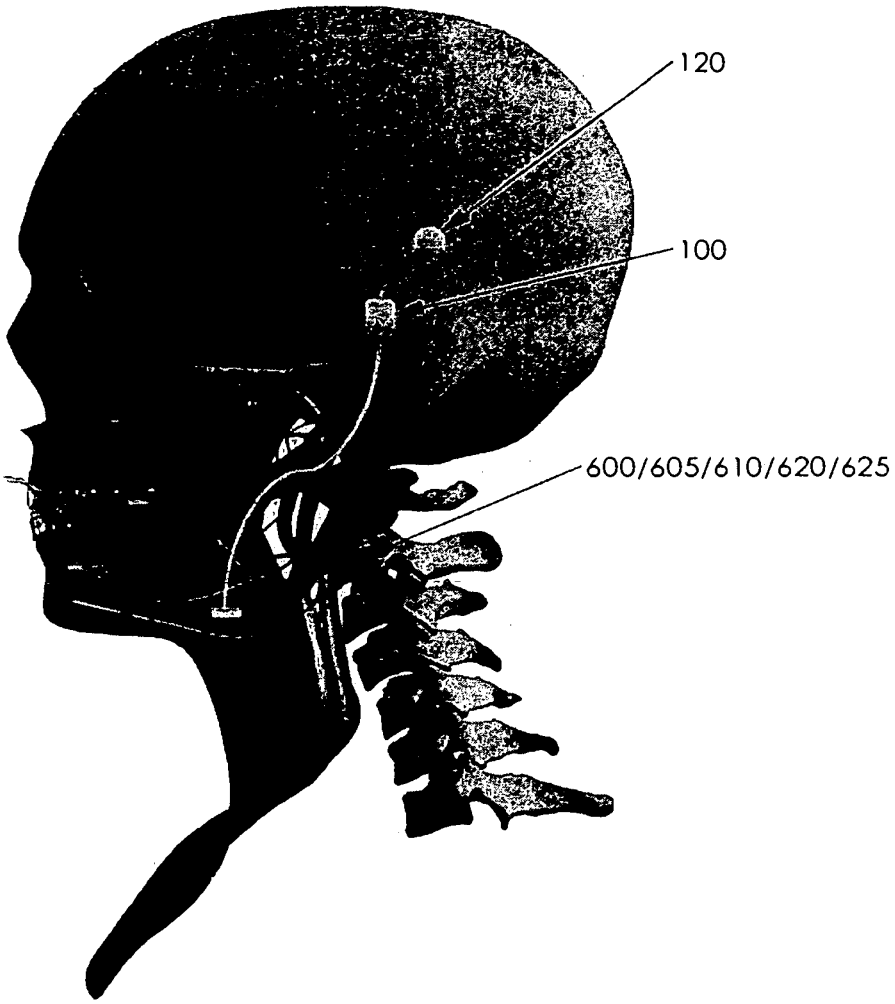


FIG. 1A

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FIG. 1B

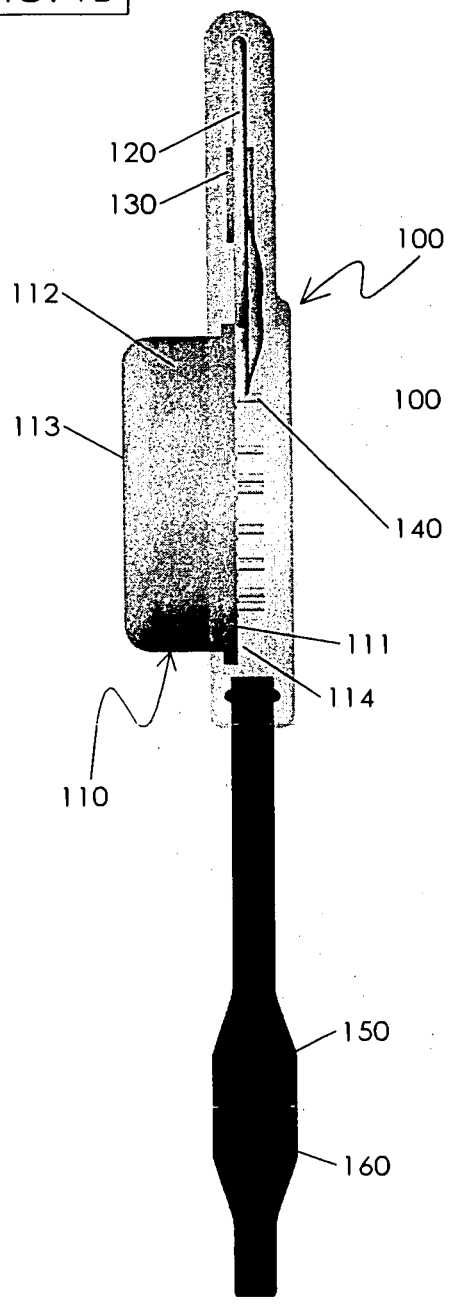


FIG. 1C

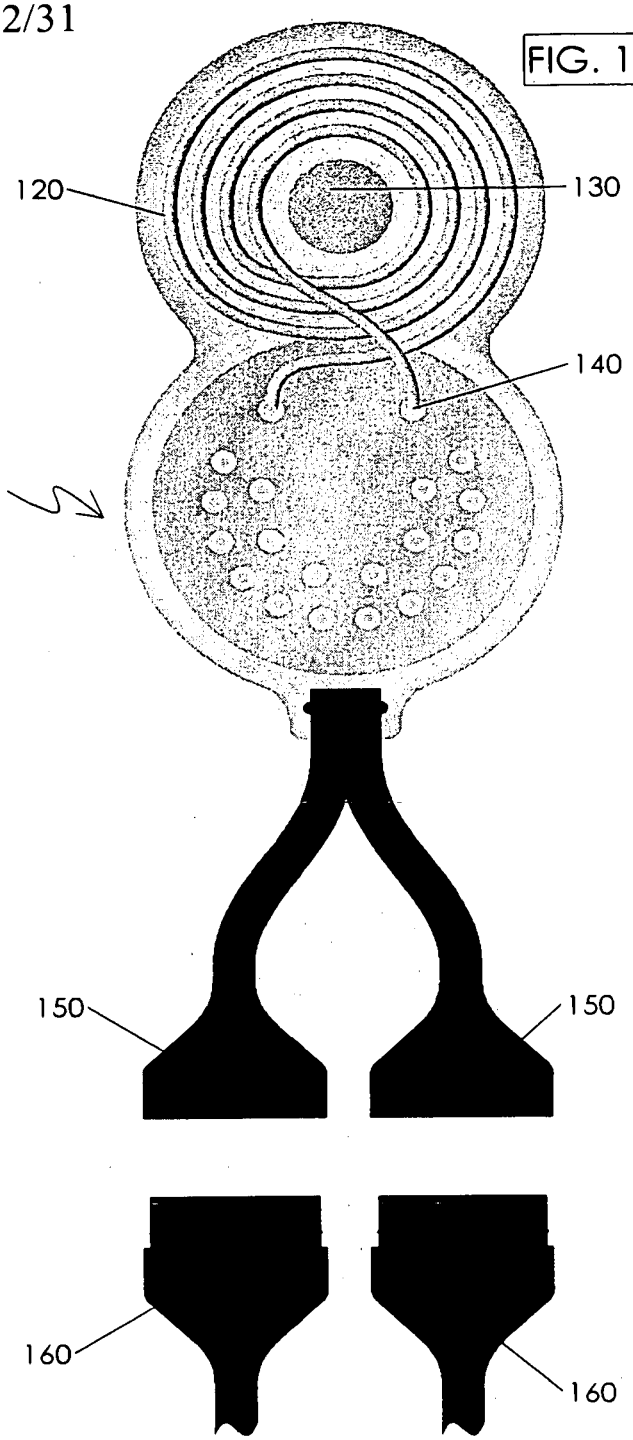


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FIG. 1D

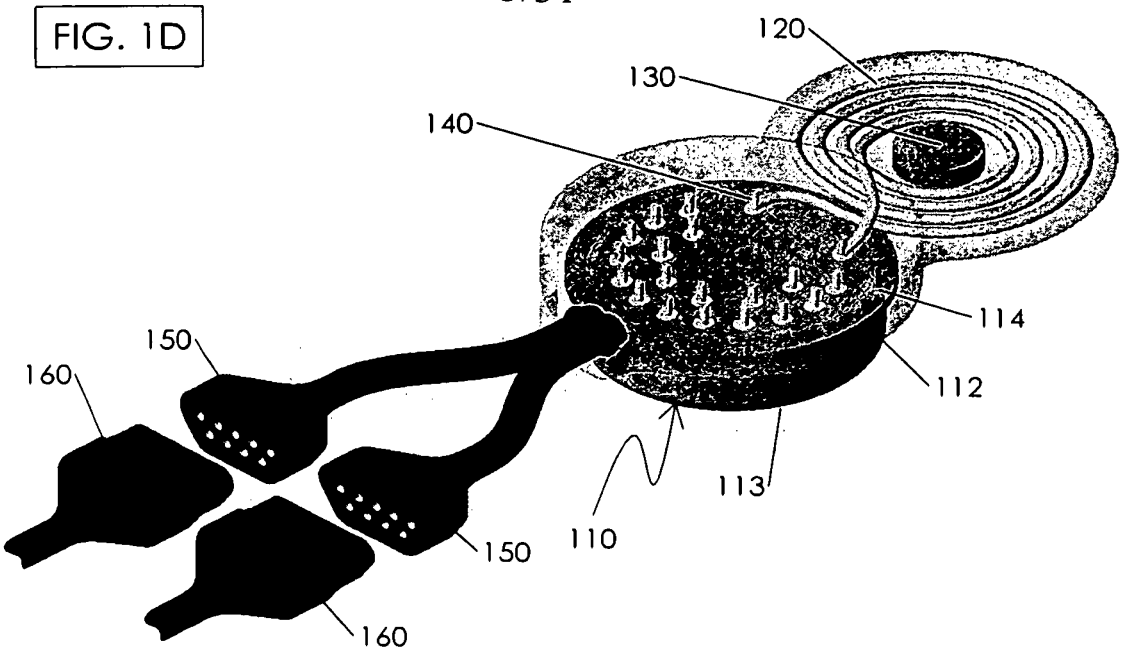


FIG. 1E

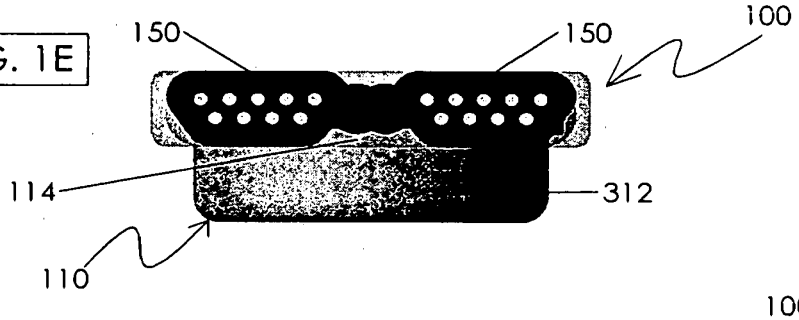


FIG. 1F

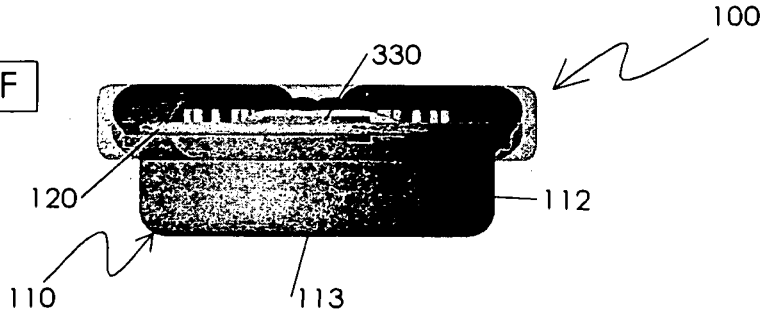


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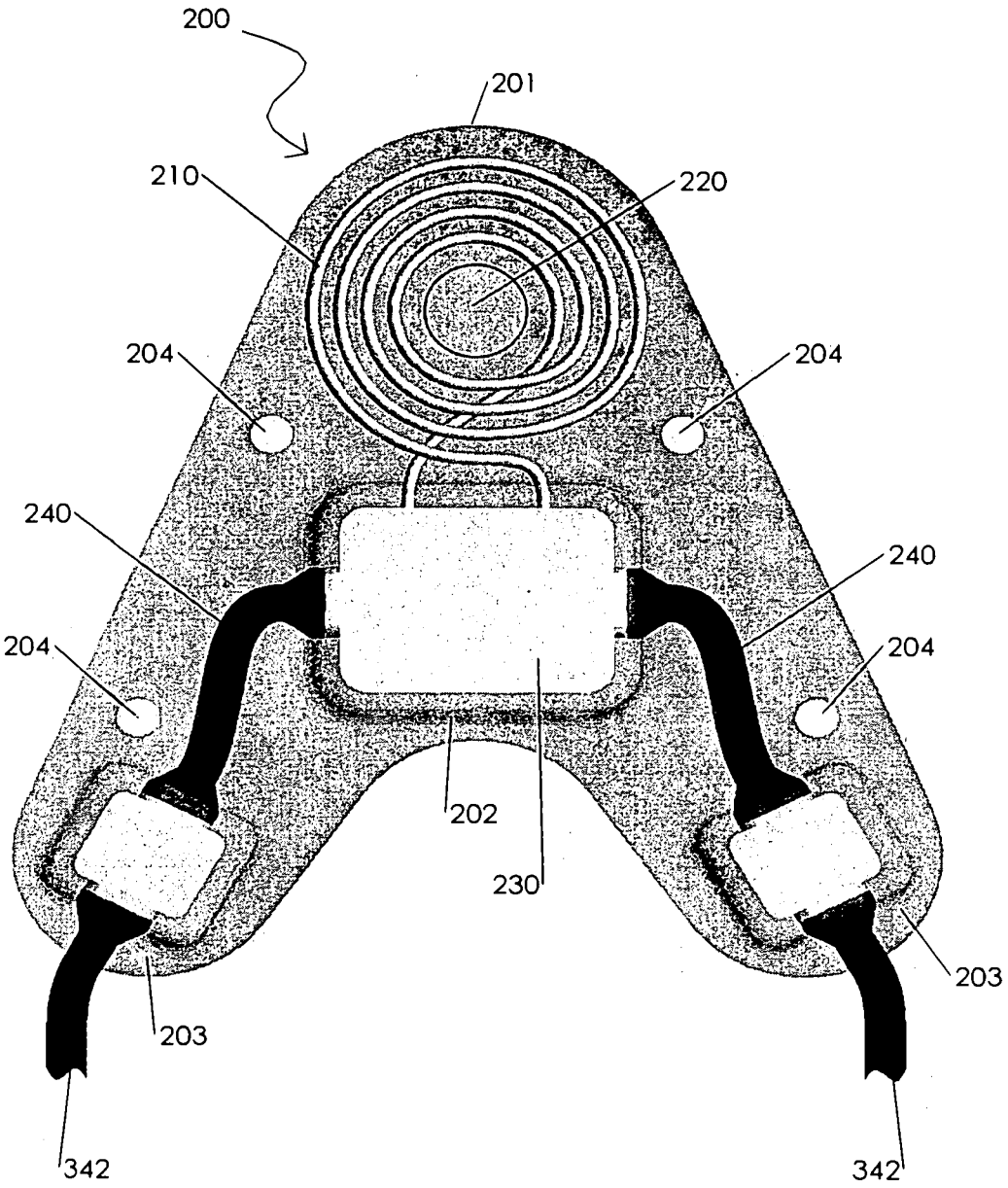


FIG. 2A

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FIG. 2B

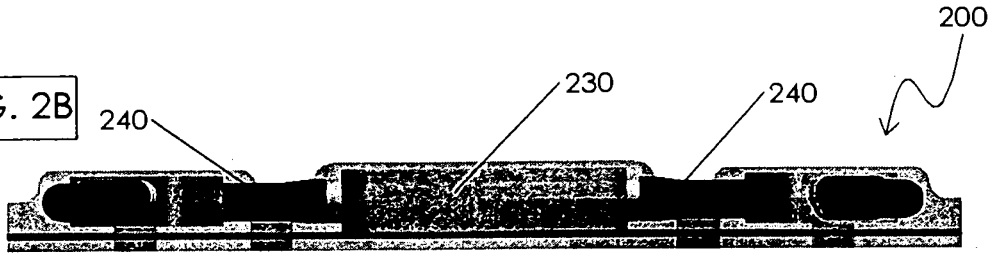


FIG. 2C

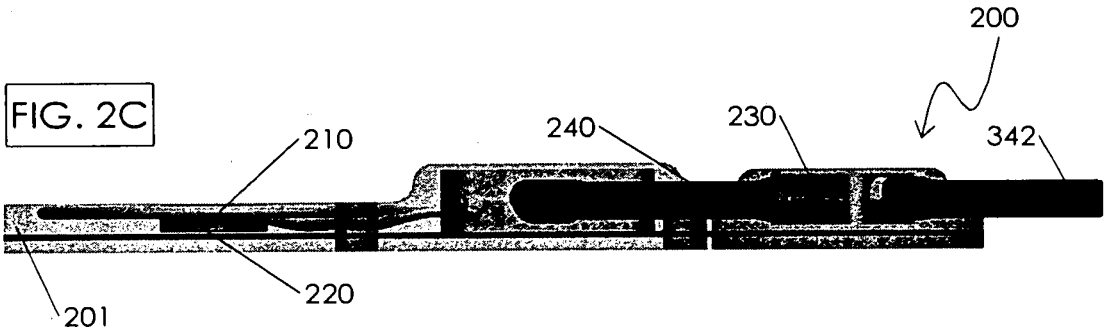


FIG. 2D

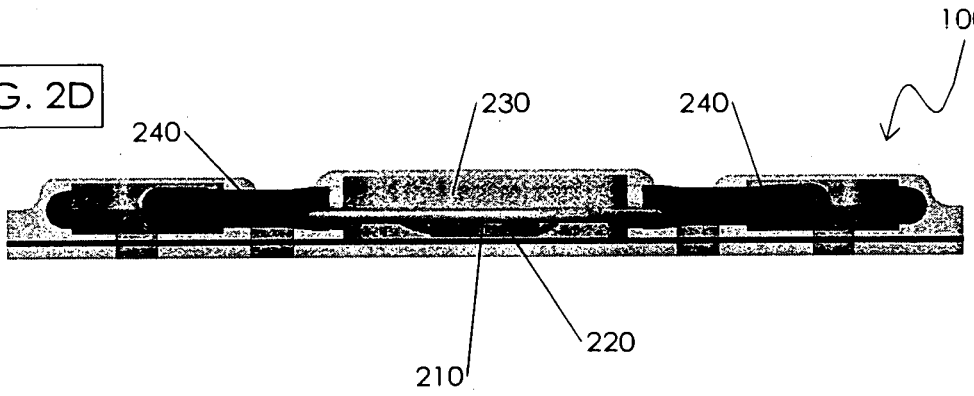


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FIG. 3A

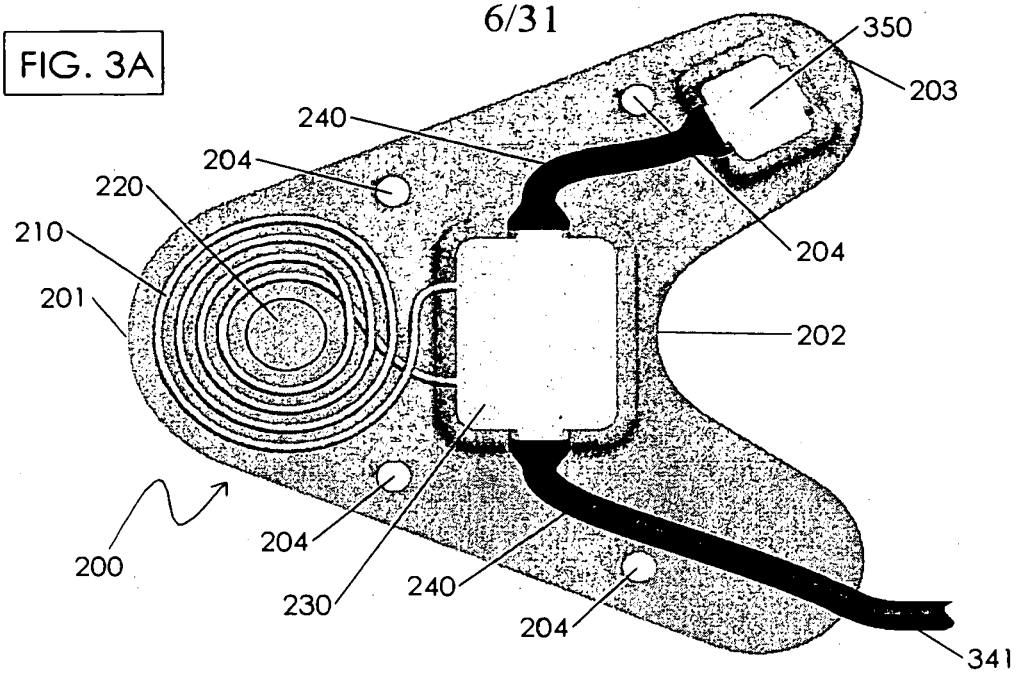


FIG. 3B

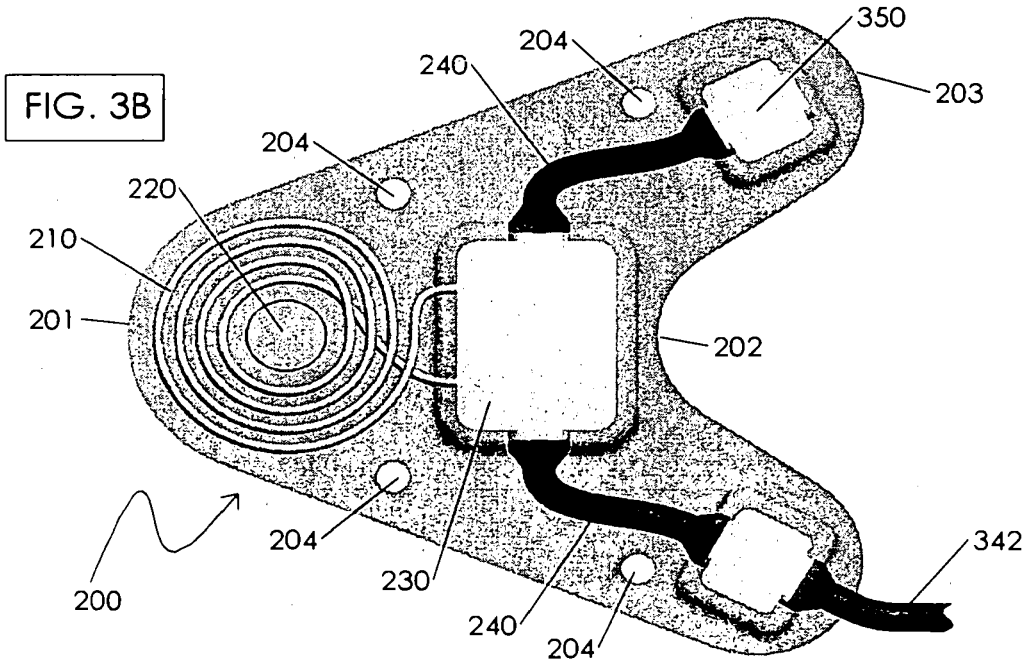


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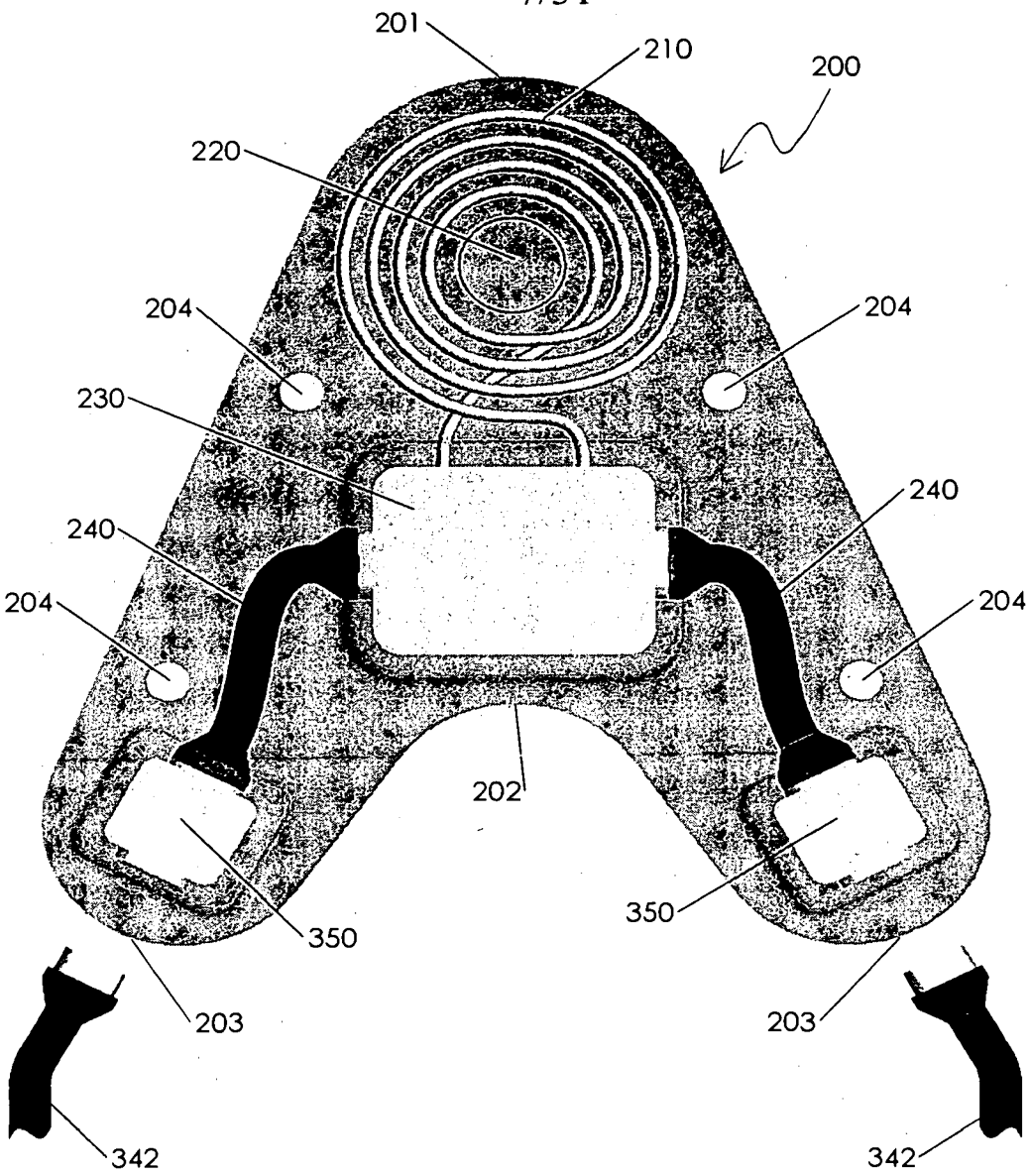


FIG. 3C

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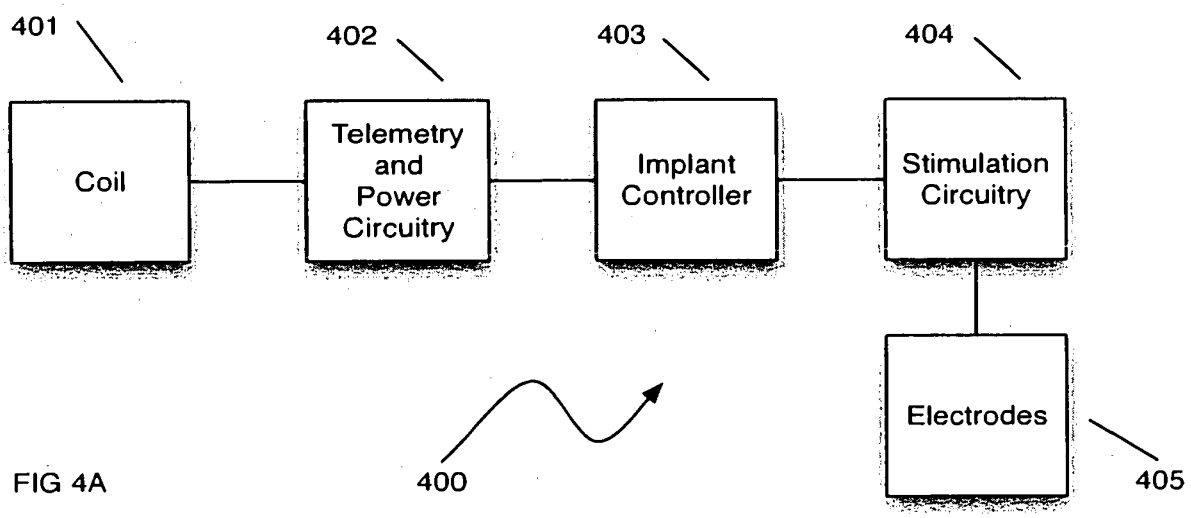


FIG 4A

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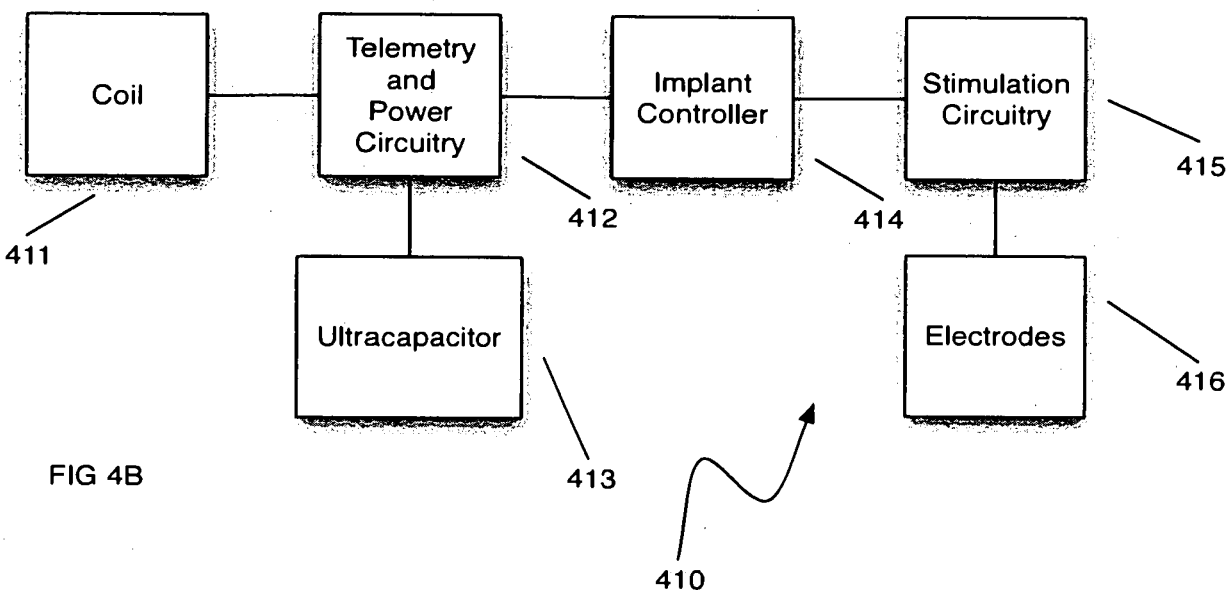


FIG 4B

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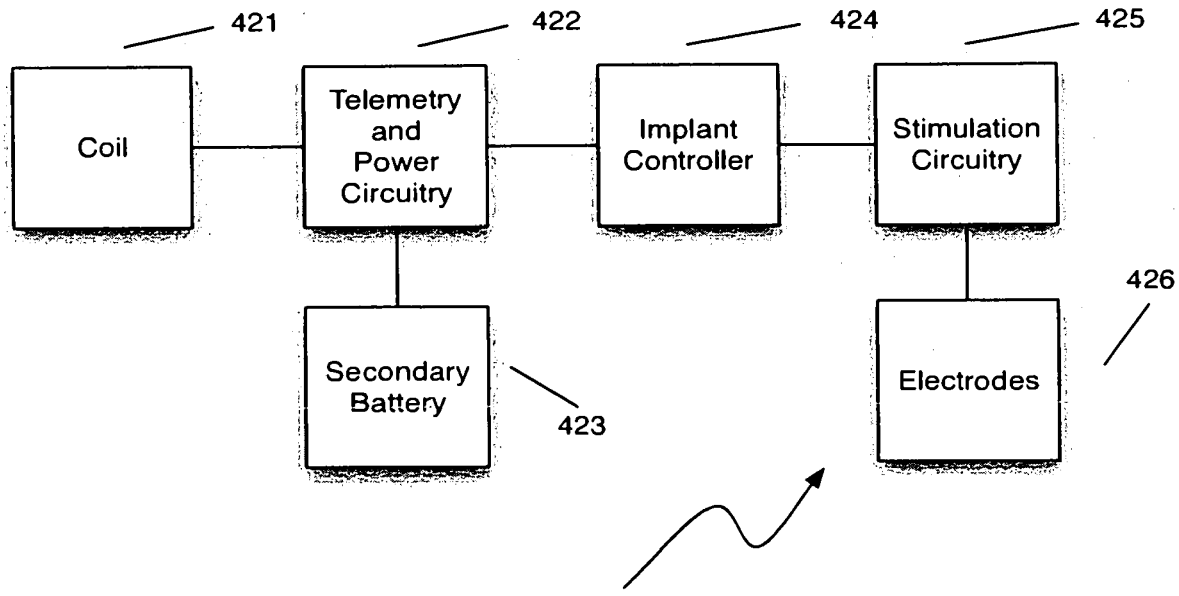


FIG 4C

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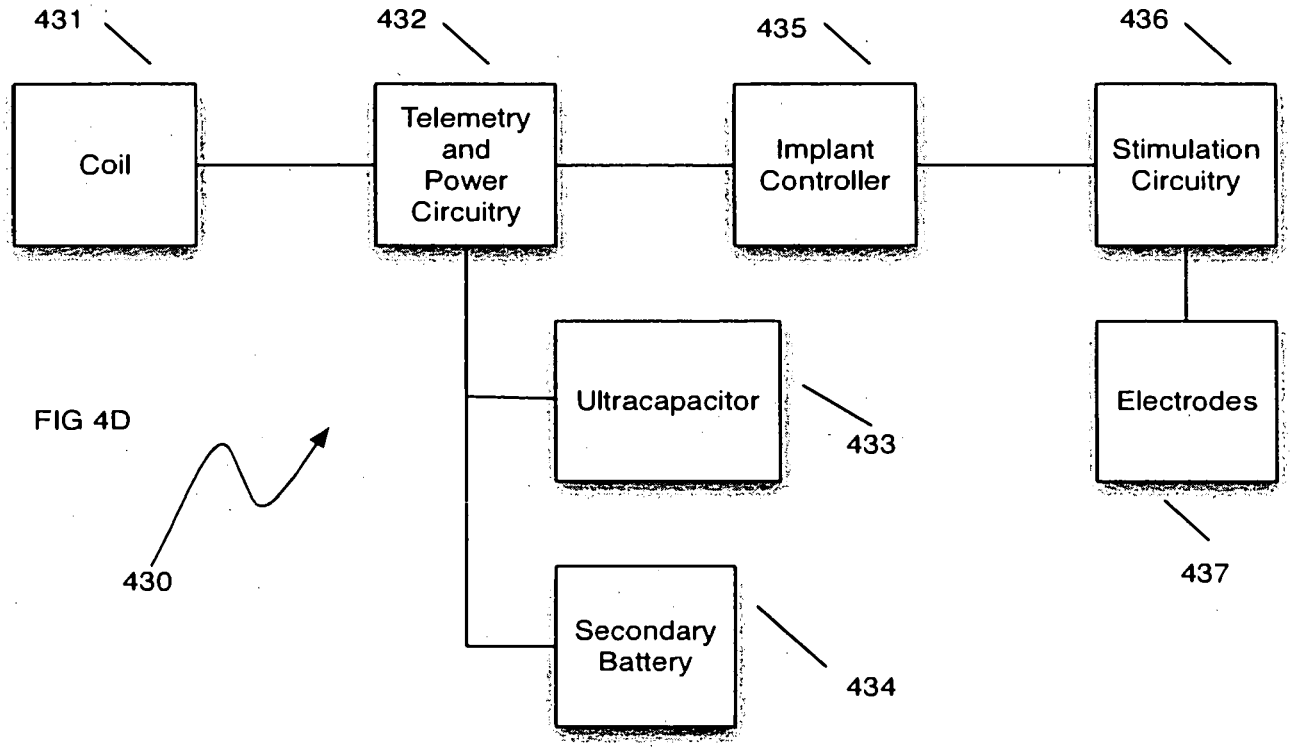


FIG 4D

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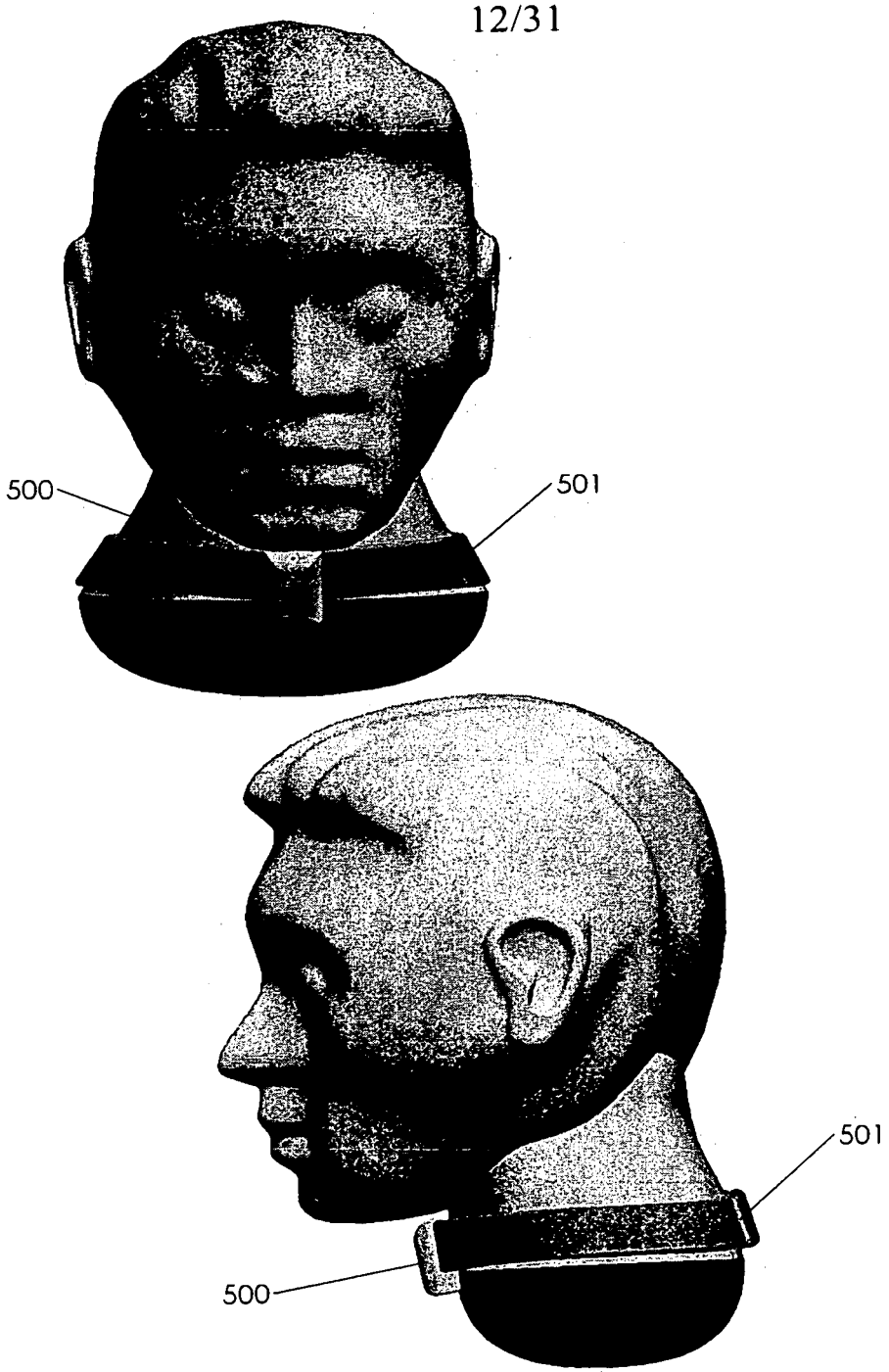


FIG. 5A

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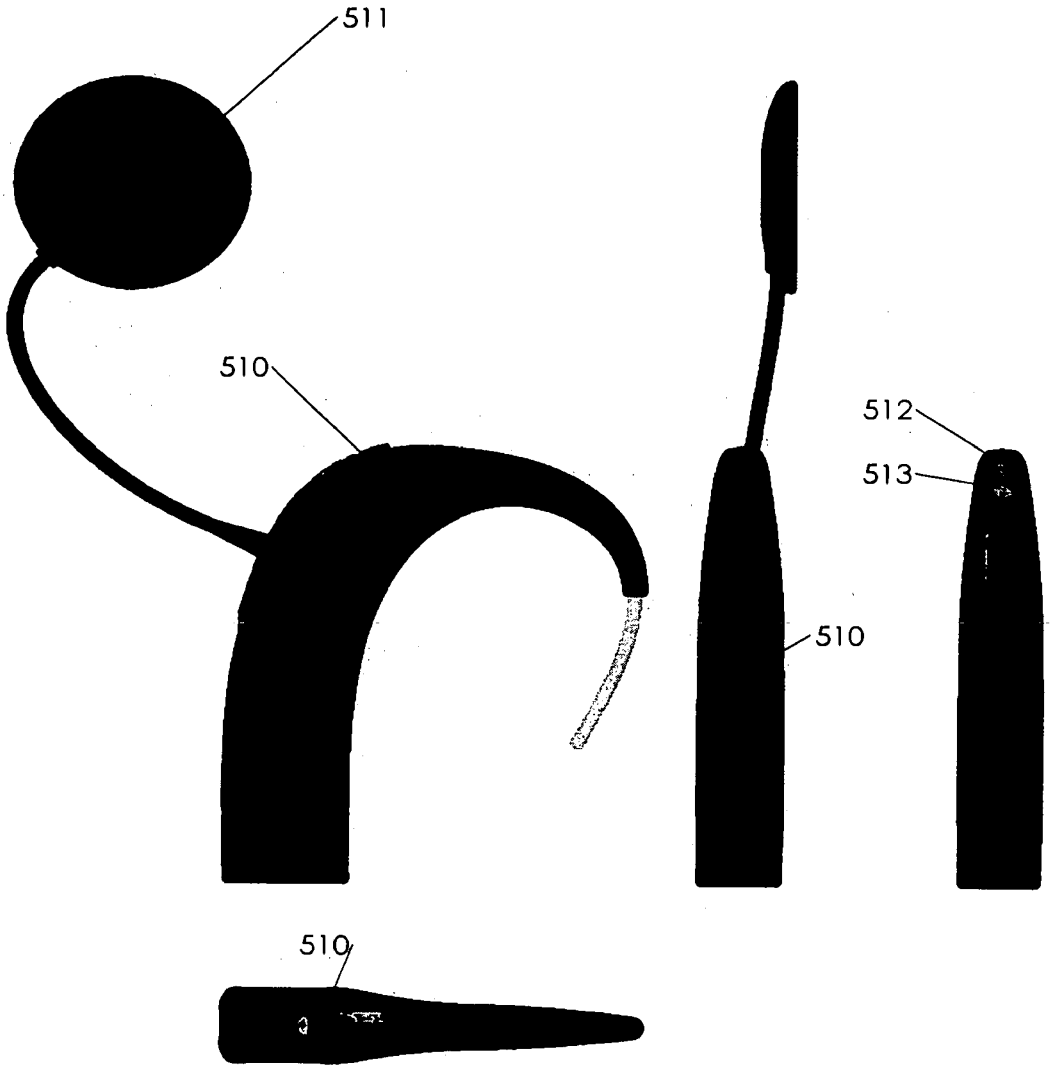


FIG. 5B

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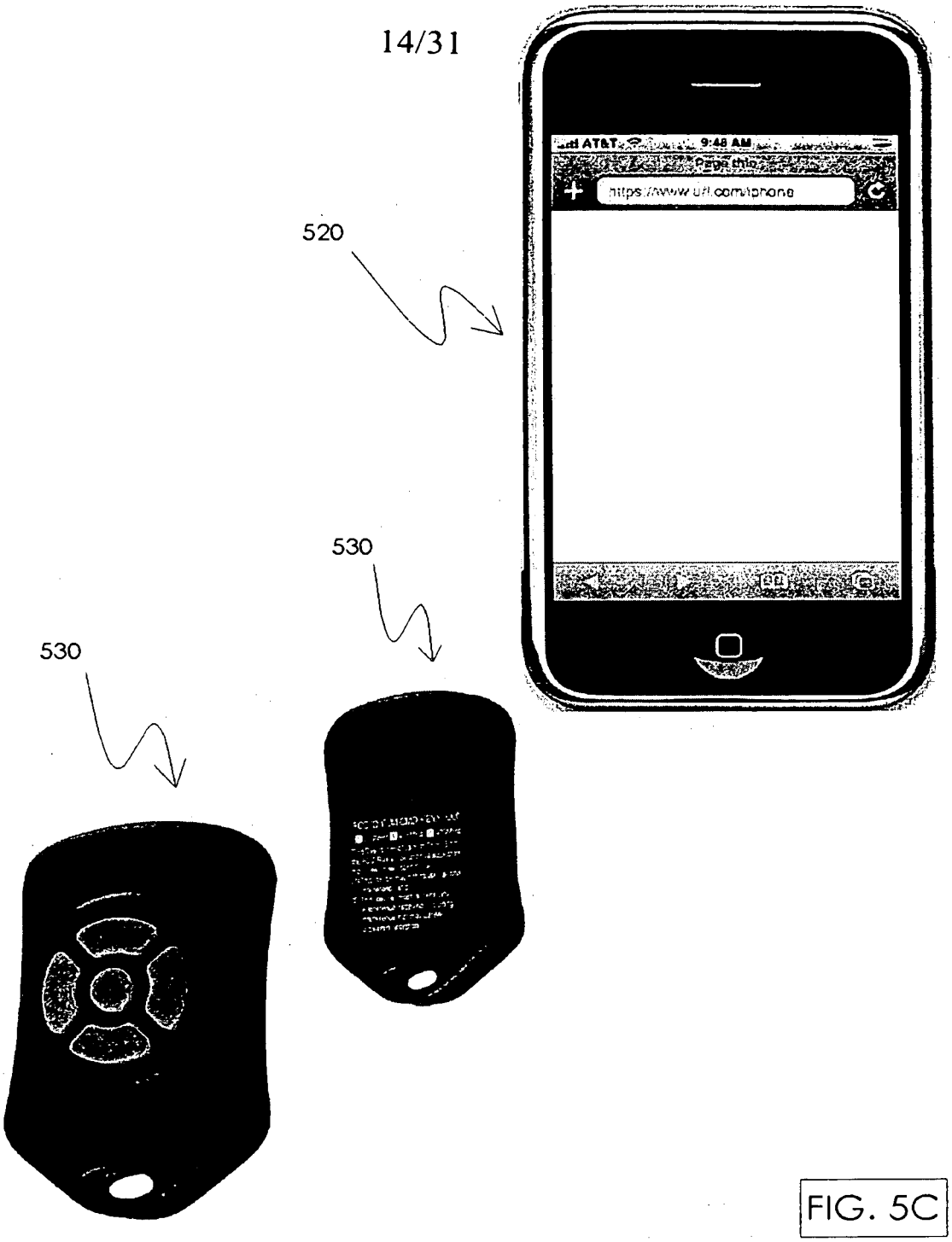


FIG. 5C

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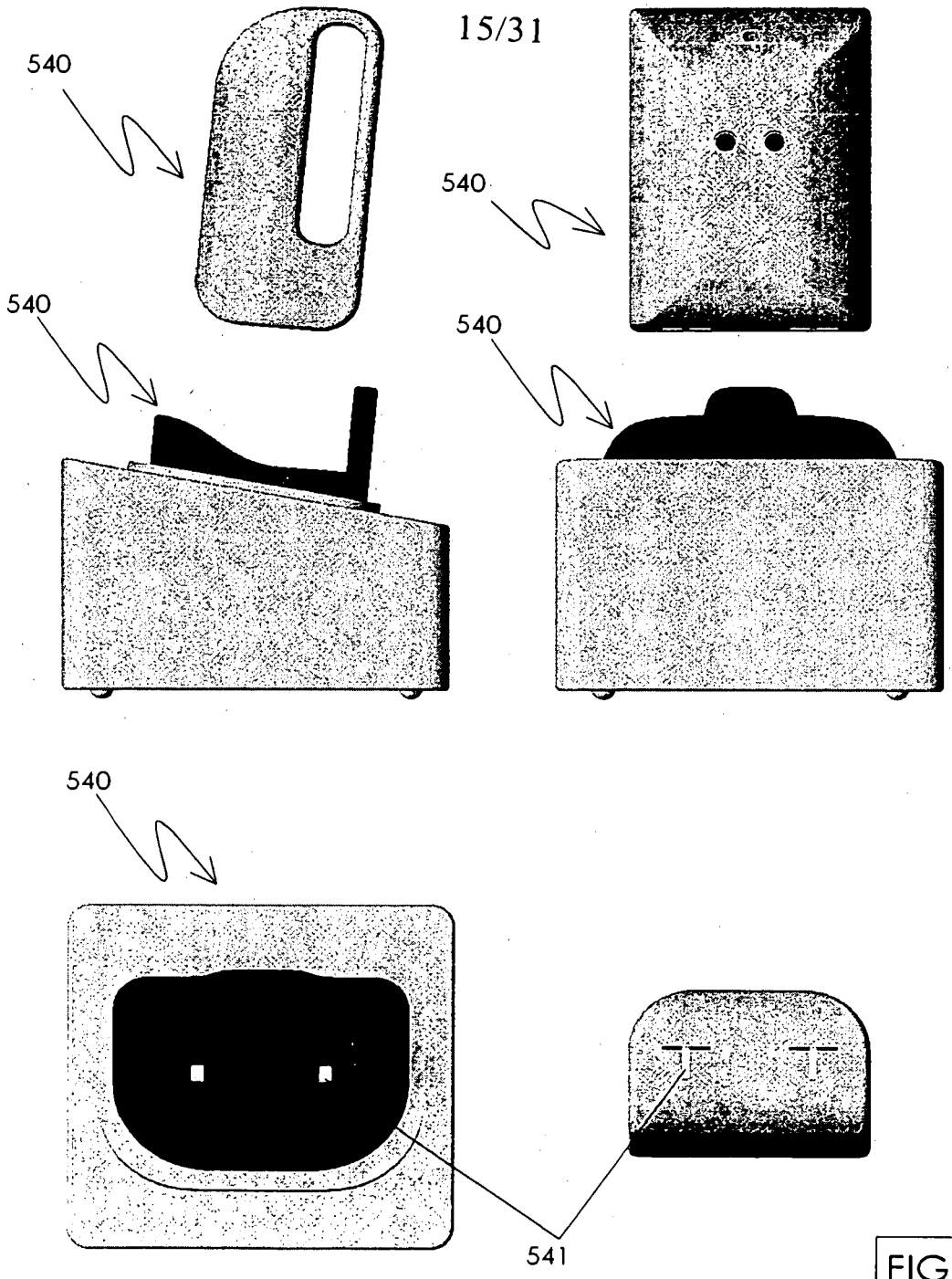


FIG. 5D

Exhibit 1002
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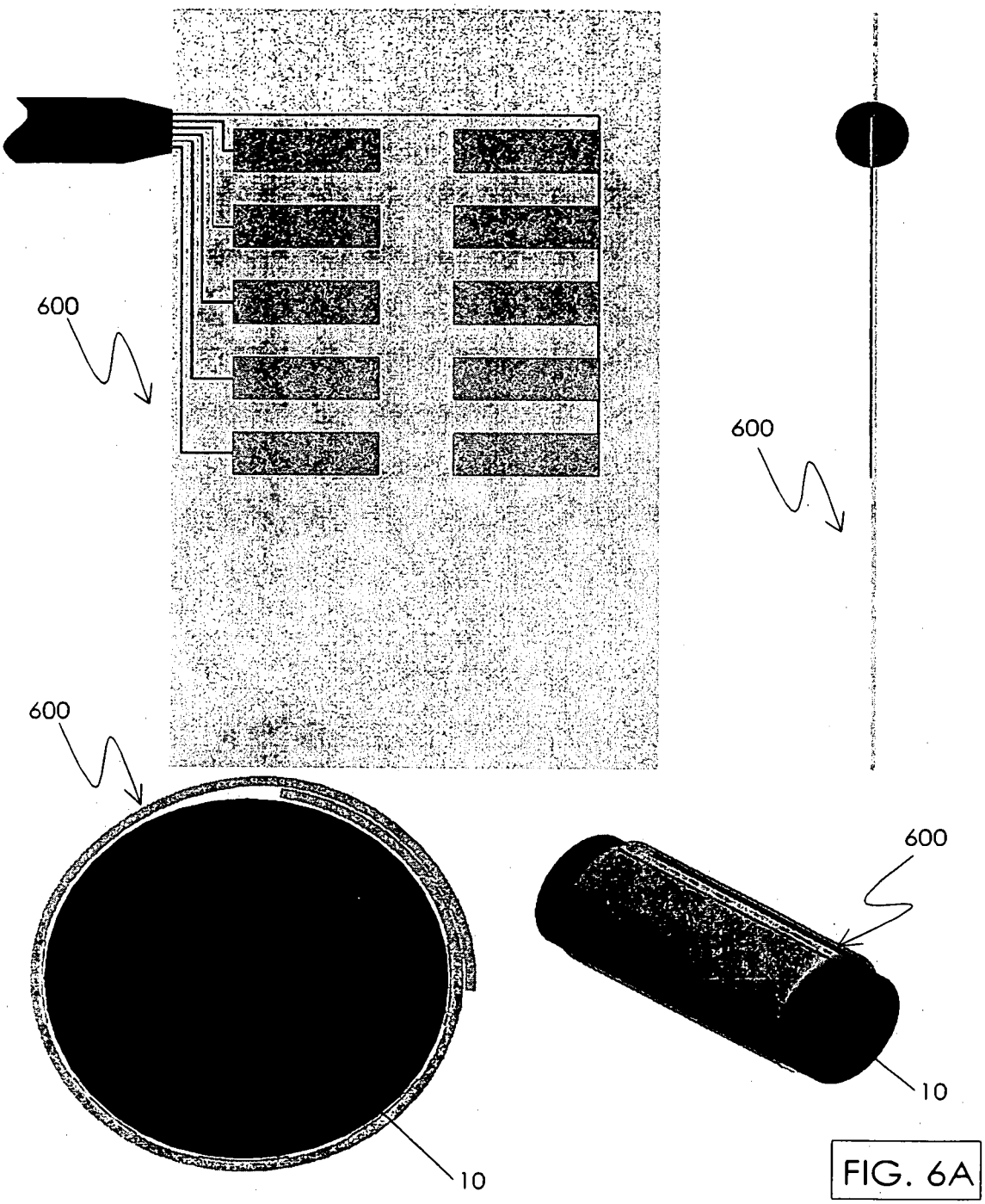


FIG. 6A

Exhibit 1002
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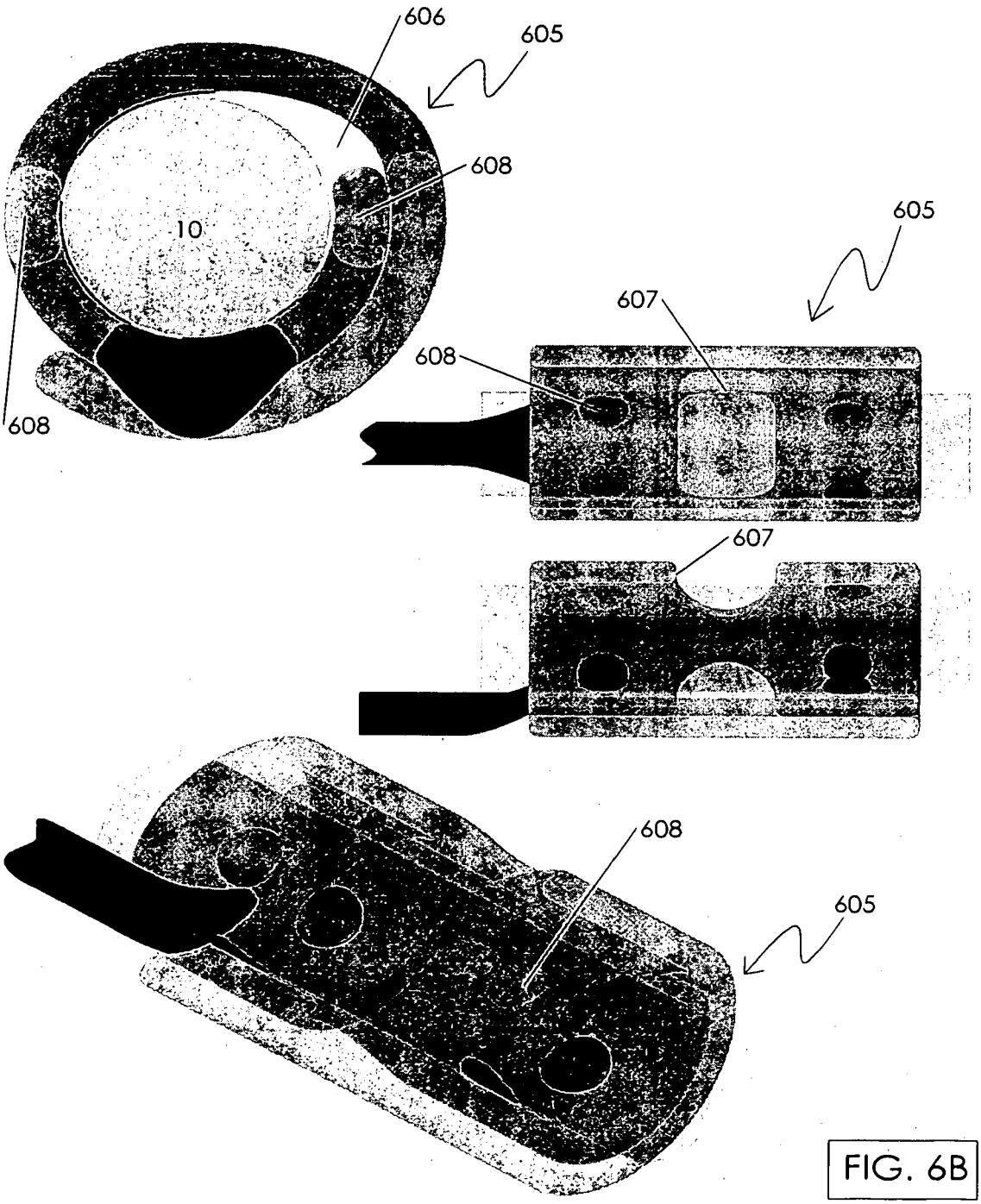


FIG. 6B

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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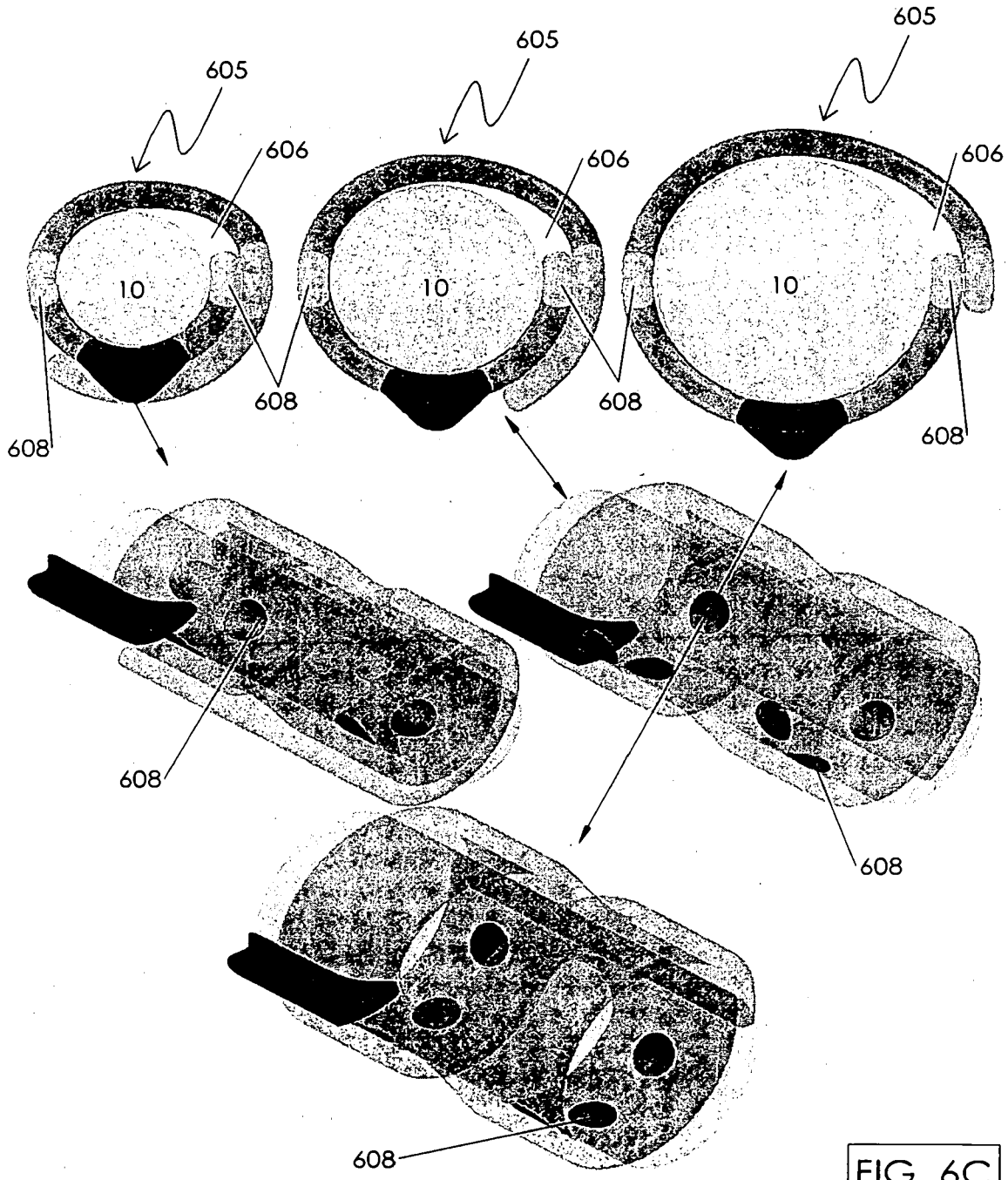


FIG. 6C

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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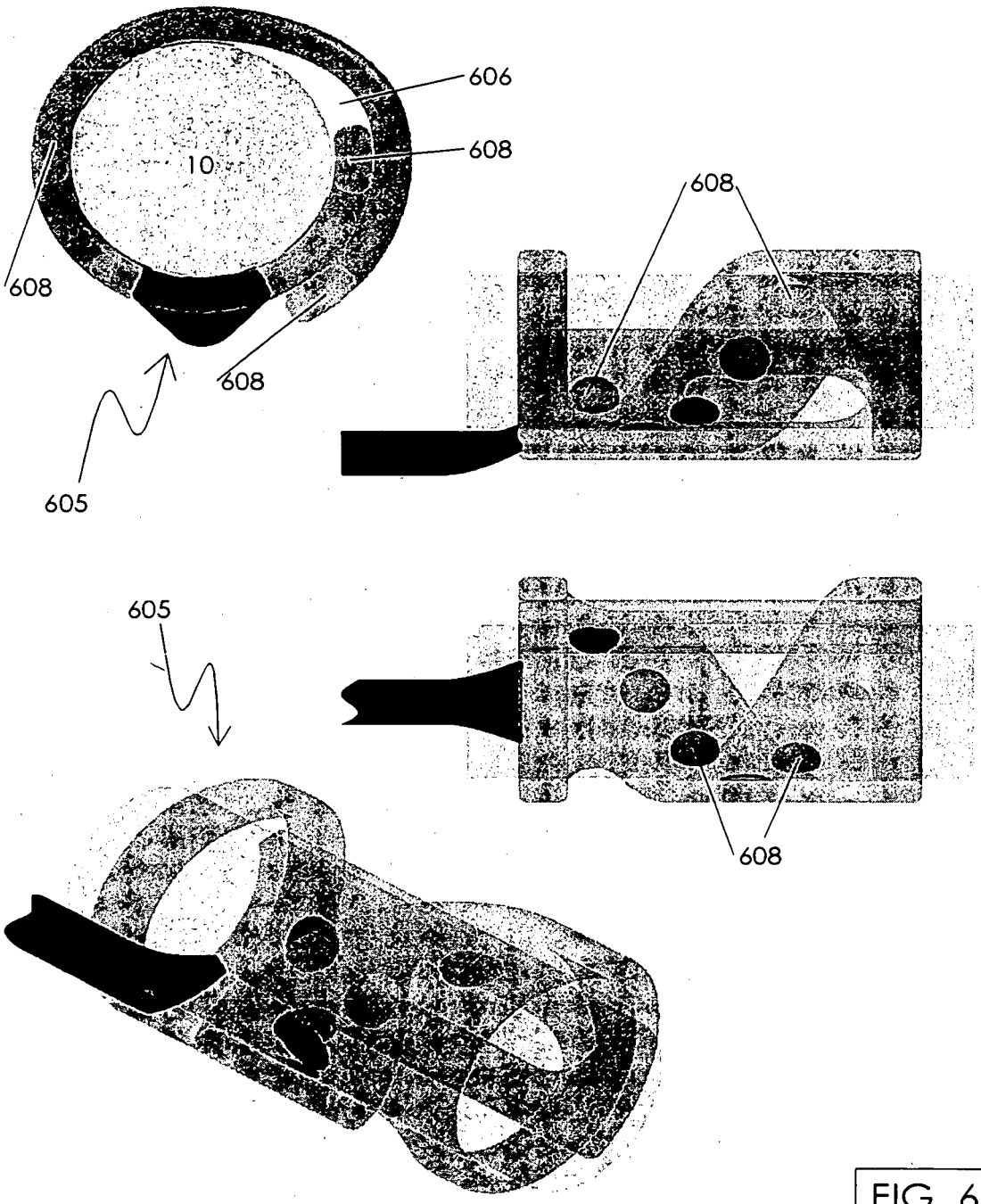


FIG. 6D

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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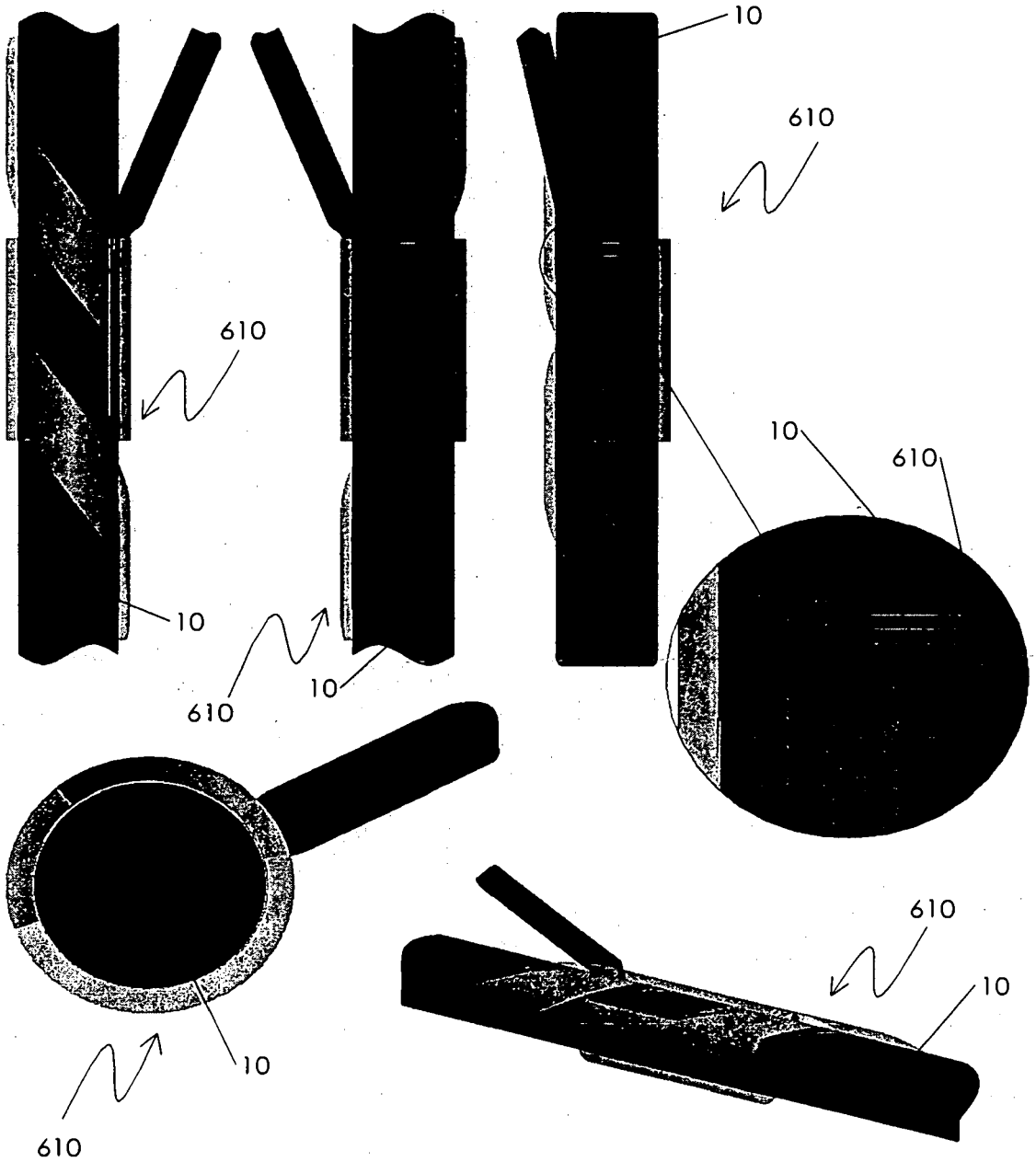


FIG. 6E

Exhibit 1002
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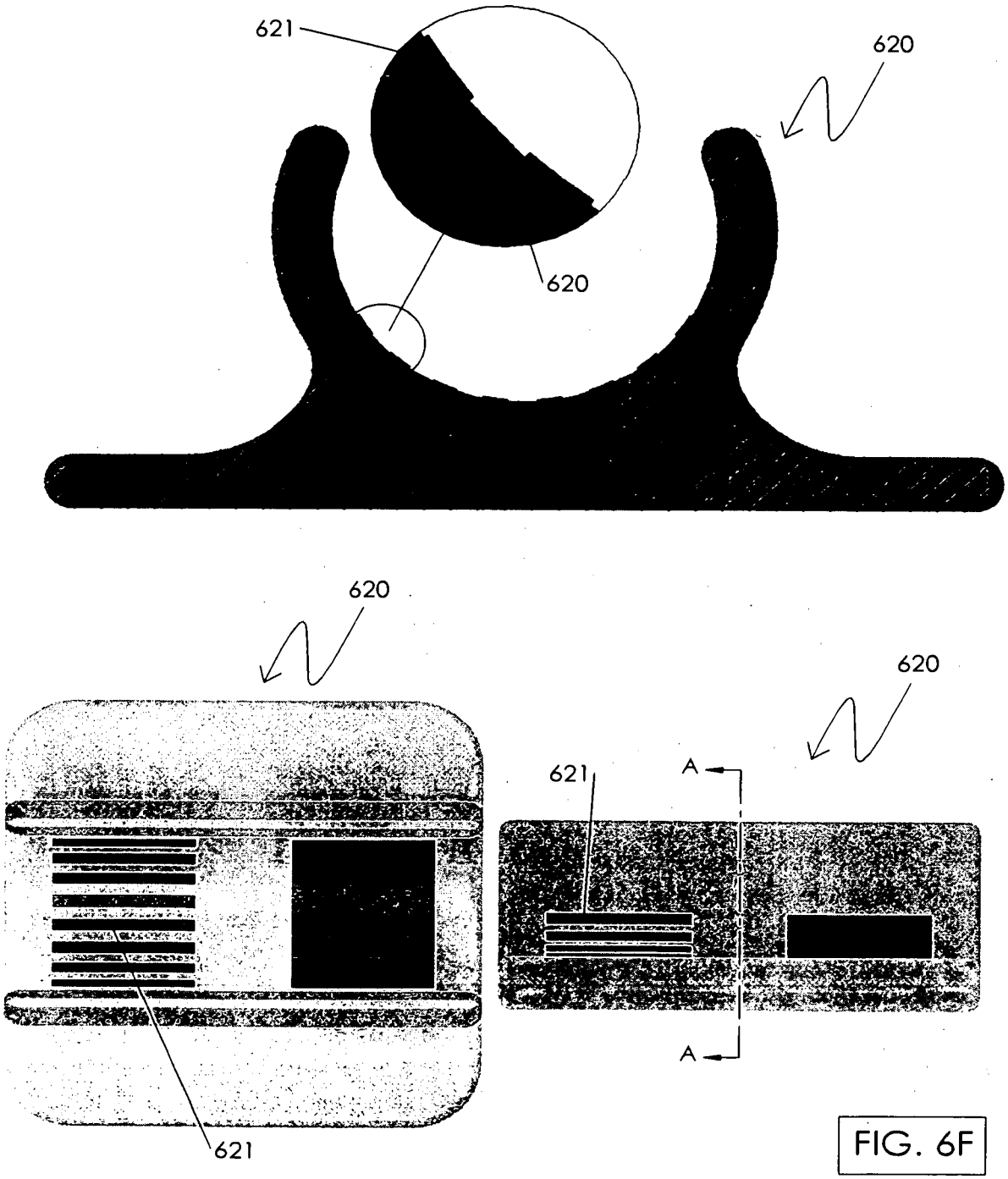


FIG. 6F

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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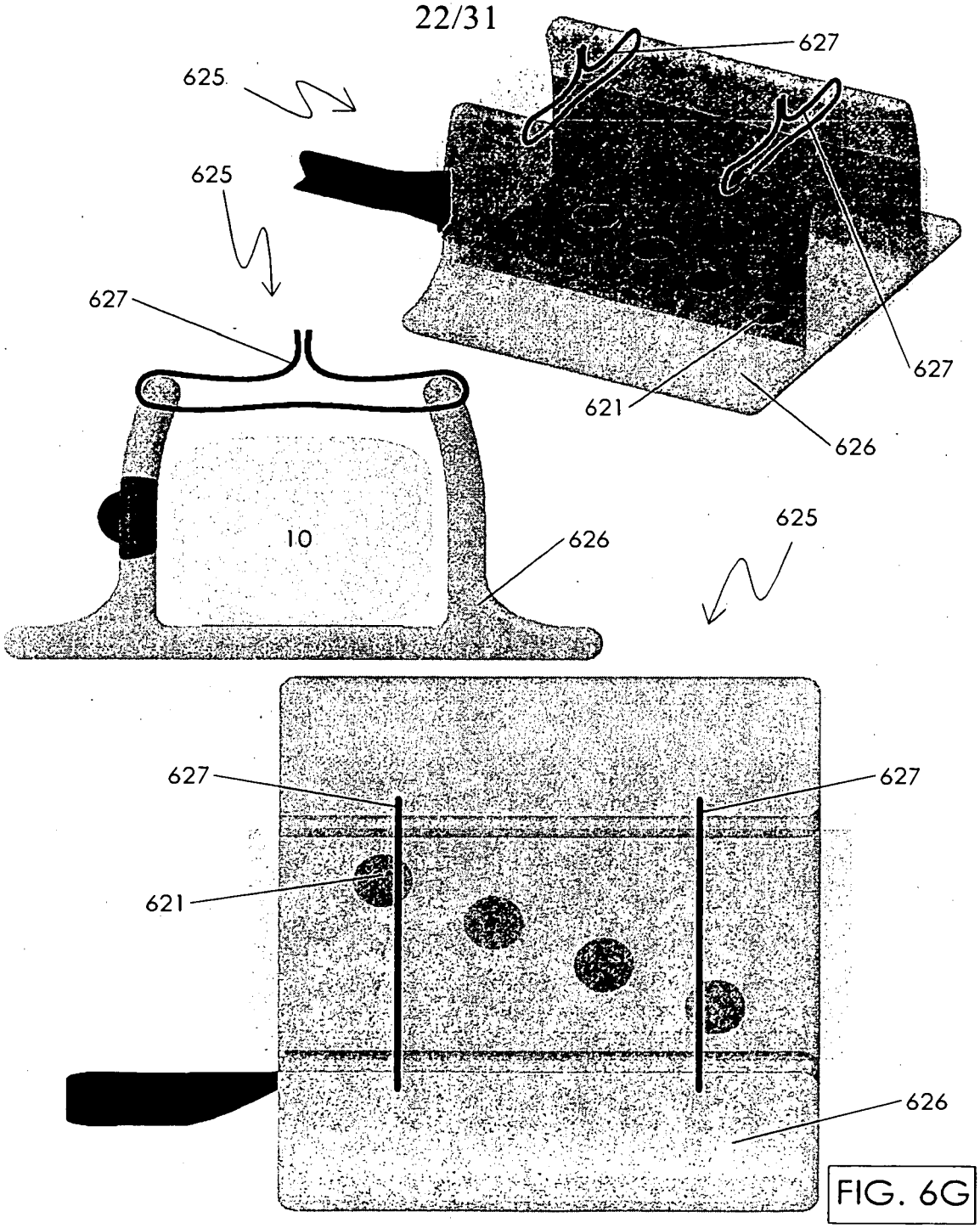


FIG. 6G

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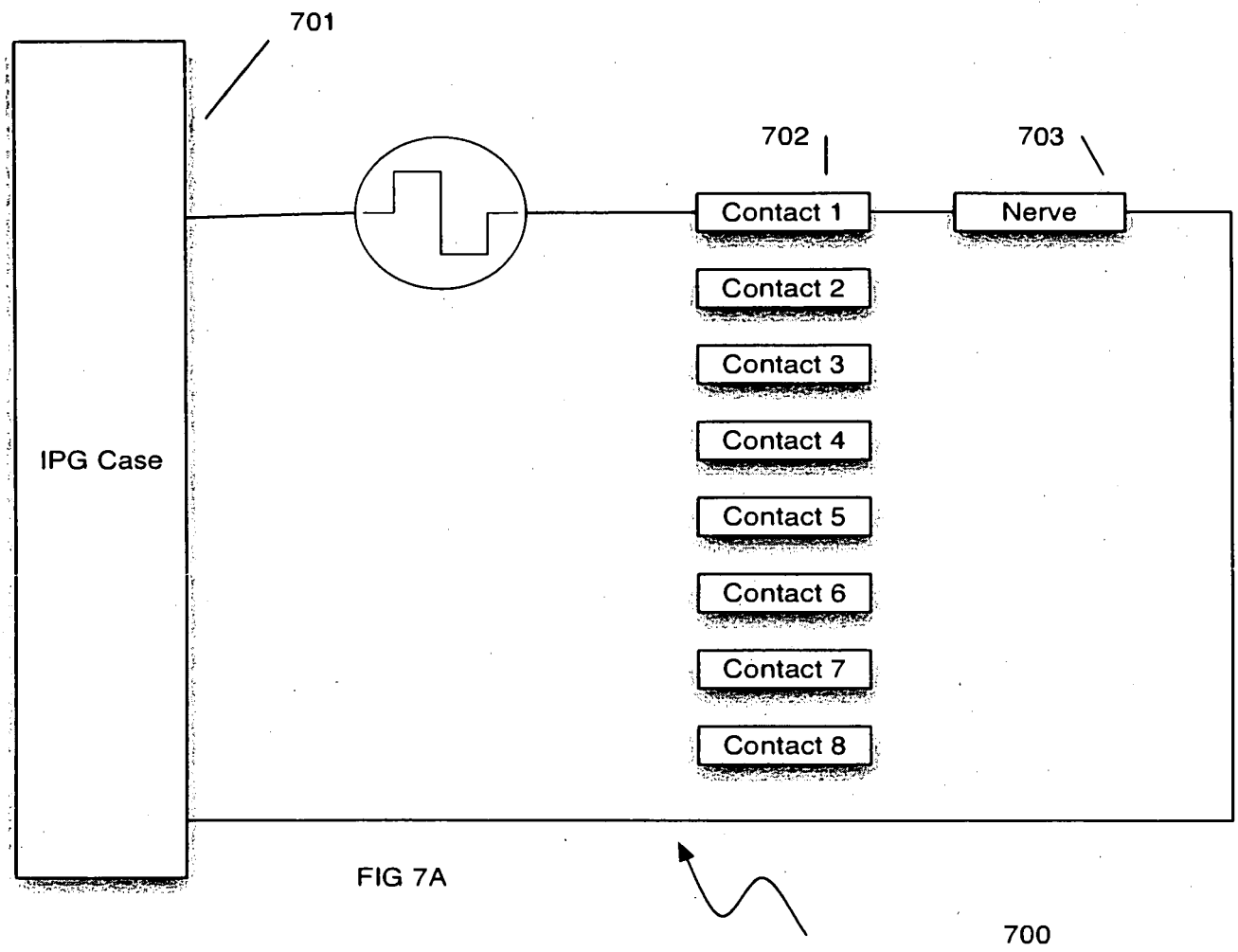


FIG 7A

Exhibit 1002
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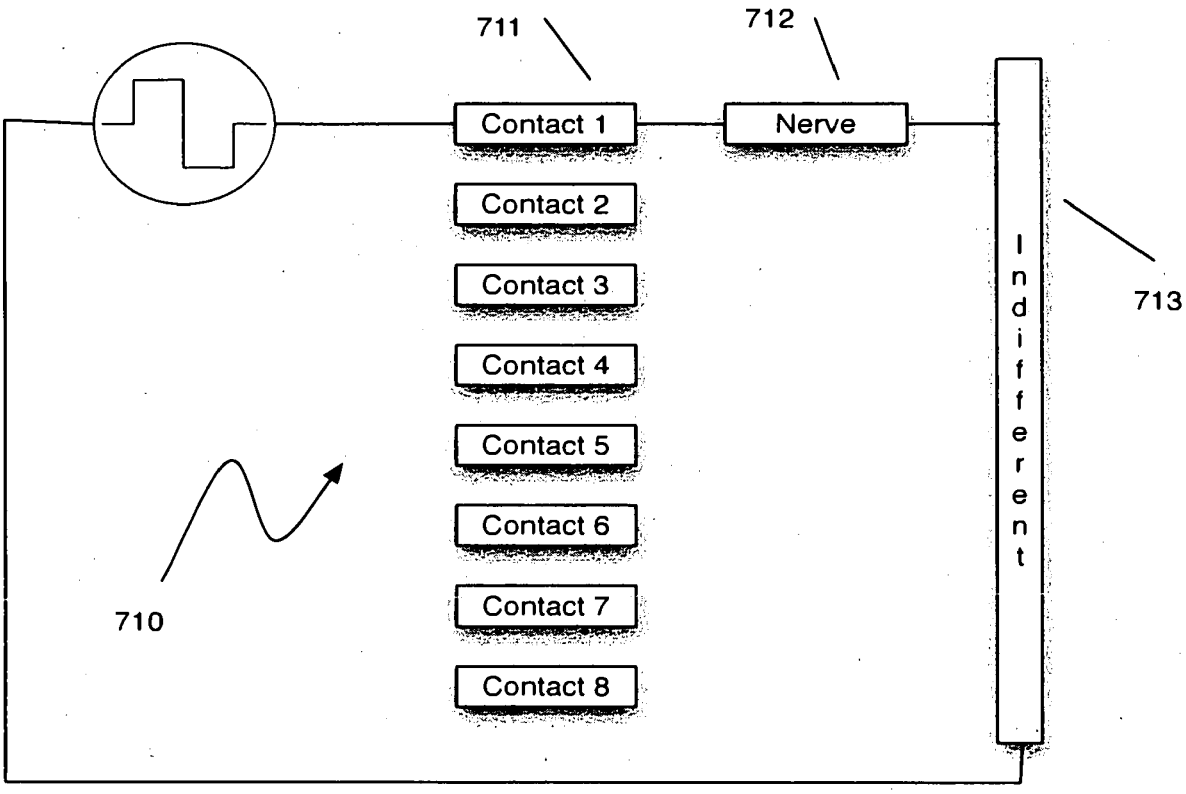


FIG 7B

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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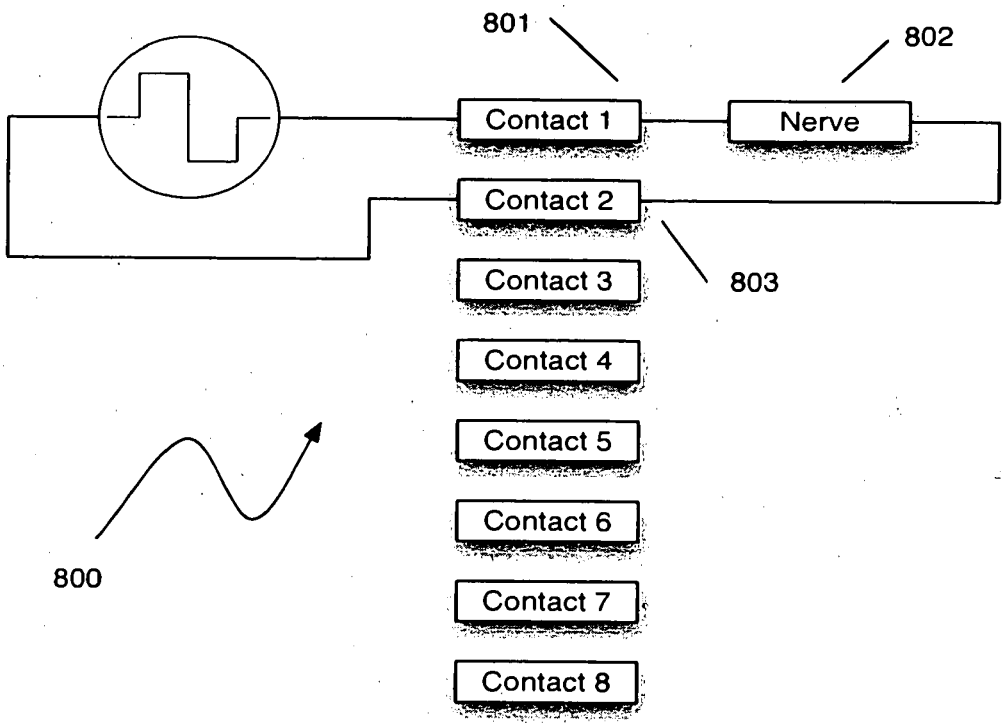


FIG 8

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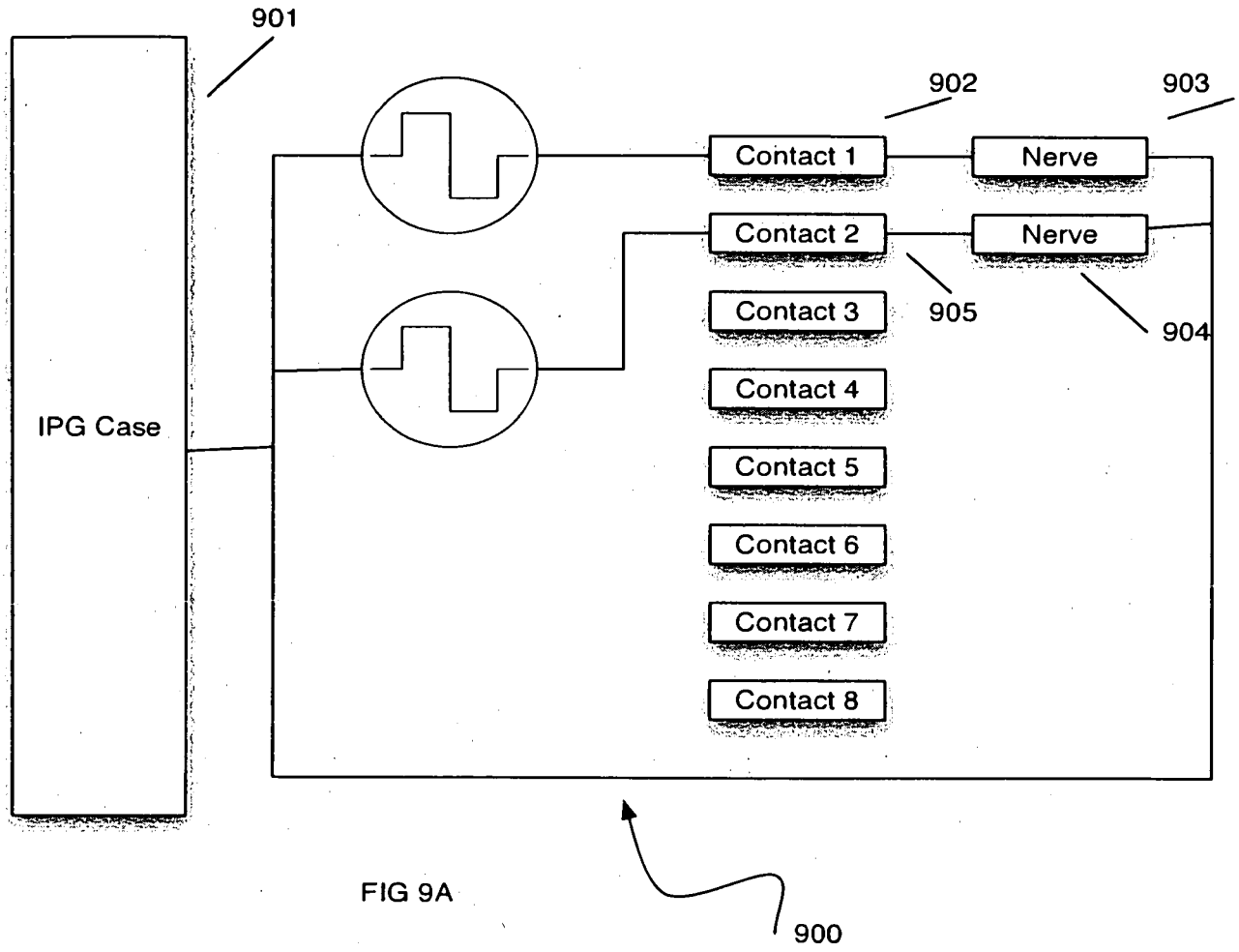


FIG 9A

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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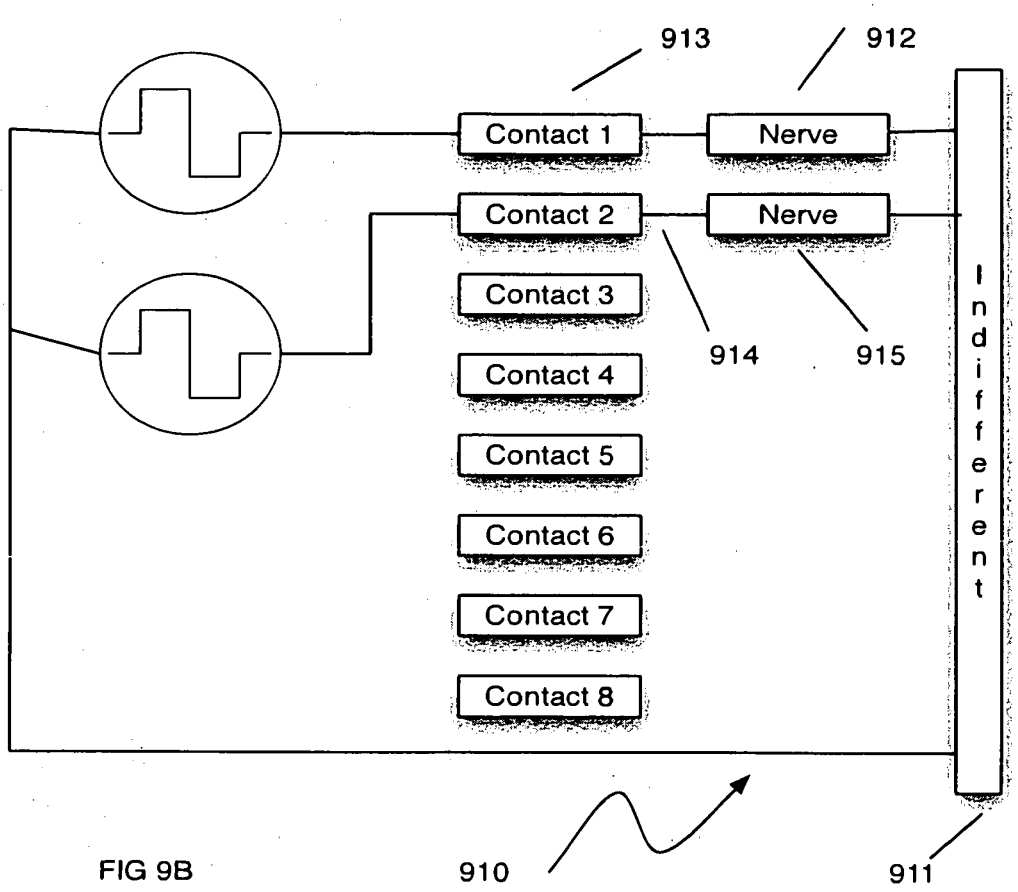


FIG 9B

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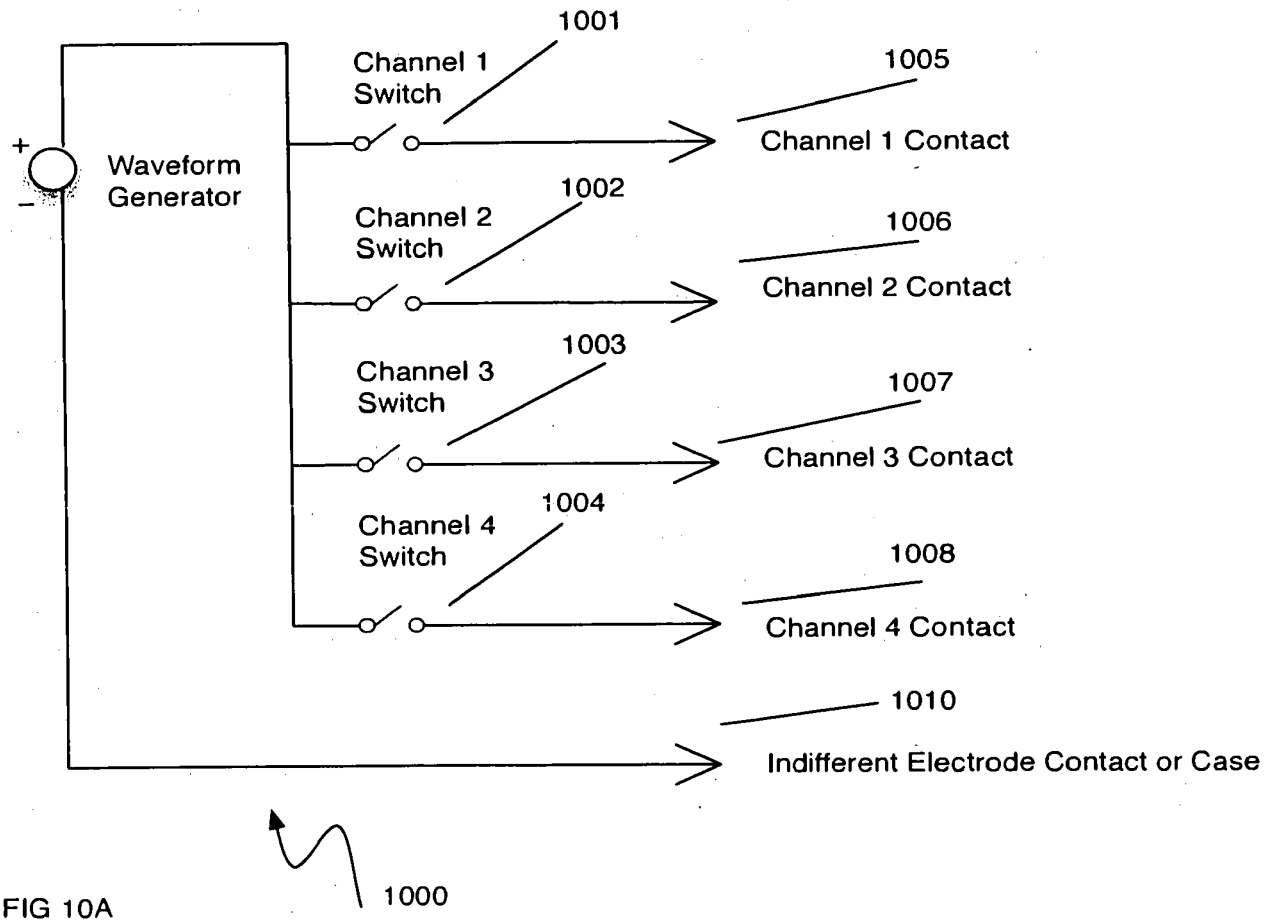


FIG 10A

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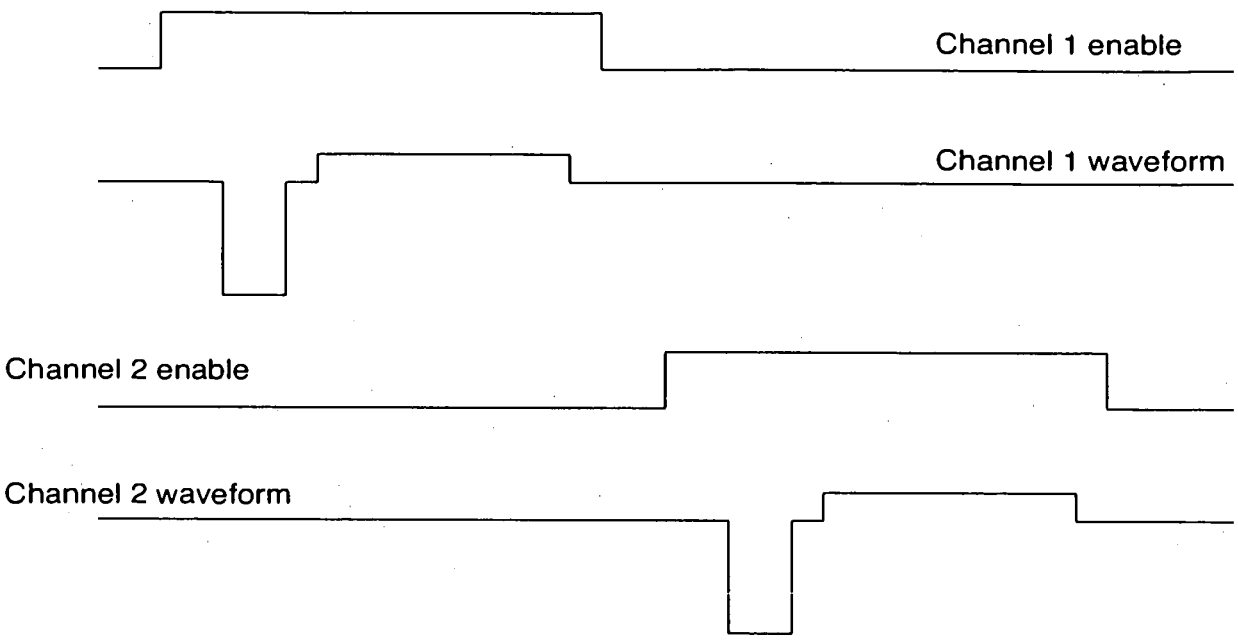


FIG 10B

Exhibit 1002
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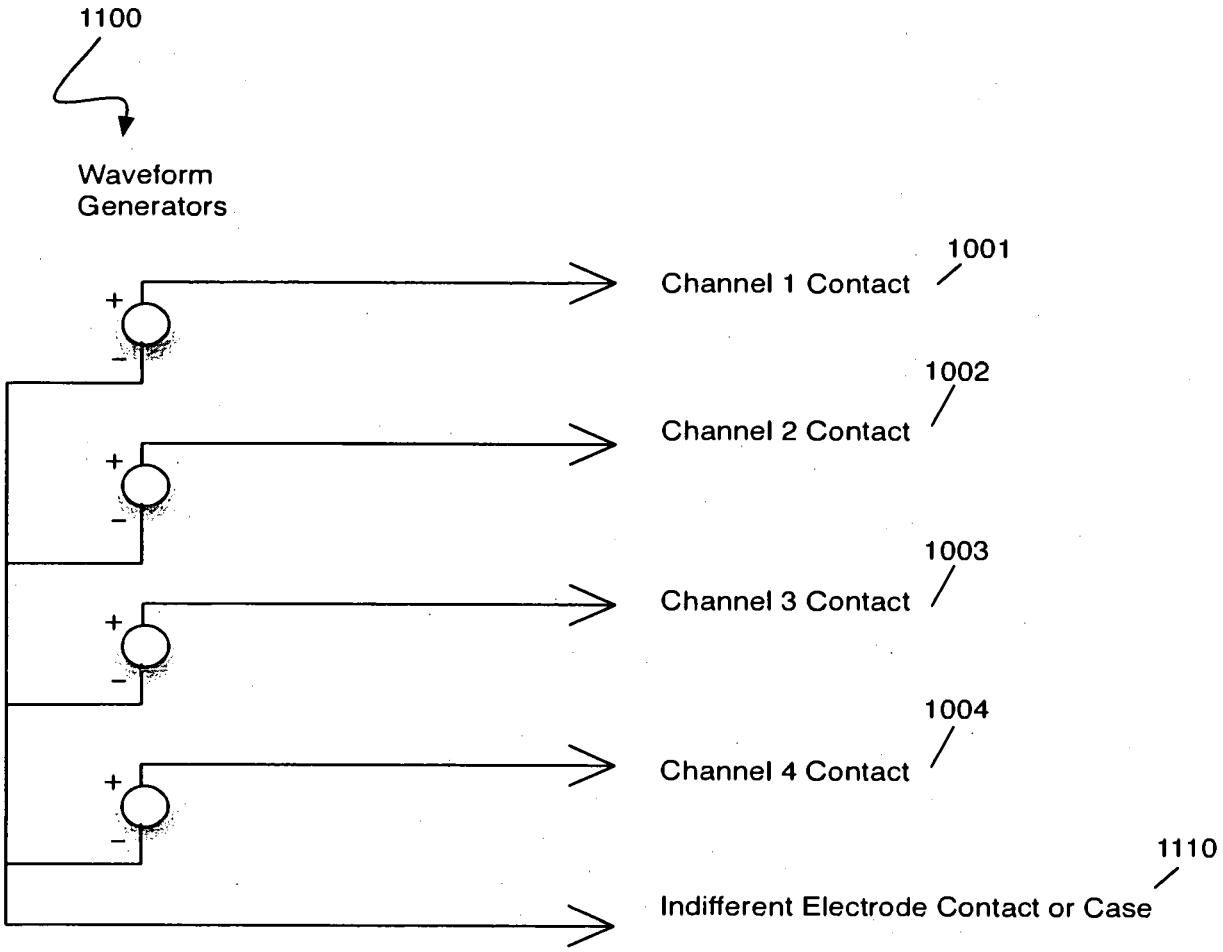


FIG 11A

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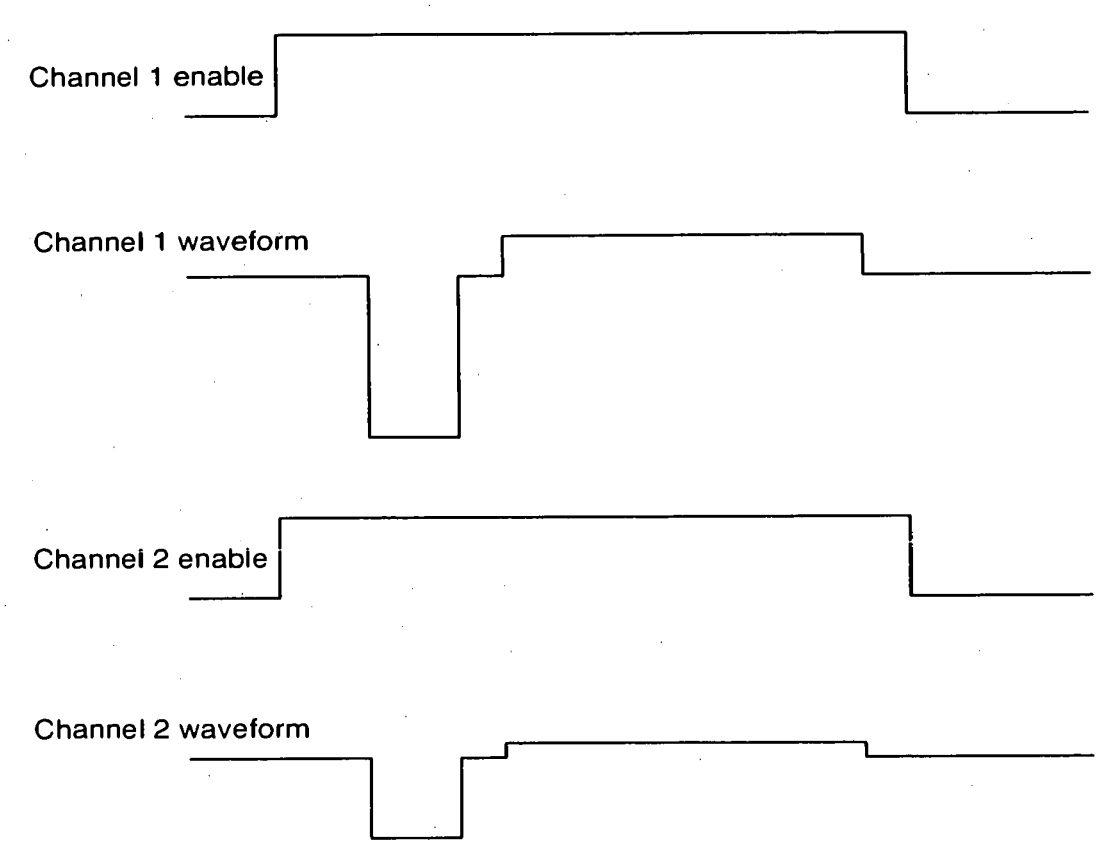


FIG 11B

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/011598

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61N 1/00 (2008.04)
USPC - 607/118
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61N 1/00 (2008.04)
USPC - 607/20,42,60,65,66,72,118,131,156; 623/10;600/9,26,377,386,390,529; 602/13

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
USPTO EAST System (US, USPG-PUB, EPO, DERWENT), MicroPatent, IP.com, DialogPro
MICROPATENT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 6,358,281 B1 (BERRANG et al) 19 March 2002 (19.03.2002) entire document	1-5, 10-17 -------- 6-9
X --- Y	US 5,824,027 A (HOFFER et al) 20 October 1998 (20.10.1998) entire document	18-19,21-22,24,26,28-42 ---------- 20,23,25,27,43-47
Y	US 5,833,714 A (LOEB) 10 November 1998 (10.11.1998) entire document	6
Y	US 2004/0138723 A1 (MALICK et al) 15 July 2004 (15.07.2004) entire document	7-9
Y	US 5,505,201 A (GRILL, JR et al) 09 April 1996 (09.04.1996) entire document	23
Y	US 5,282,468 A (KLEPINSKI) 01 February 1994 (01.02.1994) entire document	20,25
Y	US 4,353,374 A (REBBE et al) 12 October 1982 (12.10.1982) entire document	27
Y	US 6,778,858 B1 (PEETERS) 17 August 2004 (17.08.2004) entire document	43
Y	US 4,649,936 A (UNGAR et al) 17 March 1987 (17.03.1987) entire document	44
Y	US 6,240,316 B1 (RICHMOND et al) 29 May 2001 (29.05.2001) entire document	45-47

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
02 December 2008	12 DEC 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2005)

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
16 April 2009 (16.04.2009)

PCT

(10) International Publication Number
WO 2009/048581 A1

(51) International Patent Classification:
A61N 1/05 (2006.01)

(21) International Application Number:
PCT/US2008/011599

(22) International Filing Date: 9 October 2008 (09.10.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/978,519	9 October 2007 (09.10.2007)	US
61/017,614	29 December 2007 (29.12.2007)	US
61/136,102	12 August 2008 (12.08.2008)	US

(71) Applicant *(for all designated States except US)*: **IMTHERA MEDICAL, INC.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CRAIG, Stanley, R.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US). **MEADOWS, Paul, M.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US). **LIMA, Marcelo, G.** [US/US]; 4946 Smith Canyon Ct., San Diego, CA 92130 (US).

(74) Agents: **BURNS, Robert, T.** et al.; Morgan Lewis & Bockius LLP, 1111 Pennsylvania Avenue, NW, Washington, DC 20004 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,

[Continued on next page]

(54) Title: SYSTEM AND METHOD FOR NEURAL STIMULATION

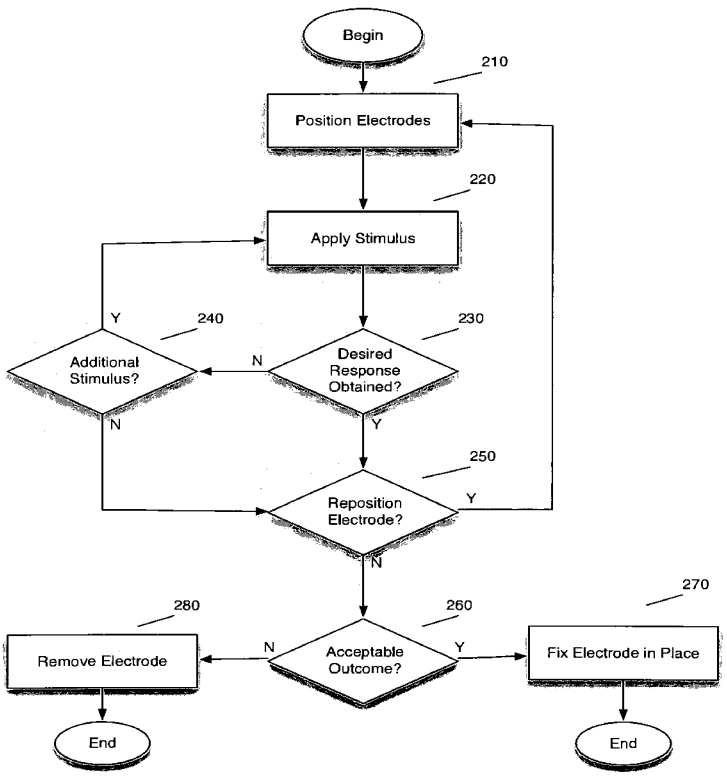


FIG 2

(57) Abstract: A system and method of neural stimulation is disclosed, comprising the steps of electrically connecting at least one electrode to a first tissue, applying a stimulus to the at least one electrode, observing a response of a second tissue, identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode, and fixing the at least one electrode in place at the identified electrode position.

WO 2009/048581 A1

ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

TITLE

SYSTEM AND METHOD FOR NEURAL STIMULATION

[0001] This application claims the benefit of United States Patent Application Nos. 60/978,519 and 61/017,614 and 61/136,102, filed on October 9, 2007 and December 29, 2007 and August 12, 2008 respectively, which are herein incorporated by reference in their entirety.

STATEMENT OF RELATED APPLICATION

[0002] This application is related to International Patent Application [Docket No. 069737-5005-WO], which also claims the benefit of United States Patent Application Nos. 60/978,519 and 61/017,614 and 61/136,102.

FIELD OF THE INVENTION

[0003] The present invention relates to a system and method for adjusting neural stimulation of a target tissue, such as a nerve, muscle, or organ.

BACKGROUND OF INVENTION

[0004] Neural stimulation is useful in treating various acute and chronic medical conditions, including pain, arthritis, sleep apnea, seizure, incontinence, and migraines, which are physiological conditions affecting millions of people worldwide. Current treatment options range from drug intervention, non-invasive approaches such as the continuous positive air pressure (CPAP) machine for sleep apnea, to invasive surgical procedures. In many instances, patient acceptance and therapy compliance are well below desired levels, rendering current treatments ineffective as long-term solutions.

[0005] Implants are a promising alternative treatment. For example, vagus nerve stimulation is thought to affect some of its connections to areas in the brain prone to seizure activity. Sacral nerve stimulation is an FDA-approved electronic stimulation therapy for reducing urge incontinence. Stimulation of peripheral nerves may help treat arthritis pain. As another

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example, pharyngeal dilation via hypoglossal nerve (XII) stimulation has been shown to be an effective treatment method for obstructive sleep apnea (OSA). The nerves are stimulated using an implanted electrode. In particular, the medial XII nerve branch (i.e., genioglossus), has demonstrated significant reductions in upper airway airflow resistance (i.e., increased pharyngeal caliber).

[0006] While electrical stimulation of nerves has been experimentally shown to remove or ameliorate certain conditions, e.g., obstructions in the upper airway in the case of sleep apnea, current implementation methods typically require accurate and selective stimulation of a target tissue. Therefore, a need exists for a system and method for identifying an optimal location on a target tissue, e.g., a muscle or nerve, and placing an implant electrode at such location to achieve optimal stimulation of such target tissue.

SUMMARY OF INVENTION

[0007] The present invention includes a system and method for adjusting neural stimulation of a target, such as a nerve, muscle, or organ. In an embodiment of the invention, the method includes electrically connecting at least one electrode to a first tissue, applying a stimulus to the at least one electrode, observing a response of a second tissue, identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode, and fixing the at least one electrode in place at the identified electrode position. In certain embodiments, the stimulus applicator is disposable.

[0008] The stimulus can be a voltage signal, a current signal, and can be preprogrammed. In certain embodiments, the voltage or current signal is a controlled voltage or a controlled current signal. In other embodiments, an estimated minimum stimulus is calculated, and in yet another embodiment a stimulus profile is generated. The stimulated tissue may be selected from the group consisting of nerve tissue, muscle tissue, and organ tissue. Examples

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of a desired stimulus response include a change in airway patency, at least partial blockage of a neural impulse, and the initiation of at least one neural impulse. A response can be directly or indirectly observed, either visually or with instrumentation.

[0009] In another embodiment of the invention, a neural stimulation system includes at least one electrode electrically connected to a first tissue, means for applying a stimulus to the at least one electrode, means for observing a response of a second tissue, means for identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode, and means for fixing the at least one electrode in place at the identified electrode position.

[0010] In still another embodiment of the invention, a computer program product comprises a computer readable medium having stored thereon computer executable instructions that, when executed on a computer, causes the computer to perform a method of neural stimulation, including the steps of applying a stimulus to at least one electrode electrically connected to a first tissue, observing a response of a second tissue, and identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode.

[0011] In another embodiment of the invention, a neural stimulation system includes at least one electrode electrically connected to a first tissue, a gross adjustment stimulator coupled to and delivering a stimulus to the at least one electrode, a stimulus measurement subsystem in communication with the gross adjustment stimulator and having at least one sensor, the at least one sensor measuring a response of a second tissue, and a programming subsystem in communication with the stimulus measurement subsystem, the programming subsystem collecting data from the group consisting of stimulus data and tissue response data.

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[0012] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory and are intended to provide further explanation of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The accompanying drawings, which are included to provide a further understanding of the invention and are incorporated in and constitute a part of this specification, illustrate embodiments of the invention and, together with the description, serve to explain the principles of the invention. In the drawings:

[0014] FIG. 1 illustrates an exemplary embodiment of a gross adjustment stimulation system;

[0015] FIG. 2 illustrates an exemplary embodiment of an initial gross adjustment method; and

[0016] FIG. 3 illustrates an exemplary embodiment of a post-surgical adjustment method.

DETAILED DESCRIPTION OF THE INVENTION

[0017] The present invention relates to a gross adjustment stimulation system and methods for adjusting stimulation electrode placement for treating various acute and chronic medical conditions. Conditions treatable with implants include, but are not limited to, arthritis, sleep apnea, seizure, incontinence, and migraine. The exemplary conditions may be treated using, for example, the methods and systems disclosed in U.S. Patent Application Nos. 11/707,104 and 11/707,053, both filed February 16, 2007, and herein incorporated by reference in their entireties. Other exemplary methods and systems are described below.

[0018] I. Electrical Stimulation and Neural Recruitment

[0019] Electrical stimulation has been successfully applied to activate both peripheral sensory and motor nerves, as well as the sensory and motor nerves making up the central nervous system, (*e.g.*, the spinal cord and the brain). Generally, electrical stimulation used to

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cause activation in a nerve follows several simple rules, which are described below.

(a) Nerves closest to an activating cathodal contact are activated (recruited) before their more distant neighbors;

(b) Nerves with greater fiber diameters are recruited before nerves with narrow fibers; and

(c) Nerve recruitment is directly proportional to the amount of current delivered.

[0020] Nerves may be electrically stimulated, or recruited, using electrical stimulation pulses of current. Nerves with the lowest threshold axon fibers are recruited first and preferentially. Excitation of the nerve axons by electrical stimulation occurs when nerves close to a stimulating electrode contact have activation thresholds low enough to be excited by the electrode and are depolarized above their threshold membrane voltage.

[0021] One of the major contributors to this activation threshold is nerve diameter. Due to the electrical cable properties of the nerve, large diameter nerve fibers have a lower excitation threshold than do smaller diameter fibers, and thus are more easily excited. Nerve fibers are more likely to be recruited by an electrical stimulation pulse if they are close to the activating electrode and are of larger diameter than other fibers.

[0022] Motor nerve excitation is typically performed at very slow stimulation rates or frequencies because of the problem of overdriving the motor units activated, and because the relatively long time constants of muscle activation reduces the need for high frequency stimulation. With every pulse of stimulation delivered to a motor nerve there is a corresponding contraction of the motor units excited. This contraction is controlled by the physical and electrochemical properties of the muscle motor unit and has a much longer time constant than the excitation of the nerve that activates it. One pulse delivered to the motor unit results in a twitch, while bursts of pulses or multiple pulses at the proper frequency produce a fused contraction with little pulsatile characteristics. Depending upon the muscle

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group, this fusion or tetanic frequency can be as low as approximately 15 Hz for large muscles or as high as approximately 80 to 100 Hz for smaller muscles. Compared to sensory nerve applications, such as cochlear implant stimulation where stimulation frequencies can be many thousands of Hz, motor nerve stimulation is very slow.

[0023] Since the frequencies for motor nerve excitation are quite low, multiple electrodes can be multiplexed to single pulse generators. While only one contact is active at a time, multiple muscle groups are essentially driven at the same time using an interlaced stimulation pattern. Since the muscle dynamics are so slow compared to the nerve, the contractions produced appear simultaneous and smooth.

[0024] Multiple contact systems also allow the activation to be shared by groups of motor units within the same pool to avoid such problems as muscle fatigue, a common problem in electrically stimulated muscle. Multiple contact systems can also co-activate multiple muscle groups to achieve a desired muscle response. In activating the muscles of the hand or forearm, for instance, several contacts may be activated at the same time by delivering interlaced pulses to first one contact and then another, to activate two or more muscle groups that when added result in a force vector in the desired direction.

[0025] Even with a multiplexed multiple contact system however, the electrodes still tend to activate the nerve fibers closest to the electrode. In that sense, they are not selective, and are constrained to activate only those neurons that are closest to the contact. To compensate for this inability to truly selectively activate the optimal pool of neurons, some stimulation systems depend upon sensors to apply stimulation at optimal times so that the desired response may still be achieved. In order to activate a selected pool of neurons located somewhere between two contacts, but that represent the only pool of neurons desired, it is desirable to use a stimulator that can deliver coincident independently controlled stimulation pulses, rather than a stimulator delivering multiplexed sequential pulses.

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[0026] With a stimulator that delivers coincident stimulation pulses, the system can simultaneously deliver currents to each contact. In certain embodiments, these currents are independently controlled. The system can control these currents so that they are at sub-threshold levels (*i.e.*, below the nerve's recruitment level) for the fibers adjacent to the contact. While the fields around each contact are below the nerve's recruitment or threshold level, the fields can combine with fields from other concurrently energized electrodes to create pulses strong enough to activate a desired nerve. Thus, nerve populations that do not lie directly under a stimulation electrode contact can be preferentially and selectively activated. Since the nerves can be selectively activated, sensors are not needed to help time the stimulation delivery to achieve the desired results.

[0027] With selective stimulation and a multiple independent current source system and site specific multiple contact electrodes design, in combination with patient specific stimulus programming, only those portions of the nerve fiber or fibers responsible for non-timing dependent activation are recruited and activated, providing the opportunity for a successful open-loop stimulation application. If desired, sensors can be used to improve stimulus timing and delivery. The sensors can be used in a closed-loop system, a triggered open loop, an open loop system, or some combination of the three.

[0028] A. Sample Conditions Treatable With Implants

[0029] The methods and systems used in conjunction with the present invention can be used to treat a number of conditions by stimulating nerves associated with treating a condition. Stimulation can be such that the stimulus is transmitted by a nerve by activating excitatory pathways, or stimulation can be such that nerve transmission in a nerve is blocked by activating inhibitory pathways. In an exemplary embodiment, the nerve is the sacral nerve. In another embodiment, the nerve is the Vagus nerve. In yet another embodiment, the nerve is a peripheral nerve. Alternatively, the target tissue can be a muscle, including muscles from

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the head and neck, the torso, the upper limbs and the lower limbs. The target tissue can also be an organ of the body, for example, kidney, liver, lung, brain, skin, ovaries, intestines, arteries and veins, lymph nodes, bones, or joints.

[0030] B. Exemplary Embodiment - Obstructive Sleep Apnea

[0031] The HGN is composed of multiple nerve fibers, each of which controls one or more tongue muscles. In certain treatments, the selected HGN nerve fibers are stimulated in order to cause movement of selected tongue muscles. The invention below describes a gross adjustment stimulation system and method of placing electrodes on a target tissue to produce a desired stimulus response.

[0032] II. Gross Adjustment Stimulation System

[0033] FIG. 1 shows an exemplary embodiment of a gross adjustment stimulation system 100. The system has at least one electrode 110, a gross adjustment stimulator 120, a stimulus measurement subsystem 130, and a programming subsystem 140. Each is described below.

[0034] A. Gross Adjustment Stimulator

[0035] In the exemplary embodiment shown in FIG. 1, the gross adjustment stimulator 120 is configured to produce the stimulus that will be sent to at least one implanted electrode 110. The gross adjustment stimulator 120 stimulates the implanted electrode 110 in a manner equivalent to the device to be implanted (*e.g.*, an implantable pulse generator). As described herein, an electrode 110 may be a single electrode, multiple electrodes, or at least one electrode array. Examples of electrodes and gross adjustment stimulators include, but are not limited to, the electrodes and implantable pulse generators described in United States Patent Application Nos. 60/978,519 and 61/017,614 and 61/136,102, filed on October 9, 2007 and December 29, 2007 and August 12, 2008 respectively, which are incorporated by reference herein in their entirety.

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[0036] In certain embodiments, the gross adjustment stimulator 120 allows the physician, physician's assistant, or technician (herein generically referred to as a physician) to start and stop stimulation, and interrogate the stimulus measurement subsystem 130 for information on proper function. In certain exemplary embodiments, the gross adjustment stimulator 120 also allows the patient to direct the system to perform these functions. In certain embodiments, the gross adjustment stimulator 120 displays the status of a communication and power link to the stimulator and status of any external controller (not shown) if, for example, the gross adjustment stimulator is used with an IPG (not shown) having an external controller. In certain embodiments, the physician or patient may also choose operating modes for the stimulator, such as a sleep mode for when the patient intends to go to sleep, an exercise mode for when the patient engages in above normal levels of physical activity, and other alternative operating modes that the patient or physician may program. In certain embodiments, the physician or patient may also adjust levels of stimulation using the gross adjustment stimulator 120.

[0037] In certain exemplary embodiments, the gross adjustment stimulator 120 stimulation is a controlled voltage or controlled current signal, which may be preprogrammed. In certain embodiments, the gross adjustment stimulator 120 is powered and/or controlled by an RF or other wireless signal. In certain embodiments, gross adjustment stimulator 120 sends stimulation in the form of one or more stimulus signals to at least one electrode 110. In other embodiments, the stimulation could be sent to at least two electrodes 110, or an array of electrodes 110. In other embodiments the stimulator sends continuous or near continuous stimulation to the electrode 110 for at least a portion of the implant procedure. Non-limiting examples include one or more pulses, a pulse train, a sinusoid, a constant source signal, or other controlled stimulation forms known to those skilled in the art. Thus, stimulation of the

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target tissue and its effects on a response tissue can be controlled based on patient needs, and is not limited to a particular waveform.

[0038] In an embodiment of the invention, gross adjustment stimulator 120 may optionally include a crypto block (not shown). A crypto block is useful in coding unique signals for only the desired electrodes 110, without interfering with other electrodes controlled by another stimulator 120. Thus, where there are two or more gross adjustment stimulators 120 in the same vicinity, the crypto block creates a unique signal that will interface with only the desired electrode or electrodes 110.

[0039] In another embodiment, gross adjustment stimulator 120 may also include a data storage unit and/or a recording unit (not shown) to store and/or record data, respectively. The gross adjustment stimulator 120 may also include a computer interface (a wireless link, USB port, serial port, or fire wire, for example) to collect or transfer data to an external system. In certain embodiments, the gross adjustment stimulator 120 is disposable.

[0040] B. Stimulus Measurement Subsystem

[0041] In the exemplary embodiment shown in FIG. 1, the stimulus measurement subsystem 130 measures a target tissue's response to applied stimulus. In certain embodiments, stimulus comes from one or more implanted electrodes 110, which receive stimulus from the gross adjustment stimulator 120. Stimulus responses can be measured directly, indirectly, or some combination of the two. Measurements can be taken using sensors integrated with the implant, external to the implant, or some combination of the two. Direct and indirect sensing, and integrated and external sensors are discussed below.

[0042] 1. Direct Measurement

[0043] Direct measurement is the measurement of one or more factors directly influencing airway patency. Factors directly influencing airway patency include, but are not limited to, oral cavity size, tongue protrusion or muscle tone, and respiration airflow (*i.e.* airway

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airflow). There are many different ways to measure these factors. These factors may be visually measured, or they can be measured using mechanical, electrical, or electromechanical sensors. Oral cavity size, for example, can be measured using acoustic pharyngometry. Tongue protrusion or muscle tone can be measured using, for example, one or more of a proximity sensor, accelerometer, or pressure sensor. The sensors may be in the mouth, ear, neck, or other suitable location known to those skilled in the art. Tongue protrusion or muscle tone may also be measured with a soft tissue imaging device utilizing photography, ultrasonography or other imaging modalities known to those skilled in the art. Still other ways include observation with an endoscope, or applying a fluorescent dye pattern to the tongue surface and illuminating it using an ultraviolet or fluorescent light source.

[0044] Respiration airflow may be measured mechanically, electrically, with electromechanical sensors, or some combination of the above. One way is to use a nasal canula or a thermistor. Other ways include a respiration transducer involving thermocouples, piezo thermal sensors, pressure and differential pressure sensors, or other flow sensors known to those skilled in the art. Respiration airflow may also be measured by a pneumotachograph or a respiratory inductance plethysmograph. These ways are exemplary only, and not limited to what is discussed. Other ways known to those skilled in the art may be used without departing from the scope of the invention.

[0045] 2. Indirect Measurement

[0046] Indirect measurement is the measurement of one or more indicators influenced by airway patency. Exemplary indicators include, but are not limited to blood oxygen level, blood pressure, heart rate, torso motion (to sense, for example, relative breathing ease), and snoring. Many different sensors can measure these indirect indictors. Indirect measurements can be made using, for example, peripheral arterial tonometry. In other examples, blood oxygen level may be measured an oxygen sensor, pulse oximetry, an infrared (IR) sensor, or

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an earlobe monitoring unit. Snoring can be measured using, for example, a differential pressure sensor, a vibration sensor, or a microphone. Snoring can also be detected using a nasal canula.

[0047] 3. Sensors

[0048] The ability to sense and measure airway patency, directly or indirectly, increases the ease and accuracy of evaluating patient response to the stimulus patterns. In the exemplary embodiment shown in FIG. 1, the sensor or sensors that input data to the stimulus measurement subsystem 130 may be internal to an electrode 110 or array of electrodes 110, the gross adjustment stimulator 120 or IPG (not shown). In other exemplary embodiments, the sensor or sensors may be external to the electrode 110 or array of electrodes 110, gross adjustment stimulator 120, or IPG (not shown). In certain embodiments, at least one internal sensor is a MEMS device, such as a pressure sensor or accelerometer. In another embodiment, at least one internal sensor is an electrical sensor capable of recording a change related to changes in muscle tone. Sensor information (from internal and/or external sensors for example) may be retrieved in real time over a bidirectional link, (an RF or other wireless link known to those skilled in the art, for example) or through use of an interface placed below the surface of the skin. In certain embodiments, the sensors are external to the electrode 110 or IPG, but still internal to the patient. For example, external sensors may be located in the ear, the nasal passage, the throat, or other measurement points known to those skilled in the art. External sensors may also be located external to the patient in, for example, a medical facility, a laboratory, or a patient's home.

[0049] C. Programming Subsystem

[0050] In the exemplary embodiment of FIG. 1, a programming subsystem 140 collects data on the stimulus applied during gross adjustment. The programming subsystem 140 may also contain preprogrammed stimulus data, which may be used to apply stimulus to the at

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least one electrode 110. In other embodiments, the programming subsystem 140 collects data on the stimulus response, (tissue response, for example) and in still other exemplary embodiments the programming subsystem collects data on both the applied stimulus and the stimulus response. This data can then be used to program user specific stimulus patterns to open the airway and decrease sleep disordered breathing/obstructive sleep apnea for download to hypoglossal nerve(s) implants. In a certain embodiment, for example, at least one sensor collects data that protruder muscles a, c, and f are not affected by a given stimulus, but flattening muscles b, d, and e are stimulated when nerve fibers x, y, and z are stimulated at a frequency of n Hz. In certain exemplary embodiments, sensor information is stored in a sensor memory (not shown) in the stimulus measurement subsystem 130. The measured data is passed to or obtained by the programming subsystem 140, where it is be recorded and correlated with the applied stimulus patterns.

[0051] Sensed information data may also be passed directly to the programming subsystem 140. Once the data are collected and correlated, the programming subsystem 140 generates a stimulus profile based on the obtained information. The stimulus profile may be downloaded into an IPG (not shown) or gross adjustment stimulator 120. The signals from these sensors (internal or external) can be correlated by direct observation (by a physician, patient, or other user, for example), or can be digitized and analyzed via software algorithms to create a stimulus profile. This profile can be used to apply a stimulus that generates a desired response in the targeted tissue. In certain embodiments, software in the programming subsystem 140 generates an algorithm to suggest electrode combinations and stimulus levels to elicit the desired stimulus response.

[0052] III. Initial Gross Adjustment

[0053] FIG. 2 illustrates an exemplary embodiment of an initial gross adjustment method 200. In the exemplary method shown, at least one electrode 110 is placed in an initial

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position on or near the target tissue at step 210. The electrode 110 need not be physically connected to or touching the target tissue. The electrode 110 only needs to be close enough to the target tissue to make an electrical connection with the tissue. The target tissue may be a nerve, a muscle, or an organ of a patient's body. In certain embodiments the target tissue is the hypoglossal nerve. In step 220, at least one stimulus is applied to at least one electrode 110. Stimulus may be chosen manually, or it may be preprogrammed. In the exemplary method shown, stimulus is applied by the gross adjustment stimulator 120, but in other embodiments stimulus can be applied from another source. In certain embodiments, the gross adjustment stimulator 120 is acceptable for use in an operating room environment. Exemplary guidelines for devices acceptable for use in an operating room environment are described in *Draft Guidance for Industry and FDA Staff: Radio-Frequency Wireless Technology in Medical Devices*, released for comment on January 3, 2007, which is hereby incorporated by reference in its entirety. Stimulators configured for wireless use in an operating room need not operate wirelessly, but can if desired.

[0054] Varying stimulus patterns involving permutations of electrode contacts, delivering stimulus of varying current amplitude, duration, and/or frequency are applied to at least one electrode 110. In certain embodiments, these varying stimulus patterns are applied under the control of a physician or technician, and may be preprogrammed. These varying stimulus patterns have different effects on the nerve fibers that control tongue position, muscle tone, and size and patency of the retrolingual airway. In order to identify which nerve fibers produce the desired stimulus response in the muscles in the tongue to open the airway, stimulus is applied independently to each targeted nerve fiber population of interest. In certain embodiments, the electrode position, applied stimulus, and stimulus response are recorded to help identify the location of the electrode on the nerve that provides optimal stimulation.

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[0055] Different levels of stimulation of the nerve fibers are applied to identify the minimum stimulus required to elicit the appropriate muscle movement required to alleviate the symptoms of the physiological condition. Different levels of stimulation often elicit different responses depending on the muscle responding and depending on the different nerve or nerve fibers to be stimulated. Exemplary stimulation patterns are known in the art, or taught in U.S. Patent Application Nos. 11/707,104 and 11/707,053.

[0056] The stimulation applied in step 220 can be in many forms. While stimulation may be applied at high frequencies, lowering the stimulation frequency to the lowest required for a smooth, tetanic, and comfortable contraction, for example, reduces overall power consumption and helps reduce muscle fatigue elicited by electrical stimulation. Stimulation may also be delivered as a single pulse, a burst of pulses, or multiple pulses at one or more frequencies. Each frequency can be as low as approximately 15 Hz for large targeted muscles or as high as approximately 80 to 100 Hz for smaller muscles. In other embodiments, Stimulation frequency is adjustable from a low of 1 Hz to a maximum of 100 Hz. Alternatively, stimulation is multiplexed, and in still other embodiments stimulation is delivered in coincident pulses. Stimulation may be delivered to several contacts (not shown) on an electrode 110, or stimulation may be sequentially applied by delivering interlaced pulses to one contact and then another, to create multiple electric fields that when added result in a force vector in the desired direction to stimulate the target tissue with the desired stimulation level.

[0057] In step 230, the physician, physician's assistant, or technician (herein generically referred to as a physician) checks to see if a desired stimulus response is achieved. This step is performed during or after step 220. In certain exemplary embodiments, a desired response is a blocking of a neural impulse (for example by activating an inhibitory pathway). In certain other exemplary embodiments, a desired response is a change in airway patency.

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Changes in airway patency, either directly or indirectly, are observed during or after stimulus is applied. Checking for a desired stimulus response helps determine which combinations of contacts and current patterns are most desirable. Stimulus parameters can then be adjusted according to the severity of the apnea.

[0058] The stimulus response may be measured using the stimulus measurement subsystem 130, by other electronic means, such as a computer or other instrumentation, or even visual observation. These measurements can be direct or indirect. The stimulus measurement subsystem 130 and measurement means are described elsewhere in this application and are not repeated here. In the exemplary embodiment shown, the gross adjustment stimulator 120 applies stimulus to at least one electrode 110, and the physician checks to see if a desired stimulus response (e.g., tongue movement changes in airway patency) is achieved 230. In certain embodiments, this helps determine which combinations of contacts and current patterns are desirable for a patient. In other exemplary embodiments, a desired response is at least partial blockage of a neural impulse, and in other exemplary embodiments a desired response is the initiation of a neural impulse. Stimulus patterns producing a desired response may then be stored in the implant, patient control device, a secure archive, or the programming subsystem 140. This stimulus may be selected by the physician, or it may be preprogrammed.

[0059] If a desired stimulus response is not obtained, the physician decides at step 240 whether to apply additional stimulus. If the physician chooses to apply additional stimulus 240, the physician repeats step 220 with the desired stimulus pattern(s). Alternatively, or in addition to step 240, the physician decides at step 250 whether electrode repositioning is desirable. If repositioning is chosen, the physician chooses a new position by, for example, shifting at least one electrode 110 along a target tissue, and beginning at step 210.

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[0060] If repositioning is not desired, the physician decides at step 260 whether an acceptable outcome was achieved with the stimulus applied to the electrode in its current position. If so, the physician fixes the electrode in place at step 270. If not, the physician removes the electrode at step 280. The electrode may be fixed in place using surgical means, such as sutures, glue, fasteners, or other means known to those skilled in the art. The method may be performed with additional stimulus electrodes 110, and may be performed with an array of electrodes 110. The steps need not be performed in the order shown, nor do they all need to be performed. The method is exemplary only, and not limited to what is described.

[0061] IV. Post-Surgical Adjustment

[0062] Post-surgical adjustment may begin once the wound heals. Once the patient and wound have healed, the physician begins implant programming to maximize the nighttime retrolingual or pharyngeal airway. Programming may include a range of stimulation values, a programmable delay between switching the implant on and stimulus commencing, a ramp in stimulus intensity over time, and an automatic shut down after a preset interval. Programming may be downloaded to the implant via a wireless link, both for initial trials and for a final stimulus program for use by the patient, or it may be downloaded in USB, serial, or other connection. Programming parameters may include the full range of stimulation values as well as a programmable delay between switching the implant on and stimulus commencing, a ramp in stimulus intensity over time, and an automatic shut down after a predetermined interval. In other embodiments, the IPG itself may be used to generate the signals and stimulation patterns used during gross adjustment.

[0063] FIG. 3 illustrates an exemplary embodiment of a post-surgical adjustment method 300. In step 310 of the exemplary method shown, electrode stimulation is applied while the patient is awake and the upper respiratory tract (URT) is open. In step 320, tongue position is measured in response to the applied stimulus. In an exemplary embodiment, tongue position

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is measured with a tongue protrusion calibration device. The device is placed at the anterior of the mouth and held in place by the teeth, or lips, or other method. In certain methods, the tongue protrusion device is configured to measure anterior tongue thrust using, for example, a pressure sensor.

[0064] The patient is asked at step 330 to evaluate the relative comfort of the tongue position in response to stimulation. If a desired stimulus response is not obtained, steps 310 - 330 may be repeated with another stimulus. At step 340 the physician evaluates whether a stimulus response is desirable. When a desired stimulus response is obtained (i.e. a stimulus that produces an open airway or change in airway patency without causing discomfort to the patient), the stimulus program is saved at step 350 for later use. Stimulus may be programmed by a physician, a physician's assistant, a technician, or even the patient.

[0065] Another exemplary post-surgical adjustment method is to record the level of nerve activity present when the tongue has normal daytime tone using, for example, an electroneurogram sensor. Under this approach, the signals from the target tissue (e.g., the hypoglossal nerve) are recorded while the patient is awake. This recording can be during the patient's normal daytime routine, or it can be done while the patient is in a laboratory or medical facility. This information collected from electroneurogram sensor is used to prepare a stimulus program that mimics the daytime nerve signals to be used during while the patient sleeps to treat obstructive sleep apnea. The use of an electroneurogram sensor is exemplary only. Other sensors known to those skilled in the art could also be used to obtain the information above to create a desired stimulus program without departing from the scope of the invention.

[0066] Yet another approach or exemplary method is to program the HGN implant(s) in a laboratory, using a stimulation protocol that minimizes URT obstruction, snoring, and apneic and or hypopneic events observed in the laboratory, in order to maximize the URT patency.

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Programming may be downloaded to the implant via the RF link, both for initial trials and for a final stimulus program for use by the patient.

[0067] It will be apparent to those skilled in the art that various modifications and variations can be made in the device of the present invention without departing from the scope of the invention. Thus, it is intended that the present invention cover the modifications and variations of the present invention.

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CLAIMS

We claim:

1. A method of neural stimulation, comprising the steps of:

electrically connecting at least one electrode to a first tissue;

applying a stimulus to the at least one electrode;

observing a response of a second tissue;

identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode; and

fixing the at least one electrode in place at the identified electrode position.

2. The neural stimulation method of claim 1, wherein the applied stimulus is a voltage signal.

3. The neural stimulation method of claim 1, wherein the applied stimulus is a controlled voltage signal.

4. The neural stimulation method of claim 1, wherein the applied stimulus is a current signal.

5. The neural stimulation method of claim 1, wherein the applied stimulus is a controlled current signal

6. The neural stimulation method of claim 1, wherein the applied stimulus is preprogrammed.

7. The neural stimulation method of claim 1, wherein the stimulus applicator is disposable.

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8. The neural stimulation method of claim 1, further comprising the step of applying an additional stimulus to the at least one electrode.

9. The neural stimulation method of claim 1, further comprising the step of repositioning the at least one electrode.

10. The neural stimulation method of claim 1, further comprising the step of calculating an estimated minimum stimulus level to achieve the desired response.

11. The neural stimulation method of claim 1, further comprising the step of generating a stimulus profile.

12. The neural stimulation method of claim 11, wherein the stimulus profile comprises suggested electrode combinations and stimulus levels to elicit the desired response.

13. The neural stimulation method of claim 1, wherein the first and second tissues are selected from the group consisting of nerve tissue, muscle tissue, and organ tissue.

14. The neural stimulation method of claim 13, wherein the first tissue is nerve tissue.

15. The neural stimulation method of claim 14, wherein the nerve tissue is a hypoglossal nerve fiber.

16. The neural stimulation method of claim 13, wherein the second tissue is tongue muscle tissue.

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17. The neural stimulation method of claim 16, wherein the tongue muscle tissue is a tongue flattening muscle.

18. The neural stimulation method of claim 16, wherein the tongue muscle tissue is a tongue protruding muscle.

19. The neural stimulation method of claim 1, wherein the desired response is a change in airway patency.

20. The neural stimulation method of claim 1, wherein the desired response is the at least partial blockage of a neural impulse.

21. The neural stimulation method of claim 1, wherein the desired response is the initiation of at least one neural impulse.

22. The neural stimulation method of claim 1, wherein the response of a second tissue is observed visually.

23. The neural stimulation method of claim 1, wherein the response of a second tissue is observed using instrumentation.

24. The neural stimulation method of claim 1, wherein the response of a second tissue is directly observed.

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25. The neural stimulation method of claim 1, wherein the response of a second tissue is indirectly observed.

26. The neural stimulation method of claim 1, wherein the response of a second tissue is observed by a sensor internal to the patient.

27. The neural stimulation method of claim 1, wherein the response of a second tissue is observed by a sensor external to the patient.

28. A neural stimulation system, comprising:

at least one electrode electrically connected to a first tissue;

means for applying a stimulus to the at least one electrode;

means for observing a response of a second tissue;

means for identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode; and

means for fixing the at least one electrode in place at the identified electrode position.

29. A computer program product comprising computer readable medium having stored thereon computer executable instructions that, when executed on a computer, causes the computer to perform a method of neural stimulation comprising the steps of:

applying a stimulus to at least one electrode electrically connected to a first tissue;

observing a response of a second tissue; and

identifying an electrode position on the first tissue wherein a desired response occurs on the second tissue when the stimulus is applied to the at least one electrode.

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30. A neural stimulation system, comprising:

at least one electrode electrically connected to a first tissue;

a gross adjustment stimulator coupled to and delivering a stimulus to the at least one electrode;

a stimulus measurement subsystem in communication with the gross adjustment stimulator and having at least one sensor, the at least one sensor measuring a response of a second tissue; and

a programming subsystem in communication with the stimulus measurement subsystem, the programming subsystem collecting data from a group consisting of stimulus data and tissue response data.

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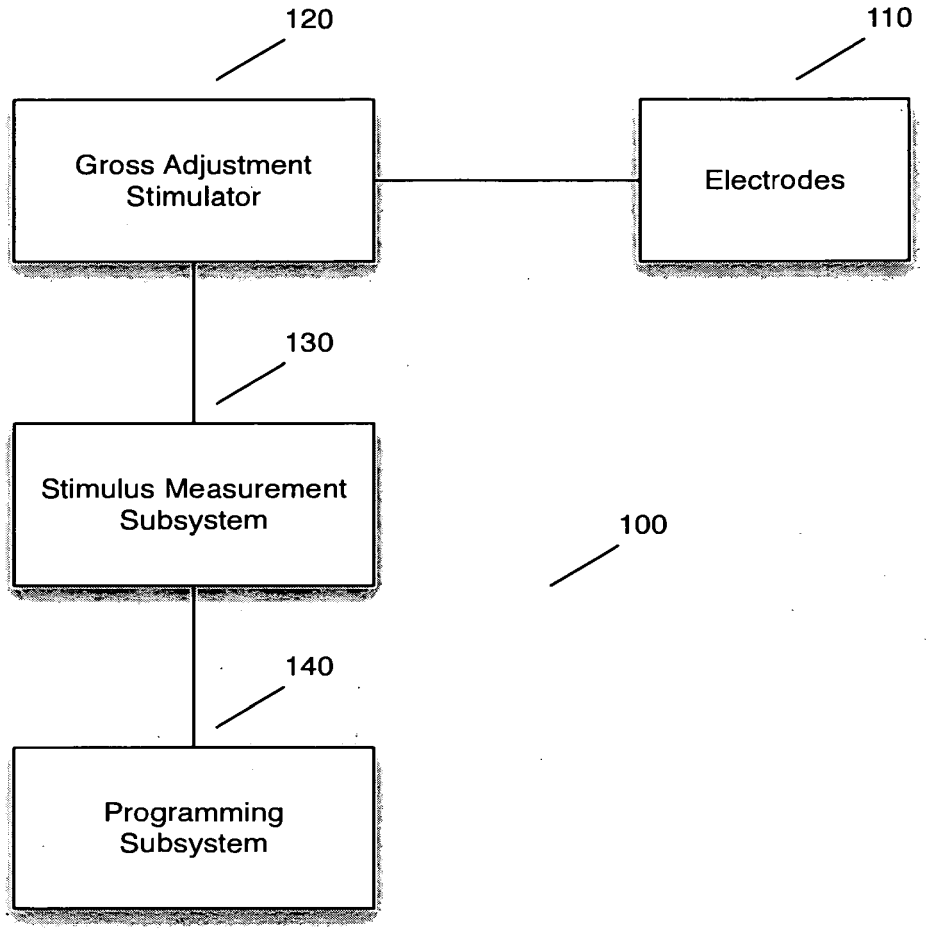


FIG 1

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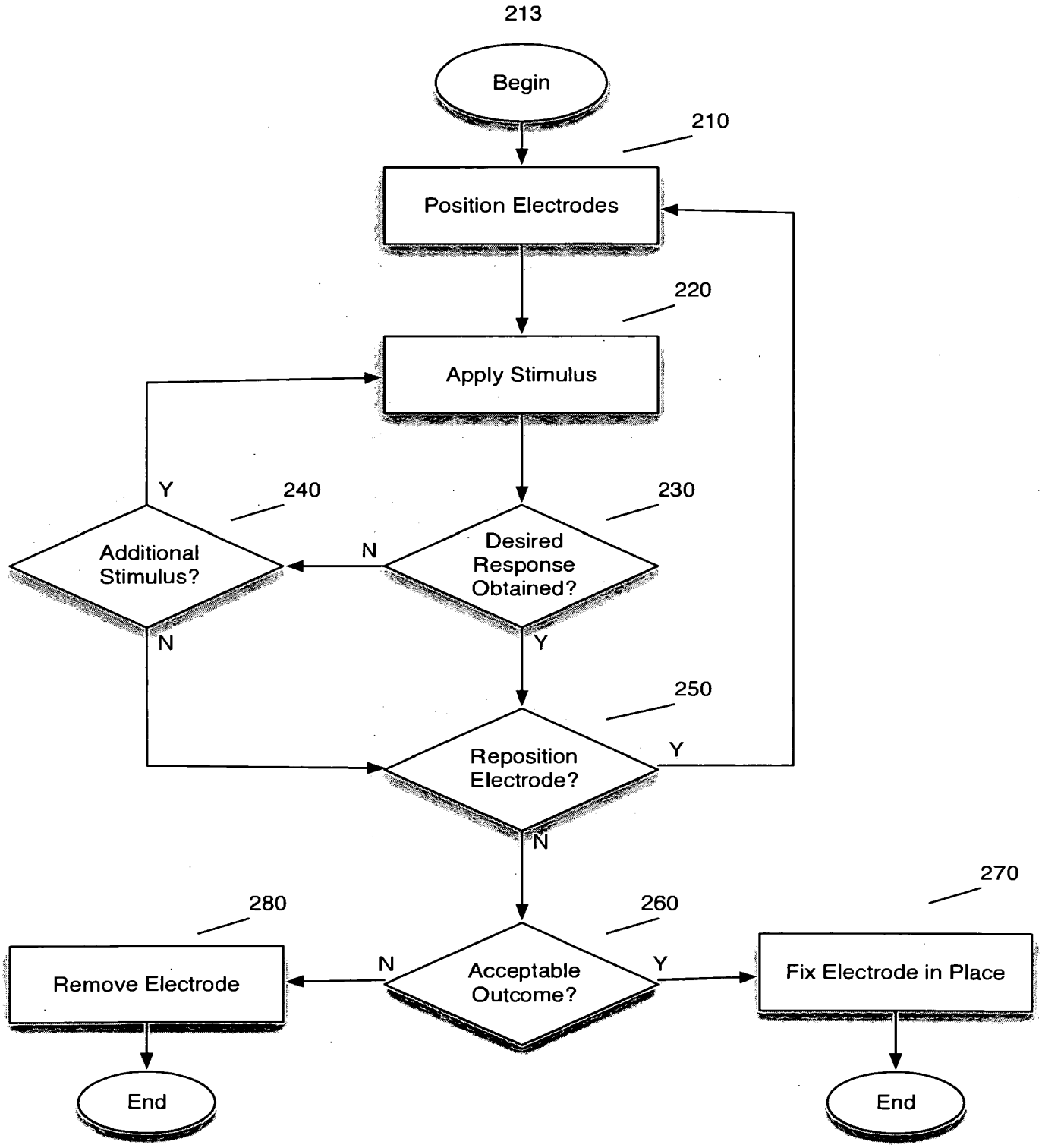


FIG 2

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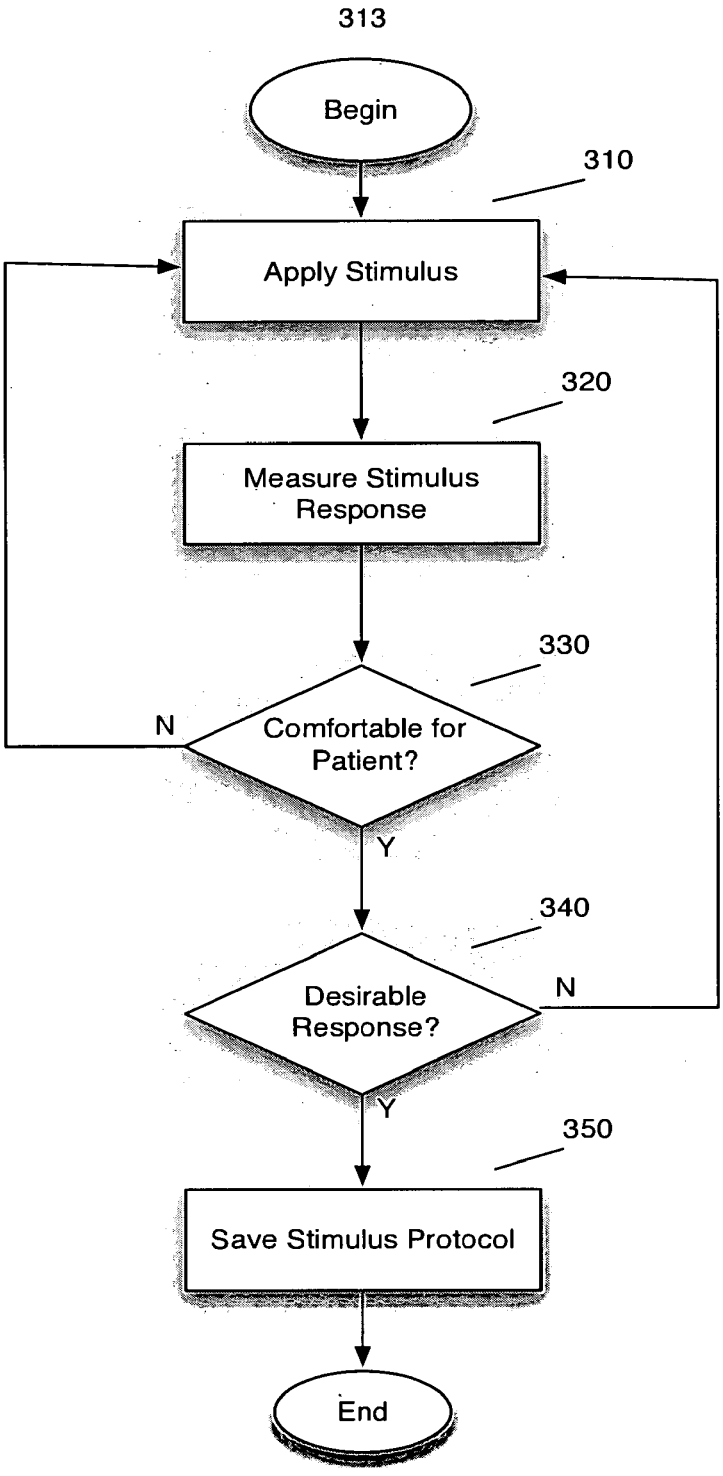


FIG 3

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/011599

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61N 1/05 (2008.04)
USPC - 607/46
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - A61N 1/00, 1/05
USPC - 607/39, 46 (2008.04)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Patbase

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2007/0233204 A1 (LIMA et al) 04 October 2007 (04.10.2007) entire document	1-30
Y	US 5,771,891 A (GOZANI) 30 June 1998 (30.06.1998) entire document	1-29
Y	US 6,266,560 B1 (ZHANG et al) 24 July 2001 (24.07.2001) entire document	7, 27, 30
Y	US 5,190,053 A (MEER) 02 March 1993 (02.03.1993) entire document	18

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
01 December 2008	12 DEC 2008
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2005)

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 November 2009 (05.11.2009)

PCT

(10) International Publication Number
WO 2009/135138 A1

(51) International Patent Classification:
A61N 1/05 (2006.01)

(21) International Application Number:
PCT/US2009/042539

(22) International Filing Date:
1 May 2009 (01.05.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/049,927 2 May 2008 (02.05.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR),

[Continued on next page]

(54) Title: SELF EXPANDING ELECTRODE CUFF

(57) Abstract: An electrode lead assembly is described. The lead assembly includes an expandable cuff electrode that includes a series of spaced apart electrode elements and a substantially re-closable opening.

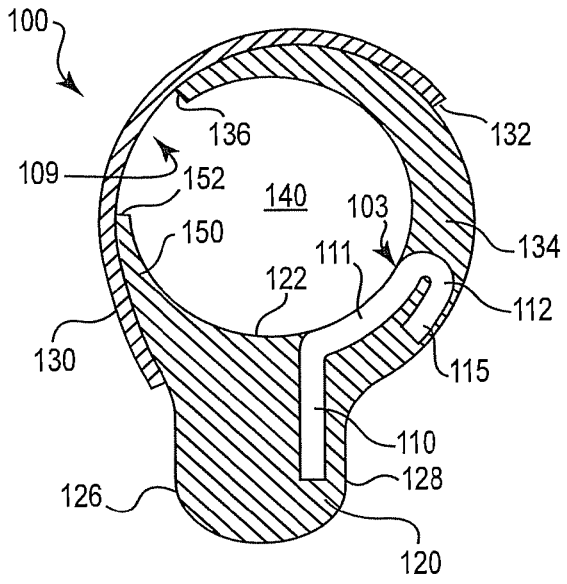


Fig. 10

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OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

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SELF EXPANDING ELECTRODE CUFF

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This application claims priority under 35 U.S.C. §119(e) to U.S. Provisional Patent Application Serial No. 61/049,927, filed on May 2, 2008, and incorporated herein by reference.

TECHNICAL FIELD

[002] The invention relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the invention relates to an expandable electrode cuff for positioning an electrode of an implantable stimulation system about a nerve for stimulation and/or monitoring of nerve tissue.

BACKGROUND

[003] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[004] One treatment for obstructive sleep apnea has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a cuff electrode place around the hypoglossal nerve.

[005] Because of the significant amount of movement in multiple directions

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that can take place under the chin, positioning an electrode to enable stimulation of the hypoglossal nerve becomes a significant challenge. On the one hand, placement of the electrode and lead in close proximity to the hypoglossal nerve can result in irritation to the nerve as a result of normal motion of the chin and neck, while on the other hand, without close adherence to the nerve, buildup of connective tissue between the nerve and the electrode cuff and lead can occur, causing low thresholds, thereby reducing the effectiveness of the delivered stimulation by the device.

[006] Another challenge in placing an electrode for nerve stimulation therapy relates to the tendency of the hypoglossal nerve to swell because the nerve is disturbed while manipulating the nerve to implant the cuff electrode and/or while securing the cuff electrode about the nerve. Once the cuff electrode secured on the nerve, swelling of the nerve can result in excess pressure on the nerve by the electrode and lead. In addition, once the electrode has initially been implanted, fibrosis tends to cause the location of the electrode to become more fixed. Therefore, during the first month following the implant of the lead and electrode, it is desirable to keep the electrode cuff properly positioned on the nerve, while at the same time not placing undue pressure on a swelling nerve. An additional challenge in placing the electrode for nerve stimulation results from the fact that stimulation currents should be confined to the hypoglossal nerve in order to prevent other nearby nerves or muscles from being stimulated, which would result in patient discomfort and loss of sleep.

BRIEF DESCRIPTION OF THE DRAWINGS

[007] Aspects and features of the present invention will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments of the present disclosure when considered in connection with the accompanying drawings, wherein:

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[008] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a self-expanding nerve cuff, according to an embodiment of the present disclosure;

[009] FIG. 2 is a side view of a lead utilized in an implantable stimulation system, according to an embodiment of the present disclosure;

[010] FIG. 3 is a perspective view of an expandable cuff electrode, according to an embodiment of the present disclosure;

[011] FIG. 4 is a sectional view as taken along lines 4—4 of Figure 3, according to an embodiment of the present disclosure;

[012] FIG. 5 is a sectional view as taken along lines 5—5 of Figure 3, according to an embodiment of the present disclosure;

[013] FIG. 6 is a sectional view of the expandable cuff of FIG. 5 in an intermediate open position, according to an embodiment of the present disclosure;

[014] FIG. 7 is a sectional view of the expandable electrode cuff of FIG. 5 in a fully open position, according to an embodiment of the present disclosure;

[015] FIG. 8 is a sectional view of an expandable electrode cuff in an intermediate open position, according to an embodiment of the present disclosure;

[016] FIG. 9 is a sectional view of an expandable electrode cuff in a larger diameter, fully engaged position, according to an embodiment of the present disclosure;

[017] FIG. 10 is a sectional view of an expandable electrode cuff in another larger diameter, fully engaged position, according to an embodiment of the present disclosure;

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[018] FIG. 11 is a sectional view of an expandable electrode cuff in a fully engaged position, according to an embodiment of the present disclosure;

[019] FIG. 12 is a sectional view of an expandable electrode cuff in a fully engaged position, according to an embodiment of the present disclosure;

[020] FIG. 13 is a sectional view of an expandable electrode cuff in a fully engaged position, according to an embodiment of the present disclosure;

[021] FIG. 14 is a perspective view of an expandable electrode cuff, according to an embodiment of the present disclosure;

[022] FIG. 15 is a sectional view as taken along lines 15—15 of FIG. 14, according to an embodiment of the present disclosure;

[023] FIG. 16 is a sectional view of the expandable electrode cuff of FIG. 15 with an alternate outer flange member, according to an embodiment of the present disclosure;

[024] FIG. 17 is a sectional view of an expandable electrode cuff, according to an embodiment of the present disclosure;

[025] FIG. 18 is a sectional view of an expandable electrode cuff, according to an embodiment of the present disclosure;

[026] FIG. 19 is a sectional view of an expandable electrode cuff of FIG. 18 with an alternate outer flange member, according to an embodiment of the present disclosure;

[027] FIG. 20 is a sectional view of an expandable electrode cuff of FIG. 15 with another alternate outer flange member, according to an embodiment of the present disclosure; and

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[028] FIG. 21 is a sectional view of an expandable electrode cuff of FIG. 18 with another alternate outer flange member, according to an embodiment of the present disclosure.

DESCRIPTION OF EMBODIMENTS

[029] The following detailed description is merely exemplary in nature and is not intended to limit the present disclosure or the application and uses of the embodiments of the present disclosure. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, brief summary or the following detailed description.

[030] Embodiments of the present disclosure provide an electrode cuff that, once engaged about a nerve via a re-closable opening, is automatically expandable to accommodate increases in the diameter of a nerve while still maintaining contact between electrodes of the cuff against the nerve. Among other features to be described, the electrode cuff includes a combination of opposed and/or overlapping flange members that are biased to remain in releasable contact with each other, and slidable movable relative to each other, to provide the automatic expandability without losing closure of the nerve within the electrode cuff.

[031] These embodiments, and other embodiments, will be described in association with FIGS. 1-21.

[027] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a self-expanding nerve cuff, according to an embodiment of the present disclosure. As illustrated in FIG.1, an example of an implantable stimulation system according to one embodiment of the present disclosure includes an

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implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 10, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes an electrode or electrode system 65 and extends from the IPG 55 so that the electrode system 65 is position around a desired nerve, such as the hypoglossal nerve 53 of the patient 10, to enable stimulation of the nerve 53, as described below in detail. An exemplary implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., incorporated herein by reference in its entirety, and further includes a sensor lead 57 electrically coupled to the IPG 55 and extending from the IPG 55 so that a sensor or transducer 60 can be positioned in the patient 10 for sensing of respiratory effort.

[028] The sensor 60 may be a pressure sensor that is surgically implanted in a region that has pressure continuity with the intrapleural space, such as the suprasternal notch, the space between the trachea and esophagus, or by being attached to either of the trachea or esophagus. The sensor 60 may also be positioned intercostally, or secured in a position for sensing pressure at the posterior side of the manubrium. The suprasternal notch 62 and manubrium 63 of the sternum 64 are well known structures on the upper chest that are in anatomical continuity with the intrapleural space. It is also well known that changes in intrapleural pressure provide a characteristic respiratory effort waveform.

[029] The location for placement of the sensor 60 is, at least in part, chosen as a function of a delay, i.e. the propagation time associated with a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position. The chosen location is also a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. the amount of filtering that is necessary to remove waveforms other than the waveform associated with the desired sensed

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characteristic, such as the filtering required to remove cardiac waveform activity, for example. The positioning of the sensor 60 enables the IPG 55 to receive respiratory effort waveform information utilized to determine increased respiratory effort, which is then used by the IPG 55 to control delivery of therapy in response to determined increases in respiratory effort.

[030] FIG. 2 is a side view of a lead utilized in an implantable stimulation system according to an embodiment of the present disclosure. In one embodiment, as illustrated in FIG. 2, a lead 80 includes a lead body 82, connector 88, and an expandable cuff electrode 90. The lead body 82 extends from a proximal end 84 to a distal end 86, with the connector 88 being positioned at the proximal end 84 of the lead body 82 for electrically connecting the lead 80 to the IPG 55. The expandable electrode cuff 90 is located at the distal end 86 of the lead body 82 and is configured to be positioned around a target nerve, such as a hypoglossal nerve or other nerve. The electrode cuff 90 includes one or more electrodes 92 embedded within a wall of the electrode cuff 90 so that when the electrode cuff 90 is positioned around the nerve, the respective electrodes 92 are in contact with the nerve. In one aspect, the lead body 82 includes conductors (not shown) extending within the lead body 82 to electrically connect the electrodes 92 and the connector 88 so that the electrodes 92 are electrically coupled to the IPG 55 via respective connector pins 94 of the connector 88, as is known in the art.

[031] FIG. 3 is a perspective view of an expandable electrode cuff 100, according to one embodiment of the present disclosure, which can be deployed in place of the cuff electrode 90 in lead 80. As illustrated in FIG. 3, cuff 100 includes a cuff body 101 and an array 102 of electrodes 103. In general terms, the cuff body 101 defines a lumen 140 through which a target nerve will extend. Among other features, the cuff body 101 includes a pair of resilient fingers 134, 150 (e.g., flange members) that have a generally arcuate shape and that extend from a base portion 120 of cuff body 101. In general terms, by pulling the ends of the resiliently, biased fingers 134,150 apart from each other, access to lumen

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140 is provided for engaging a target nerve. Upon release of the fingers 134, 150, the cuff body 101 resumes the shape illustrated in FIG. 3. As will be further described later, once positioned on a nerve, the materials and construction of the fingers 134, 150 permit automatic expansion of the size of lumen 140 to accommodate expansion of the size of the nerve encircled by the cuff body 101. In this manner, the electrodes 103 are held in close contact against the nerve while allowing for expansion of a diameter of lumen 140 defined between fingers 134, 150 and base 120.

[032] In one embodiment, the array 102 of electrodes 103 are embedded within a wall of the cuff body 101 with the respective electrodes 103 spaced apart from each other along a length of the cuff body 101. In some embodiments, as illustrated in FIG. 3, the electrodes 103 are aligned in series along a single longitudinal axis on a common side or portion of the cuff body 101. However, in other embodiments, the electrodes 103 are staggered laterally relative to a single longitudinal axis or arranged in other patterns. In one embodiment, electrode 103 has a width (W2) of about 0.050 inches.

[033] In some embodiments, cuff 100 additionally includes an outer flap or flange member that is biased and configured to maintain releasable coverage of at least a portion of an outer surface of the cuff body 101 and of the re-closable opening 109 between the distal ends of fingers 134, 150, as will be described in more detail in association with at least Figures 4-10. However, in other embodiments, this outer flap is omitted. In either case, Figure 3 illustrates cuff body 101 without an outer flap for illustrative clarity in viewing the features and attributes of cuff body 101 that would otherwise be obscured by the presence of an outer flap.

[034] FIG. 4 is a sectional view of the expandable electrode cuff 100, as taken along lines 4—4 of FIG. 3, according to an embodiment of the present disclosure. As illustrated in FIG. 4, cuff 100 defines lumen 140 and provides a row of spaced apart electrodes 103 for contacting a nerve encircled by the cuff 100. Among

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other features, the cuff body 101 also includes a conductive coil 105 extending through a length of the body portion 120 and positioned to electrically connect to each of the respective electrodes 103. In some embodiments, it is understood that the coil 105 includes three separate coil components so that each electrode 103 is separately controllable via a respective one of the coil components to enable applying independent stimulation signals to the nerve from each electrode 103. In addition, in another aspect, base portion 120 includes a proximal extension 121 that extends proximally to mechanically connect the cuff body 101 to the lead body 82 while a proximal portion of the coil 105 is electrically connected to a conductive element of lead body 82. In one aspect, this proximal extension 121 serves as a strain relief to distribute forces from the lead body 82 to the electrode cuff 100 over a wider section of the lead body 82.

[035] In one aspect, each electrode 103 includes a lower end to which a connector or crimp tube 107 (shown in FIG. 5) is mechanically and electrically attached, with a portion of the electrode coil 105 being mechanically and electrically connected to the crimp tube 107. In one non-limiting example, the crimp tube 107 and electrode 103 are metals suitable to be welded together to effect their mechanical and electrical connection together. In one aspect, the electrode is made from a biocompatible, non-corrosive electrically conductive material. In one non-limiting example, the electrode is made from a platinum-iridium material, such as a material including 90% platinum and 10% iridium. In another aspect, the coil 105 is made of a silver core MP35N type of conductor, although other types of non-silver conductors may be used. The silver component lowers the impedance of the lead, thereby providing a more efficient lead. Because of the specific attributes of these conductive materials, the material of the lead 82 is mechanically connected via crimping a portion of lead 82 to the crimp tube 107, thereby establishing the electrical connection between the coil 105 and the electrode 103.

[036] FIG. 5 is a sectional view of an expandable electrode cuff as taken along lines 5—5 of FIG. 3, according to an embodiment of the present disclosure. As

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illustrated in FIG. 5, in one embodiment an expandable electrode cuff 100 includes a base portion 120, a first flange member 130, a second flange member 134, and a third flange member 150. The base portion 102 includes a top wall 122, a bottom wall 124, a first side wall 126, and a second side wall 128. The second flange member 134 and the third flange member 150 comprise arcuate shaped fingers that are shaped, biased, and have a length to define a generally circular shaped lumen 140. The second flange member 134 extends generally outward from the second side wall 128 and from the top wall 122 of the base portion 120 with at least a portion of the second flange member 134 being spaced apart from the top wall 122 of the base portion 120. On the other hand, the third flange member 150 extends generally outward from the first side wall 126 and from the top wall 122 of the base portion 120.

[037] In one aspect, the second flange member 134 has an arcuate length substantially greater than an arcuate length of the third flange member 150. In one embodiment, the second flange member 134 has an arcuate length substantially greater than (such as 3 times longer) than an arcuate length of the third flange member 150. Moreover, in another aspect, the second flange member 134 includes a proximal portion 162 having a substantially greater width (such as 3 to 5 times greater) than a width of a distal portion 136 of the second flange member 134 and than a width of a distal portion 152 of the third flange member 150, as will be later described in more detail.

[038] In some embodiments, the first flange member 130 includes a proximal end 131 and a distal end or portion 132 with the proximal end 131 being bonded to the third flange member 150 along a portion of an outer wall 152 of the third flange member 150. The first flange member 130 has a length sufficient to extend about, and be in releasable contact with, the periphery or outer surface of both the third flange member 150 and a majority of a length of the second flange member 134. In this arrangement, the first flange member 130 also extends over, and is spaced apart from, the top wall 122 of the base portion 120. In some embodiments, the first flange member 130 has an arcuate length equal to or

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greater than about one-half the circumference of an outer surface of the cuff 100 defined by the second and third flange members 134, 150. In this arrangement, with the first flange member 130 extending coextensively with (and in releasable contact with) a majority of the arcuate length of the second flange member 134, the first flange member 130 is biased to maintain coverage across the substantially re-closable opening 109 (between the distal ends 136, 152 of the respective second and third flange members 134, 150) even when a diameter of the lumen 140 increases.

[039] In one aspect, the free distal portion (including distal end 132) of the first flange member 130 extends in a first direction or orientation opposite to the direction (or orientation) in which the free distal portion (including distal end 136) of the second flange member 134 extends. In this arrangement, with the first flange member 130 and the second flange member 134 being biased in an overlapping, releasably contacting relationship, each of the distal ends 132, 136 of the respective first and second flange members 130, 134 will move in opposite directions upon expansion of the lumen 140 in response to a swollen nerve or during positioning of the cuff 100 about a nerve, as will be further described in association with at least FIGS. 9-10.

[040] In the expandable electrode cuff 100 of the embodiment of FIG. 5, the base portion 120, second flange member 134 and the third flange member 150 are formed from a single, unitary molded piece, with the first flange member 130 bonded to the molded piece. In other words, this single, unitary molded piece comprising the base member 120, second flange member 134, and third flange member 150 forms a monolithic component to which the first flange member 130 is attached. In some embodiments, first flange member 130 is attached via an adhesive (such as a polyurethane adhesive) or other bond.

[041] FIG. 5 also illustrates one of the electrodes 103 that is embedded in cuff body 101, as previously illustrated in FIGS. 3-4. As illustrated in FIG. 5, electrode 103 includes a proximal base portion 110, a body portion 111, and a

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distal hook portion 112 with the distal hook portion 112 defining a recess 114 that extends between a distal tip portion 115 and body portion 111. In one aspect, each electrode 103 is a generally rigid member having electrically conductive properties, as will be later described in more detail. As illustrated in FIG. 5, the proximal base portion 110 is a generally straight portion while the body portion 111 extending distally from the base portion 110 includes a generally arcuate shape approximating the radius of curvature of the inner wall 142 of cuff body 101 that defines lumen 140. In one aspect, the body portion 111 forms a generally obtuse angle relative to the proximal base portion 110. In some embodiments, the obtuse angle (α) falls within a range of about 120 degrees to about 140 degrees. In one embodiment, the obtuse angle (α) is about 130 degrees.

[042] In one embodiment, the arcuate length of the body portion 111 of electrode 103 generally corresponds to about a 45 degree arc (as represented by the arc β in FIG. 5) about the generally circular lumen 140. However, in some embodiments, the arcuate length of the body portion 111 of electrode 103 falls within a range that generally corresponds to about a 20 degree arc to about a 60 degree arc about the generally circular lumen 140 defined by cuff body 101.

[043] In some embodiments, at least the body portion 111 of electrodes 103 has a thickness of about 0.006 inches. In some embodiments, the combination of the width W2 and the arcuate length (L1) of the body portion 111 defines a surface area available for contact against the target nerve. By limiting the arcuate length of the body portion 111 to a relatively short length that generally corresponds to about a 45 degree arc of the lumen 140, the generally rigid body portion 111 will be subject to little, if any, bending so that the body portion 111 and electrode 103 will be less likely to experience fracture or fatigue failures. However, given the relatively short length of body portion 111, the body portion 111 (and the rest of the electrode 103) is configured with a substantial width.

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[044] In one embodiment, the aspect ratio of the length to width of the electrode is about 1.2. However, in some embodiments, this aspect ratio can fall within a range from about to about 1 to 1.5. In this way, a generally optimal surface area of body portion 111 of electrode 103 is exposed to the nerve while maintaining a length of body portion 111 below a threshold at which a fatigue failure might be more likely to occur. In one aspect, the body portion 111 has a length that is long enough to engage a substantial portion (at least ¼ or a 45 degree arc) of a cross-section of the target nerve such that the exposed body portion 111 is limited to a length that minimizes the likelihood of fatigue through mechanical flexing while relatively maximizing the surface area of the exposed body portion 111 to maintain safe current densities.

[045] In another aspect, during construction of the cuff 100, the cuff body 101 is molded in a manner to capture or embed the respective electrodes 103 within a portion of the cuff body 101. During this molding process, the material generally encapsulates the electrode 103, including filling in the recess 114 at the distal hook portion 112 of the electrode 103. In some embodiments, cuff body 101 is formed or molded as a single, monolithic member. However, in other embodiments, cuff body 101 is formed from two or more separate components. In either case, the cuff body 101 is molded or constructed to securely maintain electrode 103 within a fixed position relative to the remainder of the cuff body 102. In this regard, with the proximal base portion 110 of the electrode 103 extending within the base portion 120 and with the distal hook portion 112 extending within second flange member 134 at a location laterally spaced apart from the proximal base portion 110 of electrode 103, this arrangement ensures stability in the location of the electrode 103 relative to the cuff body 101. Moreover, as illustrated in FIG. 5, body portion 111 of electrode 103 is embedded within the thickest portion of the second flange member 134 so that cuff body 101 is substantially more rigid (i.e., less flexible) in the region of body portion 111 of electrode 103. Moreover, with this arrangement, body portion 111 becomes exposed at a lumen 140 to enable direct contact with a nerve extending through lumen 140.

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[046] In one aspect, because the electrode 103, and in particular the body portion 111, is made of a generally rigid material, the electrode 103 is substantially less likely to be subject to bending and/or fatigue failures during use within the body. Moreover, because the electrode is generally rigid and is molded within the least flexible portion (e.g., the proximal portion 162 of second flange member 134) of the cuff body 101 as described above, the electrode 103 will not be subject to delamination (as typically occurs in foil-based electrode configurations of conventional electrode cuff arrangements) because the proximal portion 162 of the second flange member 134 that incorporates the body portion 111 and distal hook portion 112 of electrode 103 will not be subject to bending relative to the electrode 103, as will be later described in more detail in association with FIGS. 6-10, and FIG. 7 in particular. In one aspect, by full embedding the electrodes 103 (except for the exposed side of body portion 111), the cuff body 101 protects the nerve from the edges and corners of the electrode.

[047] As described below in reference to FIGS. 5-10, the electrode cuff 100 is expandable both during implantation of the electrode cuff 100 (and associated lead 80), and is also automatically expandable (in response to a change in nerve diameter) after the electrode cuff 100 is positioned around a desired nerve for delivery of electrical stimulation therapy to the nerve, as was previously described in relation to FIGS. 3-5.

[048] During it's normal, unbiased state, prior to insertion around the nerve, the electrode cuff 100 is in a fully engaged position (shown in FIG. 5) in which, the second flange member 134 extends generally upward and outward from the second side wall 128 and over (i.e. above and spaced apart from) the top wall 122 of the base portion 120 with the distal end 136 terminating adjacent the distal end 152 of the third flange member 150. In this fully engaged position, the third flange member 150 extends generally upward and outward from the first side wall 126 and from the top wall 122 of the base portion 120 such that the third flange member 150 does not extend over the top wall 132. In one embodiment, the distal end 136 of the second flange member 134 is positioned adjacent to

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and in releasable contact against the distal end 152 of the third flange member 150 while in other embodiments, the respective distal ends 136 and 152 are in close proximity but do not contact each other. In general terms, these respective ends meet at a location along the first flange member 130 closer to the proximal end 131 than the distal end 132 of the first flange member 130. Together, the distal ends 136, 152 of the respective second and third flange members 134, 150 form a substantially re-closable opening 109 that provides selective access to lumen 140 and that generally maintains a nerve securely within the lumen 140, unless affirmative steps are taken to remove the electrode cuff 100 from the nerve.

[049] In another aspect, while in this fully engaged position illustrated in FIG. 5, with the attachment of its proximal end 131 to the third flange member 150, the first flange member 130 extends generally outward from the first side wall 126 of the base portion 120 to be coextensive with and in releasable contact with an outer side wall 147 of the third flange member 150. It will be understood that the region of attachment of the first flange member 130 to the third flange member 134 extends over a significant portion of a length of the third flange member 150 to ensure a robust attachment. From this region, the first flange member 130 extends further over (e.g. above and spaced apart from) the top wall 122 of the base portion to be coextensive with, and in releasable contact with, an outer side wall 146 of the second flange member 134 until the distal end 132 terminates adjacent the top wall 122 of the base portion 120 on the second side 128 of the base portion.

[050] In one aspect, the first flange member 130 has a length greater than a length of the second flange member 134 so that when the electrode cuff 100 is in the fully engaged position, the first, second and third flange members 130, 134 and 150 form a lumen 140 for receiving a nerve therein. With this in mind, an inner side wall 141 of the second flange member 134 and an inner side wall 154 of the third flange member 150 act together to form an inner wall 142 of the lumen 140 so as to position the electrodes 103 (shown in FIGS. 3-5), which are

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embedded within the second flange member 134, adjacent to the nerve (not shown in FIG. 3). In addition, when the electrode cuff 100 is in the fully engaged position shown in FIG. 5, an inner side wall 144 of the first flange member 130 is positioned in releasable contact against the outer side wall 146 of the second flange member 134 and against the outer side wall 147 of the third flange member 150. With this arrangement, an outer wall 148 of the first flange member 130 forms an outer wall 143 of the lumen 140. In this way, when the electrode cuff 100 is in the fully engaged position shown in FIG. 5, both the first flange member 130 and the second flange member 134 extend over (e.g., above and spaced apart from) the base portion 120 such that the first flange member 130 forms an outer layer of the electrode cuff 100, and such that the second and third flange members 134 and 150 form an inner layer of the electrode cuff 100 for engaging the nerve.

[051] Depending on the size of the nerve about which the cuff 100 is mounted, the electrode cuff 100 may be either in the fully engaged position of FIG. 5 or in a partially fully engaged position (FIGS. 9-10), which occurs in the event that the cuff automatically expands in size to accommodate a larger sized diameter nerve or a swollen nerve. In a partially fully engaged position, the general configuration of the electrode cuff 100 remains generally the same as the fully engaged position except that, because the first flange member 130 is slidably movable relative to the second flange member 134 and because the generally flexible, distal portion of the second flange member 134 permits rotational movement of the second flange member 134 away from the third flange member 150, the distal end 132 of the first flange member 130 will be positioned along the outer side wall 146 of the second flange member 134 in a location spaced further away from the second side wall 128 than shown in FIG. 5. Likewise, upon rotation of the second flange member 134 away from the third flange member 150, the substantially re-closable opening between the distal end 136 of the second flange member 134 and the distal end 152 of the third flange member 150 will at least partially open as a gap between the distal ends 136, 152, as will be further described below. Nevertheless, despite this gap, in the partially fully engaged

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position the lumen 140 remains generally closed because the first flange member 130 has a length sufficient to still extend across the gap (in the substantially re-closable opening) between the respective distal ends 136, 152 and to extend further over (and in releasable contact with) substantial remaining portions of the second flange member 134.

[052] In some embodiments, the respective flange members 130, 134, 150 are configured with a relative thickness, shape, and sufficient flexibility (in the resilient materials forming them) such that a force that would cause the cuff electrode 109 to expand to a larger diameter size is less than the capillary blood flow pressures in the vessels along the nerve. In one aspect, this arrangement ensures that the cuff electrode 100 will not restrict blood flow to the nerve.

[053] FIG. 6 is a sectional view of the expandable cuff of FIG. 5 in an intermediate open position, according to an embodiment of the present disclosure. As illustrated in FIG. 6, during positioning of the electrode cuff 100 over the desired nerve so that the nerve can be properly located within the lumen 140, the electrode cuff 100 is advanced from the fully engaged position shown in FIG. 5, to an intermediate open position shown in FIG. 6. In this intermediate position, beginning with distal end 132, the first flange member 130 is pulled in a first direction (represented by arrow A) away from the second side wall 128 of base portion 120 and away from the second flange member 134 to cause the distal end 132 of the first flange member 130 to extend generally outward in an opposite direction from the first side wall 126 of the base portion 120. As a result, when the electrode cuff 100 is in the intermediate open position, the first flange member 130 is positioned so as to not extend over (e.g. above and spaced apart from) the top wall 122 of the base portion 320. However, in this position, the lumen 140 remains generally closed because the second flange member 134 remains positioned to extend over the top wall 122 of the base portion 120, with the distal end 136 of the second flange member 134 terminating adjacent to the distal end 152 of the third flange member 150. Finally, when the cuff 100 is in the intermediate open position of FIG. 6, the inner side wall 144 of

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the first flange member 130 is no longer positioned over and adjacent to the outer side wall 146 of the second flange member 134.

[054] FIG. 7 is a sectional view of the expandable electrode cuff of FIG. 5 in a fully open position, according to an embodiment of the present disclosure. As illustrated in FIG. 7, once the electrode cuff 100 is in the intermediate open position, the distal end 136 of the second flange member 134 is moved away from the distal end 152 of the third flange member 150 in a second direction (opposite the first direction A in FIG. 6). With this maneuver, a majority of the second flange member 134 is rotated away from third flange member 150 (as represented by directional arrow R) to no longer extend over or above the top wall 122 or above the first side wall of the base portion 120. In this arrangement, the distal end 136 of the second flange member 134 extends outward in the opposite direction from the second side wall 128 of the base portion 120, resulting in the inner wall 142 of the second flange member 134 no longer forming the lumen 140 when the electrode cuff 100 is in the fully open position of FIG. 7. In addition, in this position, the large gap in the re-closable opening 109 defined between the distal ends 136, 152 of the respective second and third flange members 134, 150 facilitate installation of the cuff 100 about a nerve. Accordingly, when the electrode cuff 100 is in the fully open position, this configuration includes: (1) neither the first flange member 130 nor the second flange member 134 being positioned to extend over the top wall 122 of the base portion 120 of the electrode cuff 100; (2) the inner side wall 144 of the first flange member 130 no longer overlapping (or near) the outer side wall 146 of the second flange member 134; and (3) the inner side wall 141 of the second flange member 134 no longer defining the inner wall 142 of the lumen 140 (because the lumen 140 is temporarily deconstructed).

[055] In this way, by enabling the electrode cuff 100 to be advanced between the fully engaged position (FIG. 5), the intermediate open position (FIG. 6), and the fully open position (FIG. 7), the electrode cuff 100 can be more easily positioned over a nerve during implantation of the lead 80.

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[056] As can be seen in FIGS. 5-7, the second flange member 134 according to one embodiment has a first thickness (T1 at 160) along a proximal end 162 of second flange member 134 located adjacent the top wall 122 of the base portion 120 along the second side wall 128, and has a second thickness (T2 in FIG. 7), less than the first thickness (T1 at 160), at the distal end 136 of the second flange member 134. In this arrangement, the second flange member 134 is tapered in thickness from the proximal end 162 to the distal end 136. Similarly, the third flange member 150 has a first thickness (T3 at 164 in FIG. 5) along a proximal end 166 located near the top wall 122 of the base portion 120 along the first side wall 126, and a second thickness (T4 in FIG. 7), less than the first thickness 164, at the distal end 152 of the third flange member 150. In this arrangement, the third flange member 150 is tapered in thickness from the proximal end 166 to the distal end 152. While the inner flange member 134 of FIGS. 5-7 is shown to be tapered, it is understood that the inner flange member 134, inner flange member 150, and/or the outer flange member 130 could be formed without being tapered. As described above, with the proximal portion 162 of the second flange member 134 being substantially less flexible than the distal end 136, the second flange member 134 is biased to maintain the curved shape defining lumen 140 while still permitting selective opening of the re-closable opening 109 via maneuvering the distal end 136 relative to the third flange member 150.

[057] In one embodiment, the flange members 130, 134, 150 described above are formed from polyurethane, silicon or a blend of polyurethane and silicon. Furthermore, according to some embodiments, one of the flange members could be formed of polyurethane while the other is formed of silicon. If formed from silicone, then the durometer of the flange material range would be within a range of approximately 40A – 70A. In some embodiments, the thickness of the flange material would be from approximately 0.005 inches to 0.025 inches. Nominally, if the flange is formed of a polyurethane material having a durometer of approximately 85A, the flange would be 0.0075 inches thick. In the embodiment of FIGS. 5-7, the inner flanges 134, 150 are formed from molded polyurethane

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and the outer flange 130 is formed from a portion of a polyurethane tubing. In either embodiment, the polyurethane is formed to have a "memory" that enables the flange members to be biased towards the fully engaged positioned. In some embodiments, the lumen 140 will have an inner diameter between 0.050 and 0.400 inches, while according to one embodiment, the inner diameter is approximately 0.140 inches in the fully engaged position.

[058] If the inner flange members 134, 150 are tapered, their respective proximal portion 162, 166 have a thickness of approximately 0.025 to 0.030 inches, and their respective distal ends 136, 152 have a thickness of approximately 0.001 to 0.010 inches. In addition to the features described above, in one embodiment, by providing a relatively thicker base or proximal end, this arrangement provides a strong mechanical connection relative to the base portion 120 and also provides the needed thickness to hold, and provide strain relief, for the electrodes 103. According to one embodiment, the distal end 136 of second flange member 134 has a thickness of about 0.005 inches. Similarly, in one embodiment, the distal end 152 of the third flange member 150 has a thickness of about 0.005 inches.

[059] FIG. 8 is a sectional view of the expandable electrode cuff of FIG. 5 in an intermediate open position, according to an embodiment of the present disclosure. As illustrated in FIG. 8, depending upon the circumference of the nerve, the nerve will become positioned over the top wall 122 of the base portion 120 of the electrode cuff 110, adjacent to the third flange member 150, and against body portion 111 of electrode 103 at the proximal portion 162 of second flange member 134. Accordingly, once the second flange member 134 is positioned about the nerve during the advancement of the electrode cuff 100 from the fully open position of FIG. 7 to the intermediate open position, then the distal end 136 of the second flange member 134 will be positioned to be spaced further above the proximal end 131 of the first flange member 130 and the distal end 152 of the third flange member 150 (than when the electrode cuff 100 is in the intermediate open position of FIG. 6). This arrangement results in a

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substantial gap forming in the re-closable opening 109. In this way, the size of the lumen 140 can be increased relative to when the electrode cuff 100 is in the intermediate open position of FIG. 6 to accommodate the size of the nerve during positioning of the electrode cuff 100.

[060] FIG. 9 is a sectional view of the expandable electrode cuff of FIG. 5 in a fully engaged position, according to an embodiment of the present disclosure, when cuff 100 is deployed on a larger diameter nerve as noted in association with FIG. 8. Similarly, during the advancement of the electrode cuff 100 from the intermediate open position of FIG. 8 to the fully engaged position during implant of the electrode cuff 100, first flange member 130 is allowed to return, via the biasing action, to its at-rest configuration to extend coextensively with (and in releasable contact with) the second flange member 134 and also cover the re-closable opening 109. Moreover, the distal end 132 of the outer flange member 130 may be positioned along the outer side wall 146 of the second flange member 134 to be spaced further away from the second side wall 128 than when the electrode cuff 100 is in the fully engaged position of FIG. 5, and to be above, rather than below the top wall 132 of the base portion 120 (as in FIG. 3). As a result, the diameter of the lumen 140 is increased relative to when the electrode cuff 100 is in the fully engaged position of FIG. 5 prior to being implanted, to accommodate the size of the nerve. Therefore, as illustrated in at least FIGS. 8-9, in order to accommodate the size of the nerve, the first flange member 130 and second flange member 134 are movable in oppositely-oriented directions to allow an increase in the diameter of the lumen 140.

[061] FIG. 10 is a sectional view of the expandable electrode cuff of FIG. 5, according to an embodiment of the present disclosure. As illustrated in FIG. 10, according to one embodiment, in order to address the effects of swelling of the hypoglossal nerve that may sometimes occur, particularly after the initial trauma associated with implanting the electrode cuff 100, the first and second flange members 130 and 134 are expandable so that the circumference of the lumen 140 formed by the electrode cuff 100 can be increased to accommodate

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increases in the diameter of the nerve that occur subsequent to the initial positioning of the expandable electrode cuff 100 about the nerve, as illustrated in FIG. 9. For example, during swelling of the nerve subsequent deploying the electrode cuff 100 about the nerve and implanting the rest of the lead 80, the first flange member 130 and the second flange member 134 slidably move in opposite directions relative to each other as lumen 140 expands to accommodate the increased diameter of the nerve. During this expansion, the distal end 132 of the first flange member 130 becomes positioned to be spaced further away from the second side wall 128 of the base portion 120, and to be even further above, rather than below, the top wall 122 of the base portion 120 than when the electrode cuff 100 was initially positioned about the nerve to the position illustrated in FIG. 9. At the same time, during this expansion of lumen 140, the second flange member 134 rotates away from the third flange member 150 such that the distal end 136 of the second flange member 134 becomes positioned to be spaced further above the distal end 152 of the third flange member 150, and to be further away from the first side wall 126 and the top wall 122 of the base portion 120, thereby further increasing the size of the lumen 140 to accommodate the swelling. As a result, there is a further increase in the size of the gap of re-closable opening 109. Nevertheless, as illustrated in FIG. 10, with first flange member 130 still covering (i.e., extending across) this re-closable opening 109, closure of lumen 140 about the nerve is maintained so that contact is maintained between the body portion 111 of electrodes 103 and the nerve, yet without placing undue pressure on the nerve. As the swelling of the nerve subsides some period of time after implanting the lead 80 and cuff 100, the first and second flange members 130 and 134 return towards the original fully engaged position about the nerve that occurred during positioning of the electrode cuff 100 at the time of implant of the lead 80 and electrode cuff 100, such as is illustrated in FIG. 9.

[062] By forming the first and second flange members 130, 134, described above, to extend over the base member 120 so that each of the flange members 130, 134 extend from a proximal end (e.g., 131 and 162, respectively) located on

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one side of the base member to a distal end (e.g., 132 and 136, respectively) located along the other side of the base member, the electrode cuff will continue to be positioned completely around the nerve. This overlapping, slidably movable relationship between the first flange member 130 and the second flange member 134 and the overlapping relationship between the first flange member 130 and the third flange member 150 prevents open gaps from being formed between the distal ends 136, 152 of the respective flange members 130, 134, 150 as the nerve swells. Rather, the first and second flange members 130, 134 described above enable the expansion of the flange members, as warranted, to accommodate increasing the diameter of the lumen 140 in order to maintain enclosure of the nerve within the lumen. In this way, using the electrode cuff 100 described above, the opportunity for a portion of the nerve to become displaced external to the lumen 140 is minimized because the electrode cuff 100 is able to more effectively accommodate such swelling of the nerve.

[063] In general terms, the interrelationship between a combination of the first flange member 130, second flange member 134, and third flange member 150 provides an electrode cuff that remains securely engaged about a nerve but that also automatically adjusts its diameter to accommodate a swollen nerve or nerves that have a larger diameter. In one aspect, this combination of the respective interacting flange members 130, 134, 150 achieves the secure fixation and automatic adjustability of the electrode cuff 100 without using a clamp, buckle, hinge/pin found in conventional electrode cuffs. Rather, the spatial arrangement and selective overlapping relationship between the respective flange members, as well as the resilient (e.g., configured to generally maintain or return to a pre-formed shape) material forming those flange members and the tapered configuration of the respective flange members 134, 150, enables the electrode cuff 100 to provide the secure fixation and/or automatic sizing adjustment (i.e., both the expandability and the contraction to a minimum diameter) that maintains efficacious nerve contact while minimizing undue pressure on the nerve.

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[064] FIG. 11 is a sectional view of an expandable electrode cuff 260, according to an embodiment of the present disclosure. In one embodiment, this expandable electrode cuff 260 comprises substantially the same features and attributes as the electrode cuff 100 that was previously described in association with FIGS. 5-10, except for the presence of a recess 270 in an inner wall portion 142 of the lumen 140 and the recessed position of a body portion 282 (like body portion 111 in FIG. 5) of an electrode 280 embedded within the cuff body 101. In addition, in some embodiments, instead of having a distal hook portion 112 as in the cuff 100 of FIGS. 5-10, electrode 280 omits a distal hook portion. However, at its proximal end, the electrode 280 does not terminate with the proximal base portion 284 (like proximal base portion 110 in FIG. 5). Instead, as illustrated in FIG. 11, the electrode 280 additionally includes a lateral portion 286 that extends laterally and generally perpendicular to the proximal base portion 280 in a direction generally opposite from the direction in which the body portion 282 extends laterally outwardly from the proximal base portion 280.

[065] In one aspect, the configuration of the body portion 282 and the lateral portion 286 being at opposite ends of the base portion 284, and extending outwardly in opposite directions relative to the base portion 284, provides a multi-directional shape that anchors electrode 280 securely relative to the base portion 120 and second flange member 134 of cuff 100 upon molding the cuff 100 about the electrode 280.

[066] It is also understood that in some embodiments, the configuration of the electrode 280 in the embodiment of FIG. 11 can be substituted for the electrode 103 in the embodiments of FIGS. 5-10, whether the recess 270 is present or absent.

[067] FIGS. 12-13 are sectional views of expandable electrode cuffs 300, 400, according to some embodiments of the present disclosure. In one embodiment, the respective electrode cuffs 300, 400 include at least substantially the same features and attributes of the electrode cuff 100 as previously described in

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association with FIGS. 5-10, except for modifying the relative lengths of the second flange member and the third flange member and for modifying a length and position of a first flange member relative to the base portion of the electrode cuff 300.

[068] As illustrated in FIGS. 12, electrode cuff 300 includes a second flange member 334 that is generally shorter (than the second flange member 134 of FIG. 5) and a third flange member 350 that is generally longer (than the third flange member 150 in FIG. 5) such that a point of releasable contact (such as the re-closable opening 139) between the respective distal ends 336, 352 of these flange members is generally spaced farther above the top wall 122 of base portion 120. In one non-limiting aspect, by providing a different point (in comparison to the cuff 100 of FIG. 5) of re-closable opening 309 for the second flange member 334 and the third flange member 350 to provide access to lumen 140, electrode cuff 300 provides a configuration that may be more suitable to deployment in different anatomical environments than electrode cuff 100 and/or that is more suitable to modified deployment techniques to engage a target nerve. It will be understood that at the time of construction one can select the relative lengths of the second and third flange members 334, 350 to effectively select the point of releasable contact via re-closable opening 309 between the distal ends 336, 352 of the second and third flange members 334, 350 at many desired location within along the circumference of the lumen 140.

[069] In addition, in some embodiments, the length of the first flange member 330 is increased (in comparison to a length of first flange member 130 in FIG. 5) so that the distal end 332 of the first flange member 430 terminates along the first side wall 126 instead of terminating along a proximal end 162 of second flange member 134 as in embodiment of FIG. 5. Accordingly, in this arrangement, extending from its proximal end 331, the first flange member 334 extends alongside the third flange member 350, around the entire second flange member 334, along the second side wall 128 and bottom wall 124 of the base portion 120

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before terminating along the first side wall 126 of base portion 120. In this releasably secured position, the distal end 332 of first flange member 330 is located below, and spaced apart from, the proximal end 331 of the first flange member 330.

[070] As illustrated in FIG. 12, in some embodiments, the first flange member 330 is pre-formed to include a transition region 335 configured to substantially match the contour of the transition between the second flange member 334 and the second side wall 128 of the base portion 120. This arrangement facilitates maintaining releasably secure contact of the first flange member 330 against the second flange member 334 and base portion 120. Moreover, in some embodiments, the first flange member 330 also is pre-formed to include a distal cap region 333 configured to substantially match the generally arcuate contour of the bottom wall 124 of the base portion 120 (as it extends between first side wall 126 and the second side wall 128). This arrangement facilitates maintaining releasably secure contact of the first flange member 330 against the base portion 120. Accordingly, the extra length and pre-formed shape of the first flange member 330 provides a more secure arrangement in which the distal end 331 of first flange member 330 cannot be automatically, slidable movable relative to the second flange member 334.

[071] However, it is understood that the extra length of the first flange member 330 can be provided as shown in FIG. 12 without requiring that the transition region 335 and the distal cap region 333 be pre-formed to match the contour of the reciprocating shape portions of the base portion 120 or the second flange member 334.

[072] FIG. 13 is a sectional view of an electrode cuff 400, according to an embodiment of the present disclosure. In one embodiment, electrode cuff 400 includes substantially the same features and attributes as the embodiment of FIG. 12, except for the differences noted below in association with FIG. 13. As

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illustrated in FIG. 13, according to another embodiment, the length of a first flange member 430 is increased even further so that instead of the distal end 332 of the first flange member 330 (as in FIG. 12) terminating along first side wall 126, the distal end 432 of the longer first flange member 430 terminates alongside a portion of the third flange member 450 and the first flange member 430. In this arrangement, a distal portion 433 of first flange member 430 overlaps a proximal portion 445 of the first flange member 430 so that the distal end 432 of the first flange member 430 is positioned above the proximal end 431 of the first flange member 430. In another aspect, as illustrated in FIG. 13, the first flange member 430 does not include one or more pre-formed regions that substantially match the contour of the base portion 120, as was previously described in association with some embodiments of the electrode cuff 300 of FIG. 12. Nevertheless, the relatively longer distal portions of the first flange member 430 that extend beyond the first side wall 126 of base portion still exert and provide a more secure fixation of the electrode cuff 400 so that electrode cuff 400 provides greater resistance to and/or generally prevents automatic expansion of lumen 140, as can occur more readily with the embodiment of FIG. 5 in which the first flange member 130 has a generally shorter length (and which thereby provides less frictional resistance).

[073] FIG. 14 is a perspective view of an electrode cuff 500, according to an embodiment of the present disclosure. In one embodiment, while the electrode cuff 500 includes a differently configured electrodes 503 and differently configured flange members 534, 550, it will be understood that the electrode cuff 500 includes substantially the same choice of materials for the electrodes and flange members, and is molded ~~is~~ in generally the same manner, as previously described in association with FIGS. 5-13 (unless noted otherwise).

[074] As illustrated in FIG. 14, electrode cuff 500 comprises an elongate cuff body 501 that includes at least a base portion 520, second flange member 534 and the third flange member 550. It will be understood that while electrode cuff

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500 generally includes a first flange member 530 as shown in FIG. 15, FIG. 14 omits this first flange member 530 for illustrative clarity to better depict the second and third flange members 534, 550. The base portion 520 includes a bottom wall 524, first side wall 526, and second side wall 528, and top wall 522. However, in some embodiments, the top wall 522 includes a ridge or protrusion 523 that covers a central portion of the electrode 503. As illustrated in FIG. 14, the protrusion 523 generally extends a length of the cuff body 501.

[075] As illustrated in FIG. 14 and the sectional view of FIG. 15, the second and third flange members 534, 550 are generally symmetrical in size and shape such that the proximal portions 537 of these respective flange members 534, 550 extend generally outward and upward in opposite directions from base portion 520. Because each flange member 534, 550 includes a generally arcuate concave shape to partially form lumen 540, the distal portions 571 of the respective flange members 534, 550 curve slightly inward such that their respective distal ends 536, 552 are oriented toward a point a convergence. However, in this embodiment, a large gap 539 (identified in FIG. 15) remains between the distal ends 536, 552 of the respective flange members 534, 550.

[076] In one aspect, electrode cuff 500 includes a first flange member 530 having a proximal end 531 that is secured to an outer surface of second flange member 534 with a remaining portion of the first flange member 530 (extending to an unsecured distal end 532) being in releasable contact against a distal portion 571 of the second flange member 534 and against both a distal portion 571 and proximal portion 537 of the third flange member 550. In a manner substantially similar to that described for the embodiment of FIGS. 5-10, access to a lumen 540 is provided via temporarily maneuvering the first flange member 530 away from the third flange member 550 and away from the distal portion 571 of the second flange member 534 (with the proximal end 531 remaining fixed against second flange member 534) to enable placing the cuff 500 onto a target nerve such that the nerve occupies lumen 540. Thereafter, the first flange

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member 530 is returned to the position shown in FIG. 15, thereby placing the electrode cuff 500 in a fully engaged position or configuration. In this position, the combination of the first flange member 530 with the second flange member 534 and third flange member 550 provides a re-closable opening 539.

[077] In one aspect, in a manner substantially similar to the embodiment of FIG. 5, because the first flange member 530 is slidably movable (and in releasable contact with) relative to the outer surface of the second flange member 534 and the third flange member 550, electrode cuff 500 is automatically adjustable to have an increased diameter of its lumen 540 in response to a larger size nerve or swelling of the nerve enclosed within the lumen 540.

[078] In one aspect, as illustrated in FIG. 14, the electrode cuff 500 includes an array 502 of electrodes 503 spaced apart along a length of the cuff body 501. As best seen in the sectional view of FIG. 15, each electrode 503 forms a generally wishbone cross-sectional shape. It will be understood that in some embodiments, in a manner substantially similar to that previously described in association with FIGS. 3-5, the respective electrodes 503 are electrically connected to lead 80 (FIGS. 3-4) via a coil or other conductive component that extends through a length of the base portion 520. In general terms, the electrodes 503 are formed of a conductive material and are sized and shaped to permit flexible bending of the fingers 504 of the respective electrodes 503 as the respective flange members 534, 550 (in which the electrodes 503 are embedded) are maneuvered to deploy the electrode cuff 500 on a target nerve. In one embodiment, the electrodes 503 are formed of a platinum-iridium material like that of electrodes 501 except with the electrodes 503 having a thickness and width suited to permit limited, flexible bending of the fingers 504 of the electrodes 503 as the respective flange members 534, 550 are maneuvered to deploy electrode cuff 500.

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[079] In one aspect, electrode 503 includes a generally U-shaped base portion 508 that defines a recess 509. The respective fingers 504 extend generally outward and upward, from a distal transition region 510 of the base portion 508, in generally opposite directions from each other, as illustrated in FIG. 15. When the electrode 503 is present during molding of the cuff body 501, material fills in the recess 509 of the U-shaped base 508 as the electrode 103 becomes embedded within the base portion 520 of cuff body 501 and embedded within the distal portions 571 of the respective second and third flange members 534, 550. In this arrangement, the electrode 503 is anchored in at least a three-point configuration including a first anchor point at the base portion 520 and two other anchor points at each of the respective distal portions 571 on opposite sides of the cuff 500. In one aspect, this three point anchor configuration forms a triangular shape pattern in which the first anchor point (at base portion 520) is located on an opposite side of lumen 540 from the two other anchor points (at distal portions 571) while the two other anchor points (at distal portions 571 are located on opposite sides of the lumen 540 as well. Accordingly, this three point anchor configuration provides great stability to the embedded position of the electrode 503 within the cuff body 501.

[080] As further illustrated in FIGS. 14-15, the distal portions 571 of second flange member 534 and third flange member 550 are generally tapered such that distal ends 536, 552 are slightly narrower than the wider trunk portions 570 of distal portions 571. Moreover, the generally wider trunk portions 570 are molded to embed distal ends 505 of each finger 504 of an electrode 503 within a recess 572 of the respective second, third flange members 534, 550. In one aspect, by itself, this arrangement acts to prevent delamination or separation of the fingers 504 from the respective second and third flange members 534, 550. However, this arrangement also acts in cooperation with the protrusion 523 and its proximal plug portion 525 (that fills recess 509), which also prevents separation of or delamination of the base 508 of electrode 503 from the base portion 520 of cuff 500. As illustrated in FIG. 15, the portion of each finger 504 of electrode 503 that

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extends proximally from the trunk portion 570 of each flange member 534, 550 is exposed to lumen 140 for contact against a nerve.

[081] In another aspect, like the embodiment of FIG. 5, the arcuate length of each separate finger 504 of the electrode 503 generally corresponds to a 45 degree arc of lumen 540 (as represented by arc β). With this arrangement, a sufficient surface area of electrode 503 is available for contact with the nerve while the degree or amount of bending of the fingers 504 is sufficiently limited to substantially minimize fatigue failure of portions of the electrode 503.

[082] As illustrated in FIG. 16, in one embodiment, the electrode cuff 500 of FIGS. 14-15 is modified to provide a first flange member 580 having an increased length (as compared to the length of the first flange member 53o) in a manner substantially similar to that previously described for first flange member 330 in association with FIG. 12. Accordingly, the first flange member 580 includes substantially the same features and attributes as the first flange member 330 (FIG. 12), such as including a transition region 535 and a distal cap region 533 that are pre-formed to substantially match a contour of the base portion 520 of the cuff 500 at bottom wall 524 and at a transition between third flange member 552 and the first side wall 126 of base portion 120.

[083] FIG. 17 is a sectional view of electrode cuff 600, according to one embodiment of the present disclosure. As illustrated in FIG. 17, electrode cuff 600 comprises substantially the same features and attributes as electrode cuff 500 of FIGS. 14-15, except for including a second flange member 634 having an increased length to substantially reduce the gap in re-closable opening 539 of cuff 500. Accordingly, for electrode cuff 600, the distal ends 636, 652 of the respective second and third flange members 634, 650 are in close proximity to (or releasably contact) each other to form re-closable opening 639. In this arrangement, there is even greater security of maintaining the integrity of lumen 540 about a target nerve because the large gap associated with re-closable

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opening 539 has been eliminated. In order to deploy electrode cuff 600, after temporarily pulling back the releasable portions of the first flange member 630 from second flange member 634 (with the proximal end 631 remaining fixed against the third flange member 650), the distal end 636 of the second flange member 634 is maneuvered away from the distal end 652 of the third flange member 650 to provide access to lumen 540.

[084] In one aspect, in a manner substantially similar to the previously described embodiments, the electrode cuff 600 is securable about a nerve with the first flange member 630 being slidably movable (and in releasable contact) relative to the second flange member 634 and the second flange member 634 is rotatable away from the third flange member 650 to provide automatic expansion of the lumen 540 while maintaining closure of the lumen 540 and contact of electrode 503 against the nerve, yet without placing undue pressure on the nerve.

[085] FIG. 18 is a sectional view of an electrode cuff 700, according to an embodiment of the present disclosure. As illustrated in FIG. 18, electrode cuff 700 comprises substantially the same features and attributes as electrode cuff 600, except having a modified distal ends 636A, 652A of respective second and third flange members 634A, 650A that are beveled and that releasably mate in a reciprocal manner to form re-closable opening 739. In this arrangement, the reciprocating beveled distal ends 636A, 652A facilitates releasable contact or engagement between those respective distal ends 636A, 652A, which in turn, helps to maintain the electrode cuff 700 in the fully engaged position.

[086] FIG. 19 is a sectional view of an electrode cuff 750, according to an embodiment of the present disclosure. As illustrated in FIG. 19, electrode cuff 750 comprises substantially the same features and attributes as electrode cuff 700, except having a first flange member 680 with an increased length compared to first flange member 630. In this arrangement, first flange member 680

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comprises substantially the same features and attributes as first flange member 330 (as previously described in association with FIG. 12) and/or first flange member 580 (as previously described in association with FIG. 16). Accordingly, in this instance, the proximal end 681 of first flange member 680 is fixed relative to the third flange member 650A while the remainder of the first flange member 680 is in releasable contact against the second flange member 634A and a majority of the base portion 520, with the distal end 682 of the first flange member 680 being spaced apart, and positioned below, the proximal end 681 of the first flange member 680 on the same side of cuff 750 (i.e., both adjacent to the second side wall 528 of the base portion 520).

[087] FIG. 20 is a sectional view of an expandable electrode cuff 775, according to one embodiment of the present disclosure. In one embodiment, electrode cuff 775 includes substantially the same features and attributes as electrode cuff 500 of FIG. 15, except having a substantially longer first flange member 780 that is wrapped about the cuff body 501 in at least two layers. In particular, with the proximal end 781 of first flange member 780 fixed against second flange member 534, the remaining free portion of first flange member 780 is wrapped about cuff body 501 until the distal end 782 of the first flange member 780 overlaps the position of the proximal end 781. In one embodiment, the first flange member is pre-formed to have a shape substantially similar to that shown in FIG. 20, so that it is biased to generally maintain and/or to return to that shape after temporary manipulation into a different shape.

[088] As illustrated in FIG. 20, a first layer 790 of the first flange member 630 is in releasable contact with the distal portion 570 of the second flange member 534, the third flange member 550, and a bottom wall 524 of the base portion 120. As first flange member 780 makes releasable contact against the proximal end 781 of the first flange member 780. The first flange member 780 extends further distally from that point onward as a second layer 791, overlapping the first layer 790, until the distal end of the 782 of the first flange member 780 forms a partial

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third layer by again overlapping the proximal end 781 of the first flange member 780. In one embodiment, the first flange member 630 forms at least two complete layers in its position wrapped about a circumference of the cuff body 501 while in other embodiments, more than two or less than two layers can be formed by wrapping the first flange member 780 about the circumference of the cuff body 501 of the electrode cuff 775.

[089] FIG. 21 is a sectional view of an expandable electrode cuff 800, according to one embodiment of the present disclosure. In one embodiment, electrode cuff 800 includes substantially the same features and attributes as electrode cuff 700 of FIG. 18, except having a substantially longer first flange member 810 that has substantially the same features and attributes as the first flange member 780 of FIG. 20. With this arrangement, the combination of the reciprocating beveled distal ends 636A, 652A of the respective second and third flange members 634A, 650A and of the multilayer (at least two layers) first flange member 810 wrapped about the cuff body 501B provide a robust mechanism to ensure that the second and third flange members 634A, 652A will maintain capture of the nerve within lumen 140 despite long term placement of the cuff 800 within the body.

[090] Embodiments of the present disclosure ensure long term, robust engagement of an electrode against a nerve. In some embodiments, this robust engagement is accomplished while also accommodating swelling of a nerve or larger sized nerves via automatic expansion and contraction of the lumen defined by the electrode cuff via overlapping, slidably movable flange members comprising the electrode cuff.

[091] While at least one exemplary embodiment has been presented in the foregoing detailed description, it should be appreciated that variations exist. It should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope,

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applicability, or configuration of the present disclosure in any way. Rather, the foregoing detailed description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the present disclosure as set forth in the appended claims and the legal equivalents thereof.

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WE CLAIM:

1. An electrode assembly comprising:

an elongate cuff body including:

a base; and

a pair of resilient arcuate-shaped flange members that includes a second flange member and a third flange member, the respective flange members each including a proximal portion that extends from the base outwardly and away from the other respective proximal portion and a distal portion that extends toward the other respective distal portion, wherein the base and the two flange members define a lumen and wherein the distal portions define a substantially re-closable opening, and wherein both the flange members extend a length of the cuff body; and

a row of generally rigid electrode elements embedded within the cuff body and spaced apart from each other along the length of the cuff body.

2. The electrode assembly of claim 1 wherein each electrode element includes:

a generally arcuate first portion extending along an inner surface of at least one of the respective flange members to be exposed at the lumen, wherein the exposed first portion of the electrode element is located generally opposite the substantially re-closable opening of the cuff body; and

a generally straight second portion extending into the base and away from the first portion at a generally obtuse angle relative to the first portion.

3. The electrode assembly of claim 2 wherein the first portion of each electrode element has an arcuate length that generally corresponds to a 45 degree arc of the lumen.

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4. The electrode assembly of claim 3 wherein the obtuse angle is about 130 degrees.

5. The electrode assembly of claim 2 wherein the generally arcuate shape of the first portion substantially matches a radius of curvature of the inner surface of second flange member, wherein the first portion includes a distal hook portion extending generally away from the inner surface of the second flange member, and wherein the distal hook portion defines a recess that receives a molded portion of the cuff body to secure the respective electrode element relative to the cuff body.

6. The electrode assembly of claim 1, further comprising:

a first flange member including a first end secured to an outer surface of the second flange member and extending from the secured first end to overlap, and be in releasable contact with, a portion of the second flange member, the substantially re-closable opening, and the third flange member, wherein the first flange member terminates in a second end at a location over the third flange member,

wherein the second end of the first flange member is located generally opposite the substantially re-closable opening of the cuff body.

7. The electrode assembly of claim 6, wherein the first flange member has a length sufficient for the second end to extend distally beyond the third flange member and at least around a bottom wall of the base.

8. The electrode assembly of claim 6, wherein the first flange member has a length sufficient to wrap the first flange member at least two times about the circumference of the cuff body before the second end terminates at a position overlapping the first end of the first flange member.

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9. The electrode assembly of claim 6 wherein, in a fully engaged configuration of the electrode assembly, the first flange member is slidably movable relative to, and in releasable contact with, the second flange member such that at least a portion of the first flange member extends across and covers the substantially re-closable opening.

10. The electrode assembly of claim 9 wherein a diameter of the lumen defined by the electrode cuff body is automatically expandable, in response to an increasing diameter of a nerve in the lumen, via rotation of the distal portion of the second flange member away from the distal portion of the third flange member and via slidable movement of the first flange member relative to the second flange member with the first flange member having a length sufficient to maintain overlap with the substantially re-closable opening and with a majority of a length of the second flange member during the automatic expansion.

11. The electrode assembly of claim 1, wherein the second flange member has a length substantially greater than a length of the third flange member such that the substantially re-closable opening laterally relative to, and not directly opposite, the base.

12. The electrode assembly of claim 1 wherein the proximal portions of the respective second and third flange members have a thickness substantially greater than the respective distal portions, and wherein the thickness of the proximal portion of the second flange member is substantially greater than the thickness of the third flange member such that the relative thicknesses of the second and third flange members are asymmetric.

13. The electrode assembly of claim 12 wherein each respective electrode element is positioned within the proximal portion of the second flange member generally at a region of maximum thickness of the second flange member.

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14. The electrode assembly of claim 1 wherein the inner surface of the second flange member in the region of the first portion of the respective electrode elements is recessed relative to remaining portions of the inner surface of the second flange member.

15. The electrode assembly of claim 14 wherein the generally straight second portion extends generally parallel to a cross-sectional longitudinal axis of the base of the cuff body, wherein each electrode element further comprises a generally straight third portion extending within the base of the cuff body and outwardly from the second portion in a generally opposite direction from the first portion, and wherein the third portion is generally perpendicular to the second portion.

16. An electrode assembly comprising:

an elongate cuff body including:

a base; and

a pair of resilient arcuate-shaped flange members including a second flange member and a third flange member, the respective flange members each including a proximal portion that extends from the base outwardly and away from the other respective proximal portion and a distal portion that extends toward the other respective distal portion, wherein the base and the two flange members at least partially define a lumen and wherein the distal portions define an opening providing access to the lumen, and wherein both the flange members extend a length of the cuff body; and

a row of resilient electrode elements at least partially embedded within the cuff body and spaced apart from each other along the length of the cuff body.

17. The electrode assembly of claim 16, wherein each electrode element includes:

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a generally semi-circular first portion extending along an inner surface of the respective flange members and arranged to be exposed at the lumen, wherein the exposed first portion is located generally opposite the opening of the cuff body; and

a second portion generally extending outward and away from a midpoint of the first portion into the base.

18. The electrode assembly of claim 17, wherein the second portion of the electrode elements comprises a generally U-shaped portion defining a recess between two spaced apart legs and an apex pointing away from the first portion, wherein each respective leg is connected to and extends from the first portion.

19. The electrode assembly of claim 18, wherein the first portion defines a first segment and a second segment with the first and second segments extending outward and away in opposite directions from the second portion of the electrode element, each respective first and second segment connected a respective one of the legs of the generally U-shaped second portion, and wherein the first segment is exposed at the lumen along the second flange member and the second segment is exposed at the lumen along the third flange member, and wherein the second portion extends within the base of the cuff body.

20. The electrode assembly of claim 19, wherein the respective first and second segments, which are generally exposed along the inner surface of the respective second and third flange members, each have a distal end and the respective distal ends are embedded within the distal portion of the respective second and third flange members.

21. The electrode assembly of claim 19, wherein the cuff body comprises a protrusion that extends into the recess of the generally U-shaped second portion to embed the second portion within the base of the cuff body and that is exposed at the lumen.

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22. The electrode assembly of claim 17, further comprising:

a first flange member including a first end secured to an outer surface of the second flange member and extending from the secured first end to be in releasable contact with both a portion of the second flange member and the third flange member and to overlap the portion of the second flange member, the substantially re-closable opening, and the third flange member, wherein the first flange member terminates in a second end at a location over the third flange member.

23. The electrode assembly of claim 22 wherein the first flange member has a length sufficient for the second end to extend distally beyond the third flange member and at least around a bottom wall of the base of the cuff body.

24. The electrode assembly of claim 22, wherein the first flange member has a length sufficient to wrap the first flange member at least two times about the circumference of the cuff body before the second end terminates at a position overlapping the first end of the first flange member.

25. The electrode assembly of claim 22 wherein, in a fully engaged configuration of the electrode assembly, the first flange member is slidably movable relative to, and in releasable contact with, the second flange member such that at least a portion of the first flange member extends across and covers the substantially re-closable opening.

26. The electrode assembly of claim 25 wherein a diameter of the lumen defined by the electrode cuff body is automatically expandable, in response to an increasing diameter of a nerve in the lumen, via rotation of the distal portion of the second flange member away from the distal portion of the third flange member and via slidable movement of the first flange member relative to the second flange member with the first flange member having a length sufficient to

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maintain overlap with the substantially re-closable opening and with a majority of a length of the second flange member during the automatic expansion.

27. The electrode assembly of claim 26, wherein the distal portions of the respective second and third flange members are in releasable contact with each other.

28. The electrode assembly of claim 27, wherein the respective distal portions include reciprocating beveled ends.

29. The electrode assembly of claim 16, wherein the second flange member has a length substantially greater than a length of the third flange member such that the substantially re-closable opening is laterally relative to, and not directly opposite, the base of the cuff body.

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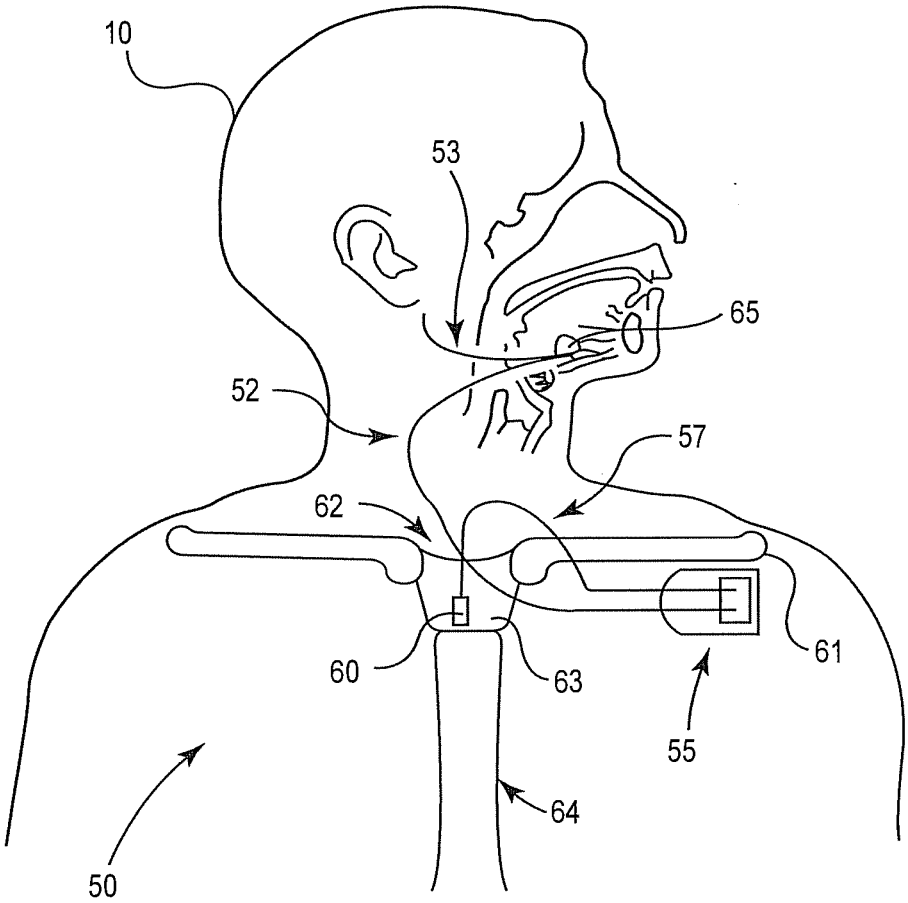


Fig. 1

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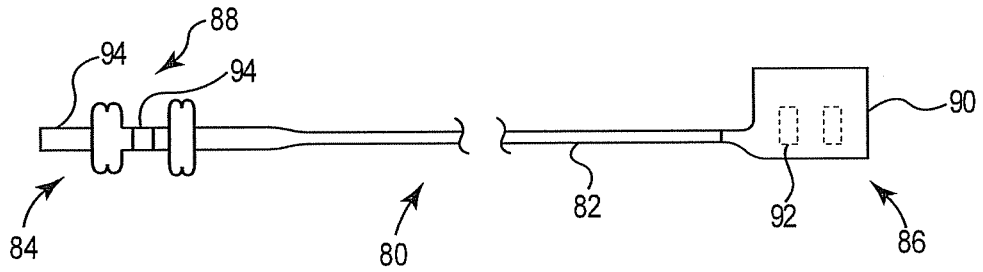

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Fig. 2

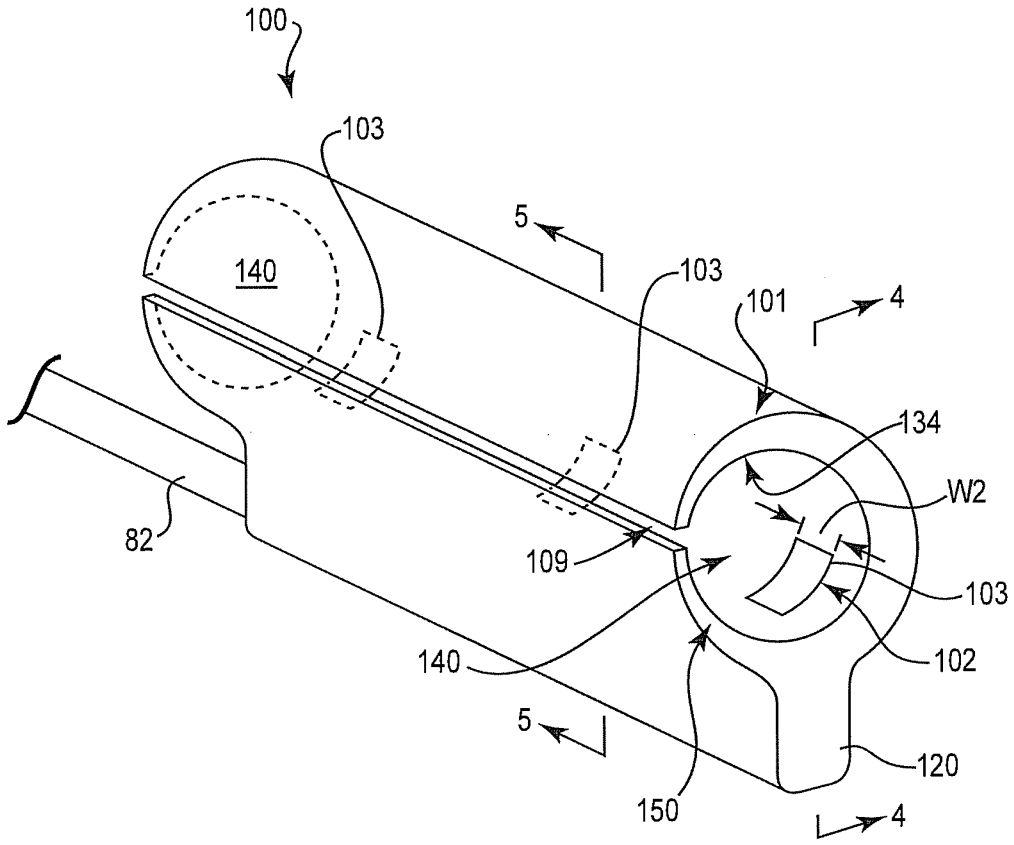

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Fig. 3

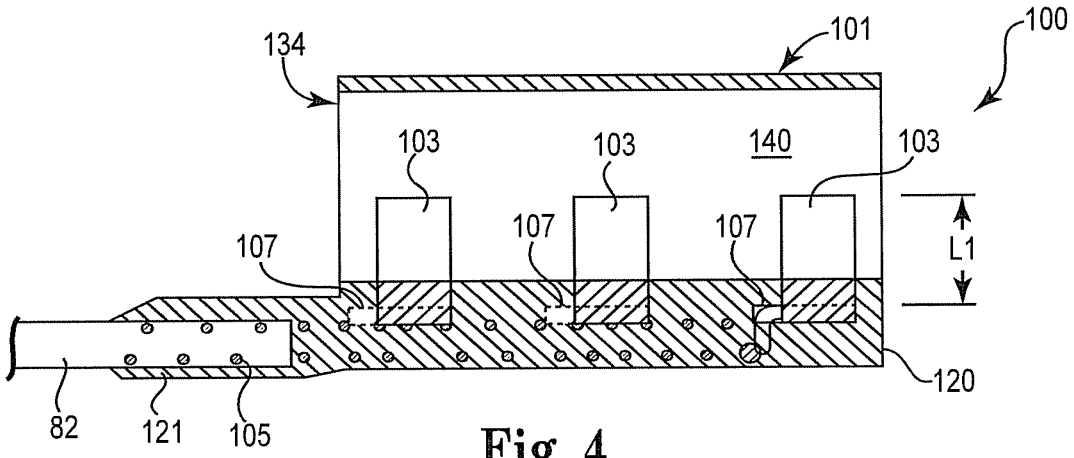

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Fig. 4

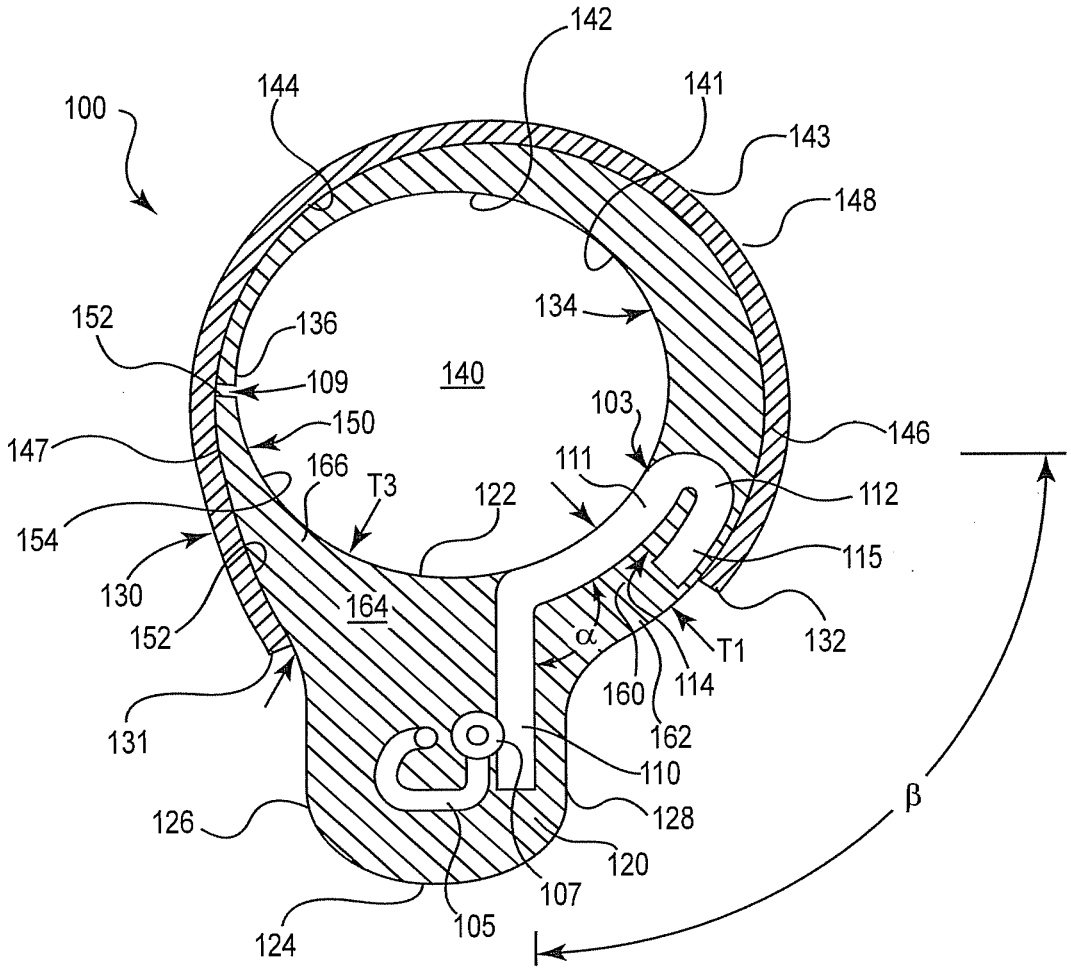

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Fig. 5

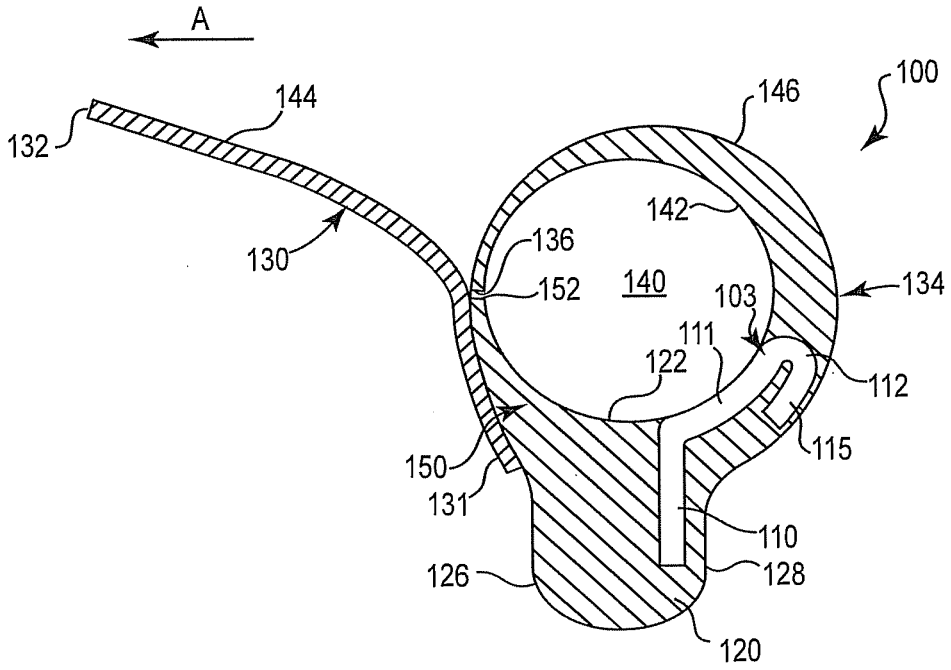

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Fig. 6

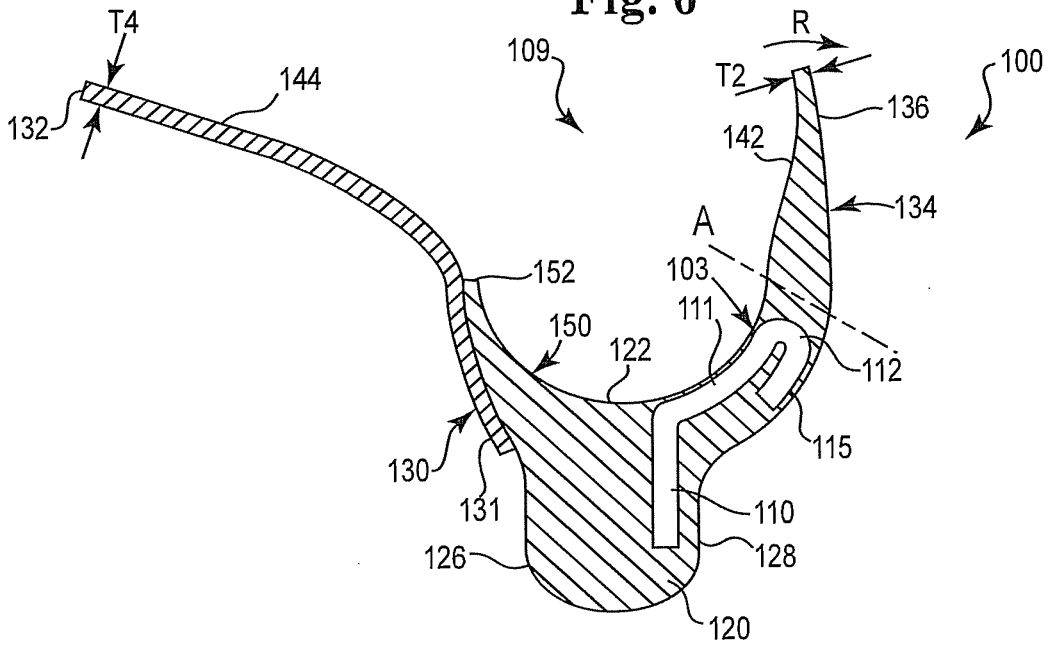

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Fig. 7

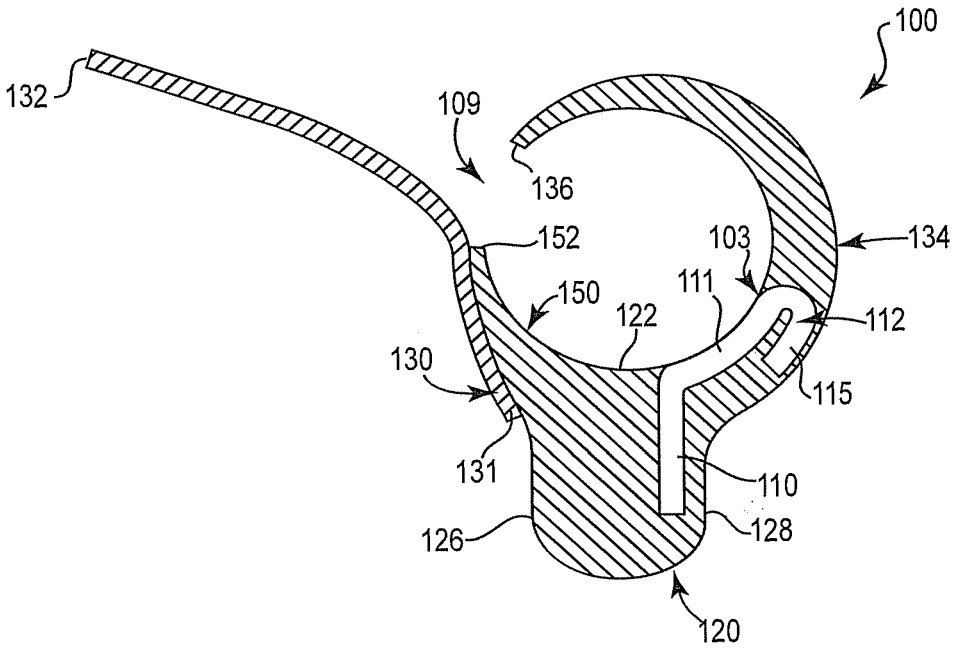

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Fig. 8

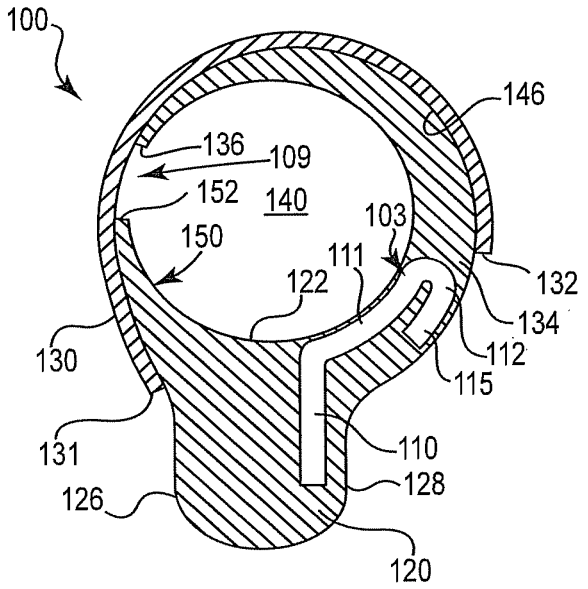

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Fig. 9

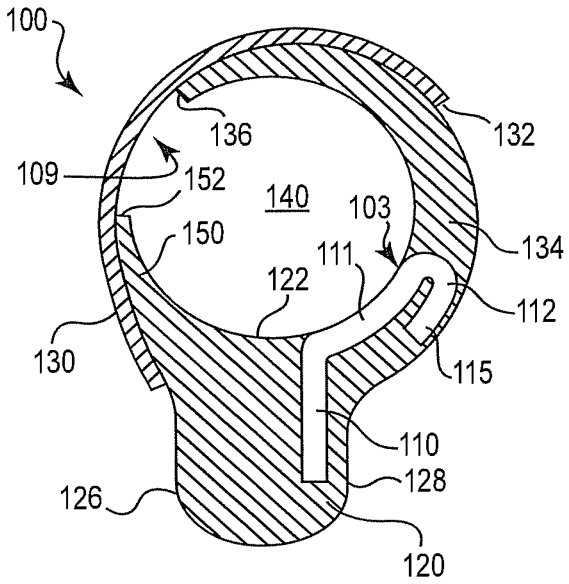

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Fig. 10

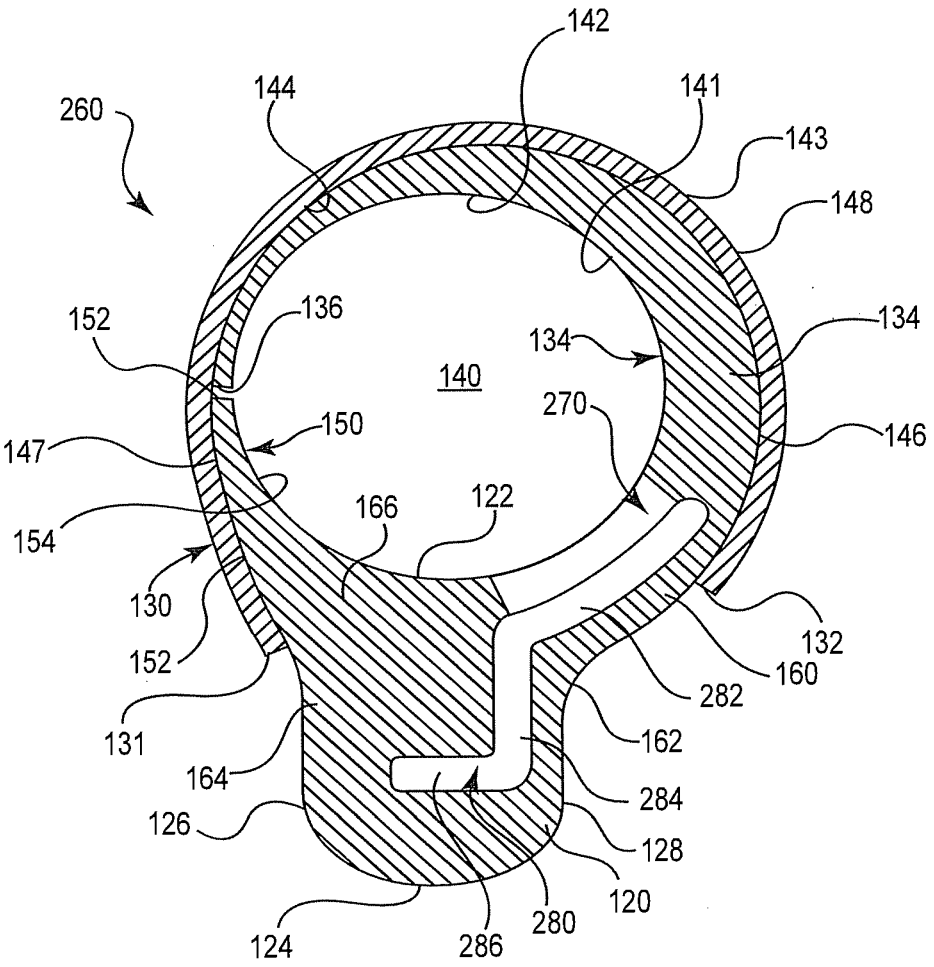

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Fig. 11

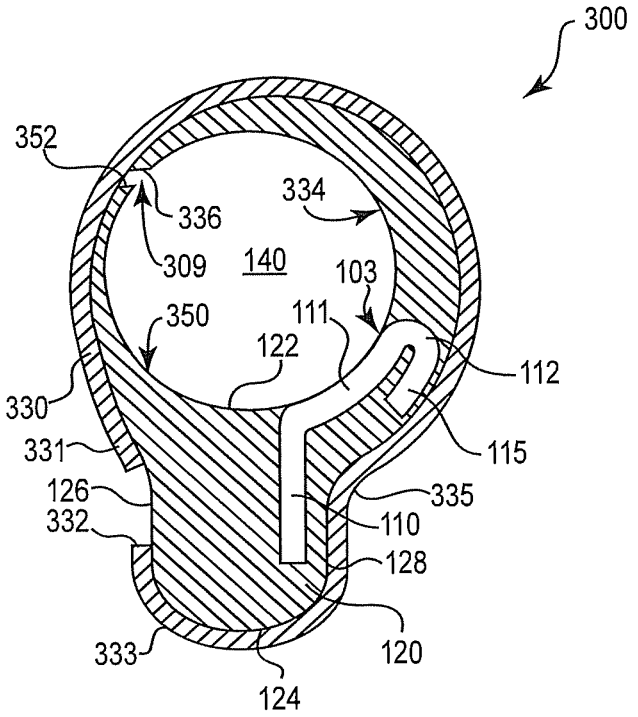

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Fig. 12

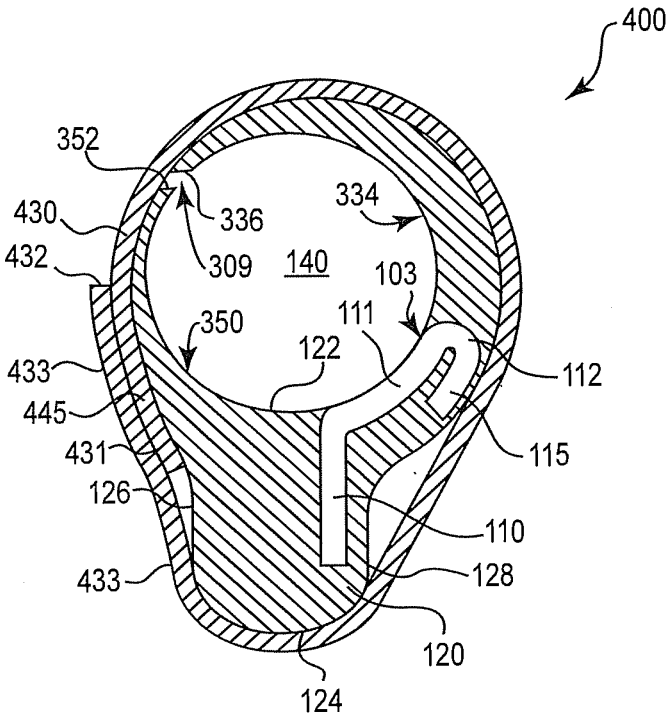

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Fig. 13

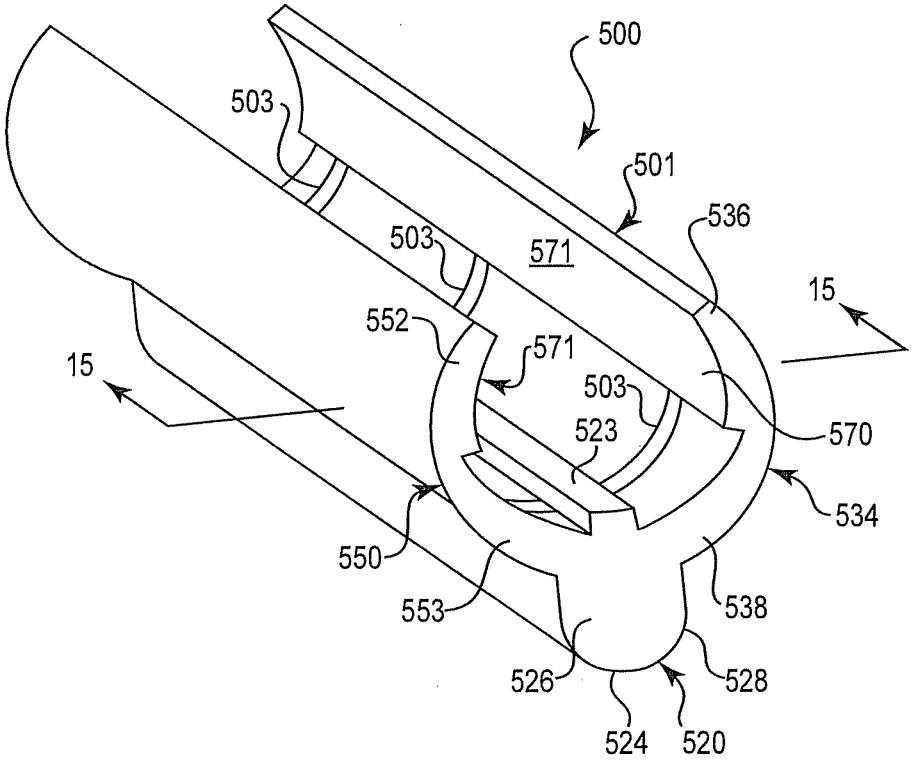

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Fig. 14

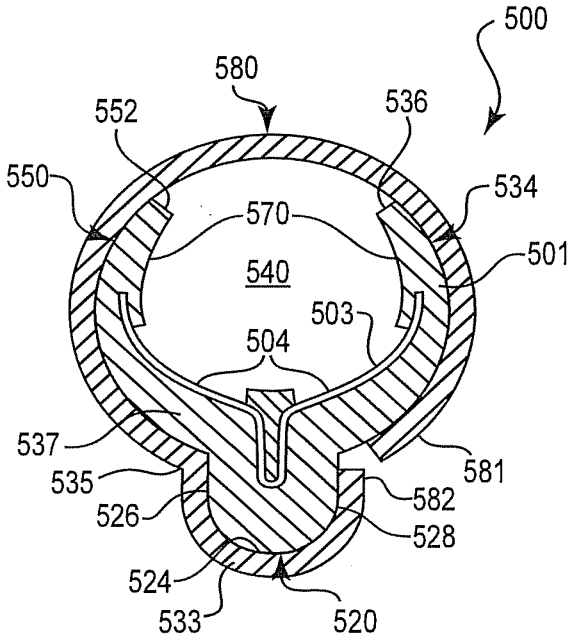

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Fig. 16

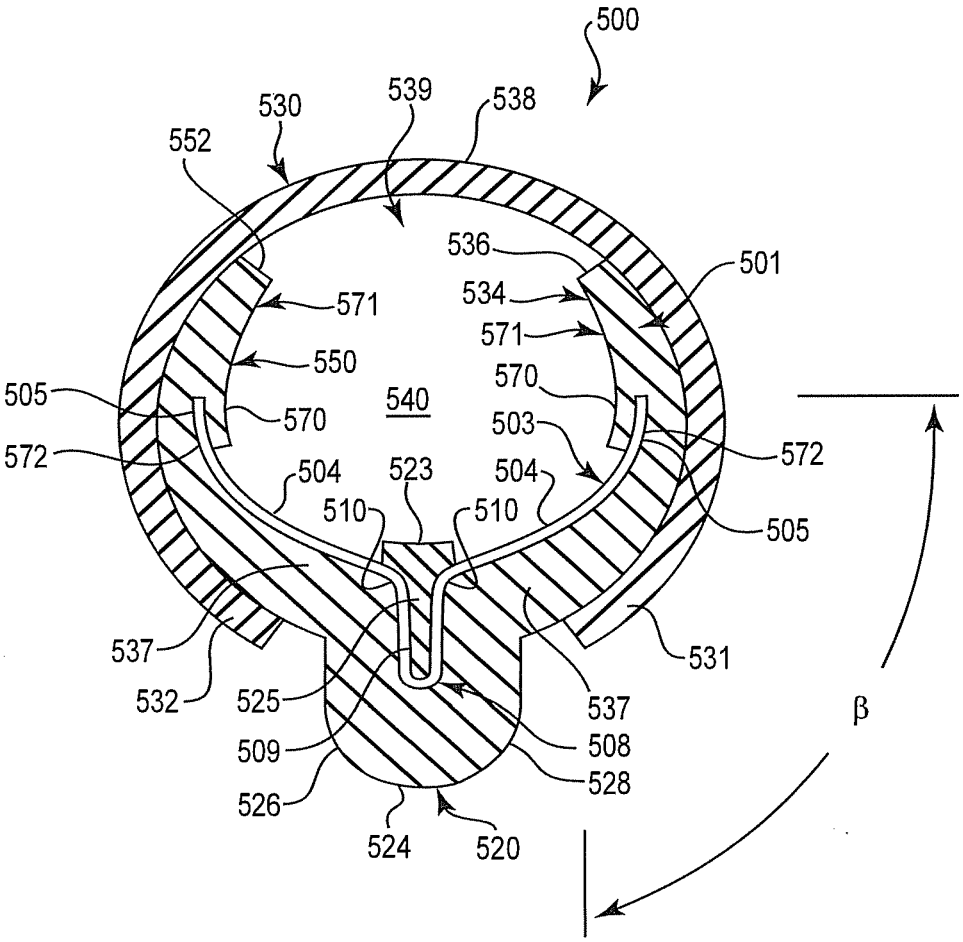

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Fig. 15

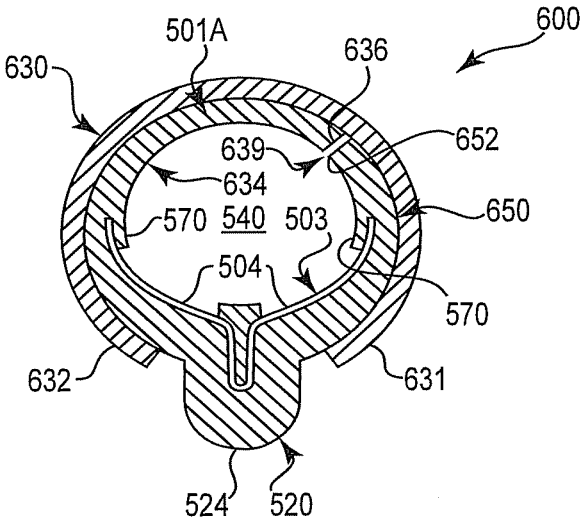


Fig. 17

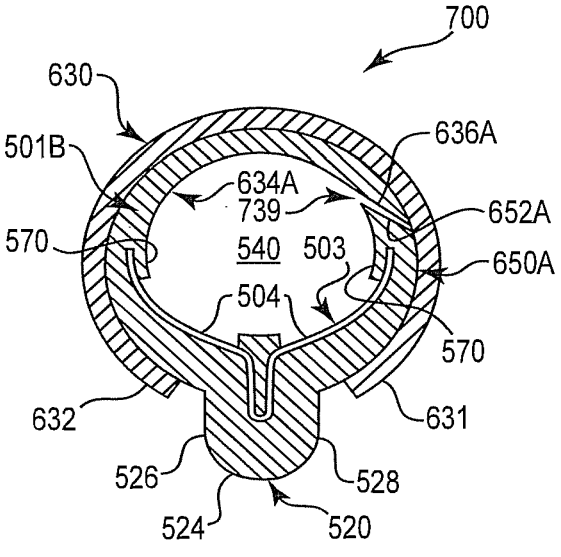


Fig. 18

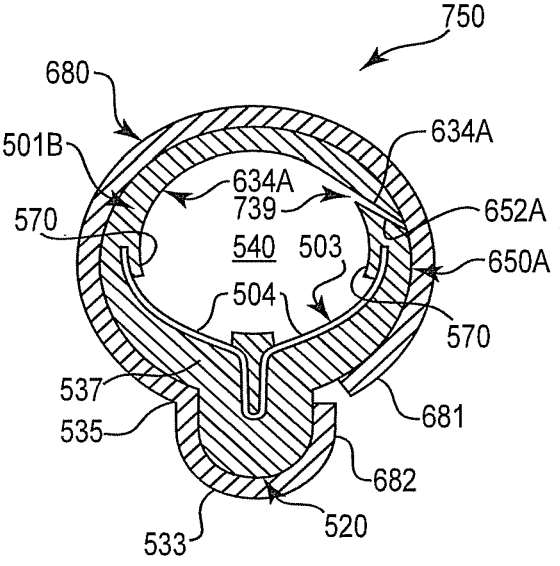


Fig. 19

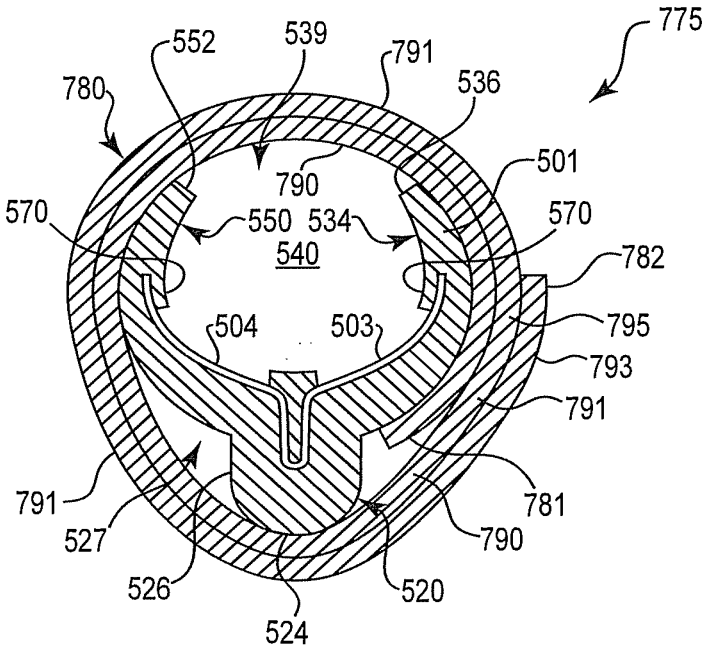

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Fig. 20

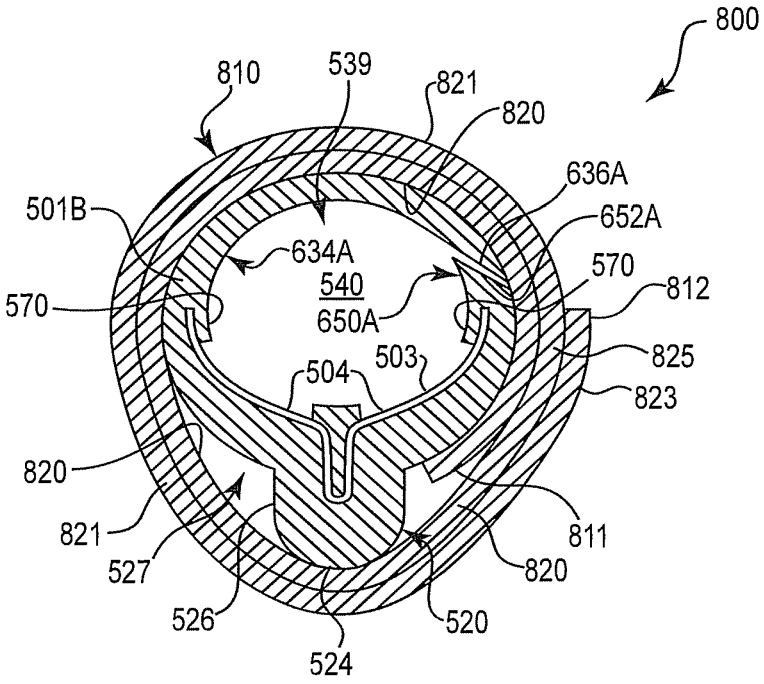

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811
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520
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Fig. 21

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/042539

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/05

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/048471 A (APNEX MEDICAL INC [US]; BOLEA STEPHEN L [US]; HOEGH THOMAS B [US]; PER) 24 April 2008 (2008-04-24) paragraphs [0065] - [0069], [0096] - [0107]; figures 6-8,16A-16F	1,2, 4-10, 12-28
Y		3,6-10, 22-26
X	US 2006/030919 A1 (MRVA JOSEPH J [US] ET AL) 9 February 2006 (2006-02-09) paragraphs [0032] - [0040]; figures 1,2A-2F,3A-3C	1,6, 9-16, 18-22, 25-29
Y		3,6-10, 22-26

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
27 July 2009	17/08/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Smit, Jos

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/042539

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 038 781 A (LYNCH H WILFRED [US]) 13 August 1991 (1991-08-13) column 4, lines 45-50 column 8, lines 19-59; figures 9-11	1,2,12, 13,15, 16, 18-21, 27,28
Y		3,6-10, 22-26
Y	ELEANOR V GOODALL ET AL: "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 43, no. 8, 1 August 1996 (1996-08-01), XP011006271 ISSN: 0018-9294 pages 851-852; figure 1	3,6,9, 10,22, 25,26
Y	NAPLES G G ET AL: "A SPIRAL NERVE CUFF ELECTRODE FOR PERIPHERAL NERVE STIMULATION" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 35, no. 11, 1 November 1988 (1988-11-01), pages 905-915, XP000036938 ISSN: 0018-9294 abstract; figure 7	6-10, 22-26
A	EP 0 865 800 A (MEDTRONIC INC [US]) 23 September 1998 (1998-09-23) the whole document	1-29
P,X	US 2008/132987 A1 (WESTLUND RANDY [US] ET AL) 5 June 2008 (2008-06-05) figures 6,9	1,16
P,X	US 2008/172116 A1 (MRVA JOSEPH J [US] ET AL) 17 July 2008 (2008-07-17) paragraphs [0061] - [0091]; figures 1-10	1,16
P,X	WO 2009/048580 A (IMTHERA MEDICAL INC [US]; MEADOWS PAUL M [US]; CRAIG STANLEY R [US]; L) 16 April 2009 (2009-04-16) paragraphs [0105] - [0120]; figures 6A-6G	1,16

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01057

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/042539

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008048471 A	24-04-2008	AU 2007313319 A1	24-04-2008
		CA 2666529 A1	24-04-2008
		US 2008103407 A1	01-05-2008
		US 2008103545 A1	01-05-2008
US 2006030919 A1	09-02-2006	WO 2006017634 A2	16-02-2006
US 5038781 A	13-08-1991	NONE	
EP 0865800 A	23-09-1998	DE 69826546 D1	04-11-2004
		DE 69826546 T2	06-10-2005
		US 7248930 B1	24-07-2007
		US 5938596 A	17-08-1999
US 2008132987 A1	05-06-2008	NONE	
US 2008172116 A1	17-07-2008	WO 2008088695 A2	24-07-2008
WO 2009048580 A	16-04-2009	WO 2009048581 A1	16-04-2009

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01058

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 November 2009 (05.11.2009)

PCT

(10) International Publication Number
WO 2009/135140 A1

(51) International Patent Classification:
A61N 1/05 (2006.01)

(21) International Application Number:
PCT/US2009/042543

(22) International Filing Date:
1 May 2009 (01.05.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
12/114,352 2 May 2008 (02.05.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ,

[Continued on next page]

(54) Title: SELF EXPANDING ELECTRODE CUFF

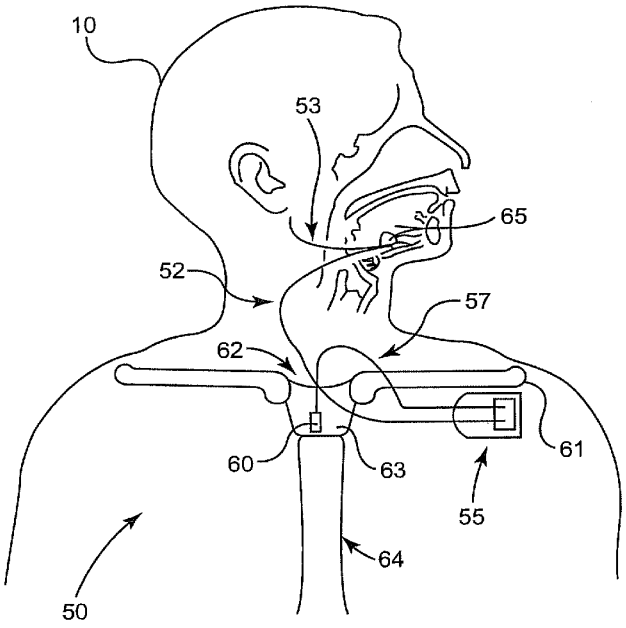


Fig. 1

(57) Abstract: An expandable electrode cuff of an implantable stimulation system that includes a base member, a first flange member extending from a proximal end along a first side wall of the base member to a first distal end, and a second flange member extending from a proximal end along a second side wall of the base member to a second distal end. The first flange member extends over both a top wall of the base member and the second flange member, and the second flange member extends over the top wall to form a lumen. The electrode cuff is capable of being advanced between a first position corresponding to both flange members extending over the top wall, a second position corresponding to the first flange member not extending over the top wall and the second flange member extending over the top wall, and a third position corresponding to both of the flange members not extending over the top wall.

WO 2009/135140 A1

TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

SELF EXPANDING ELECTRODE CUFF

TECHNICAL FIELD

[001] The invention relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the invention relates to an expandable electrode cuff for positioning an electrode of an implantable stimulation system about a nerve for stimulation and/or monitoring of nerve tissue.

BACKGROUND

[002] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[003] One treatment for obstructive sleep apnea has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a cuff electrode place around the hypoglossal nerve.

[004] Because of the significant amount of movement in multiple directions that can take place under the chin, positioning an electrode to enable stimulation of the hypoglossal nerve becomes a significant challenge. On the one hand, placement of the electrode and lead in close proximity to the hypoglossal nerve can result in irritation to the nerve as a result of normal motion of the chin and neck, while on the other hand, without close adherence to the nerve, buildup of connective tissue between the nerve and the electrode and lead can occur, causing low thresholds, thereby reducing the effectiveness of the delivered stimulation by the device.

[005] Another challenge in placing an electrode for nerve stimulation therapy relates to the tendency of the hypoglossal nerve to swell, which can result in the nerve being strangled by the electrode and lead. In addition, once the electrode cuff has initially been implanted, fibrosis tends to cause the location of the electrode cuff to become more fixed. Therefore, the first month post implant is critical to keep the electrode cuff properly positioned on the nerve, while at the same time it is important not to "suffocate" a swelling nerve. An additional challenge in placing the electrode for nerve stimulation results from the fact that stimulation currents need to be confined to the hypoglossal nerve in order to prevent other nearby nerves or muscles from being stimulated, which results in patient discomfort and loss of sleep. Therefore, what is needed is an improved electrode cuff that enables positioning of an electrode about a nerve.

BRIEF DESCRIPTION OF THE DRAWINGS

[006] Aspects and features of the present invention will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments of the invention when considered in connection with the accompanying drawings, wherein:

[007] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a self-expanding nerve cuff according to an embodiment of the invention;

[008] FIG. 2 is a side view of a lead utilized in an implantable stimulation system according to an embodiment of the invention;

[009] FIG. 3 is a front view of an expandable electrode cuff according to an embodiment of the invention;

[010] FIG. 4 is a front view of the expandable cuff of FIG. 3 in an intermediate open position according to an embodiment of the invention;

[011] FIG. 5 is a front view of the expandable electrode cuff of FIG. 3 in a fully open position according to an embodiment of the invention;

[012] FIGS. 6 is a schematic diagram illustrating positioning of an expandable electrode cuff over a desired nerve according to an embodiment of the invention;

[013] FIG. 7 is a front view of an expandable electrode cuff positioned about a nerve in an intermediate open position according to an embodiment;

[014] FIG. 8 is a front view of an expandable electrode cuff positioned about a nerve in a fully engaged position according to an embodiment;

[015] FIG. 9 is a front view of an expandable electrode cuff positioned around a nerve according to an embodiment of the invention;

[016] FIG. 10 is a front view of an expandable electrode cuff according to an embodiment of the invention;

[017] FIG. 11 is a front view of the expandable cuff of FIG. 10 in an intermediate open position according to an embodiment of the invention;

[018] FIG. 12 is a front view of the expandable electrode cuff of FIG. 10 in a fully open position according to an embodiment of the invention;

[019] FIG. 13 is a front view of an expandable electrode cuff positioned about a nerve in an intermediate open position according to an embodiment;

[020] FIG. 14 is a front view of an expandable electrode cuff positioned about a nerve in a fully engaged position according to an embodiment;

[021] FIG. 15 is a front view of an expandable electrode cuff positioned around a nerve according to an embodiment of the invention;

[022] FIG. 16 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position;

[023] FIG. 17 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position;

[024] FIG. 18 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position; and

[025] FIGS. 19-21 are front views of an expandable electrode cuff according to embodiments of the invention.

DESCRIPTION OF EMBODIMENTS

[026] The following detailed description is merely exemplary in nature and is not intended to limit the invention or the application and uses of the invention. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, brief summary or the following detailed description.

[027] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a self-expanding nerve cuff according to an embodiment of the invention. As illustrated in FIG.1, an example of an implantable stimulation system according to one embodiment of the invention includes an implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 10, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes an electrode or electrode system 65 and extends from the IPG 55 so that the electrode system 65 is position around a desired nerve, such as the hypoglossal nerve 53 of the patient 10, to enable stimulation of the nerve 53, as described below in detail. An exemplary implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., incorporated herein by reference in its entirety, and further includes a sensor lead 57 electrically coupled to the IPG 55 and extending from the IPG 55 so that a sensor or transducer 60 can be positioned in the patient 10 for sensing of respiratory effort.

[028] The sensor 60 may be a pressure sensor that is surgically implanted in a region that has pressure continuity with the intrapleural space, such as the suprasternal notch, the space between the trachea and esophagus, or by being attached to either of the trachea or esophagus. The sensor 60 may also be positioned intercostally, or secured in a position for sensing pressure at the posterior side of the manubrium. The suprasternal notch 62 and manubrium 63 of the sternum 64 are well known structures on the upper chest that are in anatomical continuity with the intrapleural space. It is also well known that changes in intrapleural pressure provide a characteristic respiratory effort waveform.

[029] The location for placement of the sensor 60 is, at least in part, chosen as a function of a delay, i.e. the propagation time associated with a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position. The chosen location is also a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. the amount of filtering that is necessary to remove waveforms other than the waveform associated with the desired sensed characteristic, such as the filtering required to remove cardiac waveform activity, for example. The positioning of the sensor 60 enables the IPG 55 to receive respiratory effort waveform information utilized to determine increased respiratory effort, which is then used by the IPG 55 to control delivery of therapy in response to determined increases in respiratory effort.

[030] FIG. 2 is a side view of a lead utilized in an implantable stimulation system according to an embodiment of the invention. As illustrated in FIG. 2, a lead 100 according to one embodiment includes a lead body 102 extending from a proximal end 104 to a distal end 106, with a connector 108 positioned at the proximal end 104 for electrically connecting the lead 100 to the IPG 55. An expandable electrode cuff 110, positioned at the distal end 106 of the lead body 102, is capable of being positioned around a nerve, such as a hypoglossal nerve for example, in order to strategically locate one or more electrodes 112 embedded within the electrode cuff 110 so as to be adjacent to the nerve when the electrode cuff 110 is positioned around the nerve. Conductors (not shown) are positioned within the lead body 102 to electrically connect the electrodes 112 and the connector 108 so that the electrodes 112 are electrically coupled to the IPG 55 via respective connector pins 114 of the connector 108, as is known in the art.

[031] FIG. 3 is a front view of an expandable electrode cuff according to an embodiment of the invention. As illustrated in FIG. 3, according to one embodiment, the expandable electrode cuff 110 is a single, unitary molded piece that includes a base portion 120 having a top wall 122 and a bottom wall 124 extending from a first side wall 126 to a second side wall 128. A first flange member 130 extends from a proximal end 131 to a distal end 312, and is located at the top wall 122 of the base portion 120 to extend from the first side wall 126 to the distal end 132. A second flange member 134 extends from a proximal end 135, and is located at the top wall

122 of the base portion 120 to extend from the second side wall 128 to the distal end 136. As will be described below, the electrode cuff 110 is expandable both during implantation of the lead 100 and electrode cuff 110, and after the electrode cuff 110 is positioned around a desired nerve for delivery of electrical stimulation therapy to the nerve.

[032] During it's normal, unbiased state, prior to insertion around the nerve, the electrode cuff 110 is in a fully engaged position, shown in FIG. 3, in which the dsital end 132 of the first flange member 130 is positioned adjacent to and may engage against the second side wall 128 at a location below the proximal end 135 of the second flange member 134 and below the top wall 122 of the base portion 120, and the distal end 136 of the second flange member 134 is positioned at a location above the proximal end 131 of the first flange member 130 and above the top wall 122 of the base portion 120 along the first side wall 126.

[033] The first flange member 130 has a length greater than the second flange member 134 so that when the electrode cuff 110 is in the fully engaged position, the first flange member 130 and the second flange member 134 form a lumen 140 for receiving a nerve therein, with an inner side wall 141 of the second flange member 134 forming an inner wall 142 of the lumen 140 so as to position the electrodes 112 (shown in FIG. 2), which are embedded within the second flange member 134, adjacent to the nerve (not shown in FIG. 3).

[034] In addition, when the electrode cuff 110 is in the fully engaged position, an inner side wall 144 of the first flange member 130 is positioned over and engages against an outer side wall 146 of the second flange member 134, and therefore an outer wall 148 of the first flange member 130 forms an outer wall 143 of the lumen 140. In this way, when the electrode cuff 110 is in the fully engaged position shown in FIG. 3, both the first flange member 130 and the second flange member 134 extend over the base portion 120, the first flange member 130 forms an outer portion of the electrode cuff 110, and the second flange member 134 forms an inner portion of the electrode cuff 110 for engaging the nerve. Depending on the size of the nerve, once positioned about a nerve, the electrode cuff 110 may be in either the fully engaged position of FIG. 3 or in a partially fully engaged position, wherein the distal end 132 of the first flange member 130 may be spaced from rather than

engaged against the second side wall 128, and the distal end 136 of the second flange member 134 may be spaced from rather than aligned with the first side wall 126 at the top wall 122 of the base portion 120, as will be described below.

[035] FIG. 4 is a front view of the expandable cuff of FIG. 3 in an intermediate open position according to an embodiment of the invention. As illustrated in FIG. 4, during positioning of the electrode cuff 110 over the desired nerve so that the nerve can be properly located within the lumen 140, the electrode cuff 110 is advanced from the fully engaged position shown in FIG. 3, to an intermediate position shown in FIG. 4, in which the distal end 132 of the first flange member 130 is advanced away from the second side wall 128, and the inner side wall 144 of the first flange member 130 is advanced away from the outer side wall 146 of the second flange member 134 so that the distal end 132 extends outward from and along the first side wall 126 of the base portion 120. As a result, when the electrode cuff 110 is in the intermediate open position, the first flange member 130 is not positioned so as to extend over the top wall 122 of the base portion 120, and the distal end 132 is no longer positioned below the top wall 122 of the base portion 120, while the second flange member 134 remains positioned to extend over the top wall 122 of the base portion 120 with the distal end 136 of the second flange member 134 positioned above the proximal end 131 of the first flange member 130. In addition, the inner side wall 144 of the first flange member 130 is no longer positioned over and adjacent to the outer side wall of 146 of the second flange member 134 when the cuff 110 is in the intermediate open position of FIG. 4.

[036] FIG. 5 is a front view of the expandable electrode cuff of FIG. 3 in a fully open position according to an embodiment of the invention. As illustrated in FIG. 5, once the electrode cuff 110 is in the intermediate open position, the distal end 136 of the second flange member 134 is advanced away from the top wall 122 of the base portion 120 and the first side wall 126 so that rather than being positioned above the proximal end 131 of the first flange member 130, the distal end 136 of the second flange member 134 extends outward from the second side wall 128 so that the second flange member 134 does not extend over the second side wall 128 of the base portion 120, resulting in the inner wall 142 of the second flange member 134 no longer forming the lumen 140 when the cuff is in the fully open position of FIG. 5. As

a result, when the electrode cuff 110 is in the fully open position, neither the first flange member 130 nor the second flange member 134 are positioned so as to extend over or near the top wall 122 of the base portion 120 of the electrode cuff 110, the inner side wall 144 of the first flange member 130 is no longer positioned over or near an outer side wall 146 of the second flange member 134, and the inner side wall 141 of the second flange member 134 no longer forms the inner wall 142 of the lumen 140. In this way, by enabling the electrode cuff 110 to be advanced between the fully engaged position, the intermediate open position, and the fully open position, the invention enables the cuff 110 to be more easily positioned over a nerve during implantation of the lead 100, as described below.

[037] FIG. 6 is a schematic diagram illustrating positioning of an expandable electrode cuff over a desired nerve according to an embodiment of the invention. As illustrated in FIG. 6, during the initial positioning of the lead and positioning of the electrode cuff 110 over a nerve, such as over a hypoglossal nerve 200, once the nerve 200 has been dissected out over a desired range, such as over 1-3 cm range, for example, the electrode cuff 110 is advanced from the normal, fully engaged position of FIG. 3 to the fully open position of FIG. 5 so that the inner flange 134 of the electrode cuff 110 is then inserted under the nerve 200 while in the fully open position, until the nerve 200 becomes positioned so as to be aligned with and against the top wall 122 of the base portion 120.

[038] The inner flange member 134 is then released so that the inner flange member 134 becomes positioned around the nerve 200. According to one embodiment, prior to be advanced from the fully open position to the intermediate position, the base portion 120 of the electrode cuff 110 is positioned inward, towards the body of the patient. As a result, once positioned under the nerve 200, the electrode cuff 110 is advanced from the fully open position to the intermediate open position (FIG. 4) so that only the second flange member 134 is positioned over the top wall 122 of the base portion 120, enclosing the nerve 200. The outer flange member 130 is then released to be positioned around the nerve 200, resulting in the electrode cuff 110 being advanced from the intermediate open position to a final engaged positioned (see FIG. 7), with both the first flange member 130 and the second flange member 134 being positioned over the top wall 122 of the base

portion 120, enclosing the nerve 200 within the lumen 140 formed by the flange members 130 and 134.

[039] FIG. 7 is a front view of an expandable electrode cuff positioned about a nerve in an intermediate open position according to an embodiment. As illustrated in FIG. 7, depending upon the circumference of the nerve 200, once the nerve 200 is positioned over the top wall 122 of the base portion 120 of the electrode cuff 110, and the inner flange member 134 is positioned about the nerve 200 during the advancement of the electrode cuff 110 from the fully open position of FIG. 5 to the intermediate open position of FIG. 7, the distal end 136 of the second flange member 134 may be positioned to be spaced further above the proximal end 131 of the first flange member 130 and further away from the first side wall 126 and the top wall 122 of the base portion 120 than when the electrode cuff 110 is in the intermediate open position of FIG. 4. As a result, the size of the lumen 140 can be increased relative to when the electrode cuff 110 is in the intermediate open position of FIG. 4 to accommodate the size of the nerve 200.

[040] FIG. 8 is a front view of an expandable electrode cuff positioned about a nerve in a fully engaged position according to an embodiment. Similarly, during the advancement of the electrode cuff from the intermediate open position of FIG. 7 to the fully engaged position during implant of the electrode cuff 110, the distal end 132 of the outer flange member 130 may be positioned to be spaced further away from the second side wall 128 of the base portion 120 than when the electrode cuff 110 is in the fully engaged position of FIG. 3, and to be above, rather than below the proximal end 135 of the second flange member 134 and the top wall 122 of the base portion 120, thereby increasing the size of the lumen 140 relative to when the electrode cuff 110 is in the fully engaged position of FIG. 3 prior to be implanted to accommodate the size of the nerve. Therefore, as illustrated in FIGS. 7 and 8, in order to accommodate the size of the nerve, the first and second flanges 130 and 134 can be advanced or expanded to increase the diameter of the lumen 140.

[041] FIG. 9 is a front view of an expandable electrode cuff positioned around a nerve according to an embodiment of the invention. If the small arteries that run along the side of the nerve are overly restricted by the electrode cuff 110, blood supply could be inhibited, causing temporary or permanent damage to the nerve.

The inventors have found that approximately 25 mmHg is the approximate amount of pressure that may be applied to the nerve without restricting blood flow. As illustrated in FIG. 9, according to one embodiment, in order to address the effects of swelling of the hypoglossal nerve 200 that may sometimes occur, particularly after the initial trauma associated with implanting the electrode cuff 110, the first and second flange members 130 and 134 are expandable so that the circumference of the lumen 140 formed by the electrode cuff 110 is able to increase to accommodate increases in the diameter of the nerve 200 that occur subsequent to the initial positioning of the expandable electrode cuff 110 about the nerve 200. For example, during swelling of the nerve 200 subsequent to implant of the device 100, the first flange member 130 and the second flange member 134 expand so that the distal end 132 of the first flange member 130 becomes positioned to be spaced further away from the second side wall 128 of the base portion 120, and to be even further above, rather than below the proximal end 135 of the second flange member 134 and the top wall 122 of the base portion 120. At the same time, the distal end 136 of the second flange member 134 becomes positioned to be spaced further above the proximal end 131 of the first flange member 130 and further away from the first side wall 126 and the top wall 122 of the base portion 120, thereby further increasing the size of the lumen 140 to accommodate the swelling. As the swelling of the nerve 200 subsides, the first and second flange members 130 and 134 return towards the original fully engaged position about the nerve 200 that occurred at the time of implant.

[042] FIG. 10 is a front view of an expandable electrode cuff according to an embodiment of the invention. As illustrated in FIG. 10, according to another embodiment, an expandable electrode cuff 310 includes a base portion 320 having a top wall 322 and a bottom wall 324 extending from a first side wall 326 to a second side wall 328, a first flange member 330, a second flange member 334, and a third flange member 350. The first flange member 330 is bonded at a proximal end 331 to the third flange member 350 along a portion of an outer wall 352 of the third flange member 350, and extends outward and over the top wall 322 of the base portion 320 from the first side wall 326 to a distal end 332. The second flange member 334 extends outward and over the top wall 322 of the base portion 320 from the second side wall 328 to a distal end 336. The third flange member 350 extends outward at

the top wall 322 of the base portion 320 from the first side wall 326 to a distal end 352.

[043] In the expandable electrode cuff 310 of the embodiment of FIG. 10, the base portion 320, second flange member 334 and the third flange member 350 are formed from a single, unitary molded piece, with the first flange member 330 bonded to the molded piece. As will be described below, the electrode cuff 310 is expandable both during implantation of the lead 100 and electrode cuff 310, and after the electrode cuff 310 is positioned around a desired nerve for delivery of electrical stimulation therapy to the nerve, similar to the electrode cuff 110 described above in the embodiment of FIGS. 3-5.

[044] During it's normal, unbiased state, prior to insertion around the nerve, the electrode cuff 310 is in a fully engaged position, shown in FIG. 10, in which the first flange member 330 extends outward and over the top wall 322 of the base portion 320 from the first side wall 326 to the distal end 332, the second flange member 334 extends outward and over the top wall 322 of the base portion 320 from the second side wall 328 to the distal end 336, and third flange member 350 extends outward at the top wall 322 of the base portion 320 from the first side wall 326 to the distal end 352 so that the third flange member 350 does not extend over the top wall 332. In addition, while in the fully engaged position, the distal end 332 of the first flange member 330 is positioned adjacent to and engaged against an outer side wall 346 of the second flange member 334 and an outer side wall 347 of the third flange member 350, and the distal end 336 of the second flange member 334 is positioned adjacent to and may be engage against the distal end 352 of the third flange member 350 at a location along the first flange member 330.

[045] The first flange member 330 has a length greater than the second flange member 334 so that when the electrode cuff 310 is in the fully engaged position, the first, second and third flange members 330, 334 and 350 form a lumen 340 for receiving a nerve therein, with an inner side wall 341 of the second flange member 134 and an inner side wall 354 of the third flange member 350 forming an inner wall 342 of the lumen 340 so as to position the electrodes 112 (shown in FIG. 2), which are embedded within the second flange member 334, adjacent to the nerve (not shown in FIG. 3). In addition, when the electrode cuff 310 is in the fully engaged

position, an inner side wall 344 of the first flange member 330 is positioned over the outer side wall 346 of the second flange member 334 and the outer side wall 347 of the third flange member 350, and an outer wall 348 of the first flange member 330 forms an outer wall 343 of the lumen 340. In this way, when the electrode cuff 310 is in the fully engaged position shown in FIG. 10, both the first flange member 330 and the second flange member 334 extend over the base portion 320, the first flange member 330 forms an outer portion of the electrode cuff 310, and the second and third flange members 334 and 350 form an inner portion of the electrode cuff 310 for engaging the nerve. Depending on the size of the nerve, once positioned about the nerve, the electrode cuff 310 may be either in the fully engaged position of FIG. 10 or in a partially fully engaged position, wherein the distal end 332 of the first flange member 330 may be positioned along the outer side wall 346 of the second flange member 334 to be spaced further away from the second side wall 328 than shown in FIG. 10, and the distal end 336 of the second flange member 334 may be spaced further away from and not engaged against the distal end 352 of the third flange member 350, as will be described below.

[046] FIG. 11 is a front view of the expandable cuff of FIG. 10 in an intermediate open position according to an embodiment of the invention. As illustrated in FIG. 11, during positioning of the electrode cuff 310 over the desired nerve so that the nerve can be properly located within the lumen 340, the electrode cuff 310 is advanced from the fully engaged position shown in FIG. 10, to an intermediate position shown in FIG. 11 in which the distal end 332 of the first flange member 330 is advanced away from the second side wall 328, and the first flange member 330 is advanced away from the second flange member 334 so that the distal end 332 extends outward in an opposite direction from the first side wall 326 of the base portion 320. As a result, when the electrode cuff 310 is in the intermediate open position, the first flange member 330 is not positioned so as to extend over the top wall 322 of the base portion 320, while the second flange member 334 remains positioned to extend over the top wall 322 of the base portion 320, with the distal end 336 adjacent to the distal end 352 of the third flange member 350. In addition, the inner side wall 344 of the first flange member 330 is no longer positioned over and adjacent to the outer side wall 346 of the second flange member 334 when the cuff 310 is in the intermediate open position of FIG. 11.

[047] FIG. 12 is a front view of the expandable electrode cuff of FIG. 10 in a fully open position according to an embodiment of the invention. As illustrated in FIG. 12, once the electrode cuff 310 is in the intermediate open position, the distal end 336 of the second flange member 334 is advanced away from the distal end 352 of the third flange member 350 and the second flange member 334 is advanced to no longer extend over the top wall 322 of the base portion 320 and the first side wall 326 so that the distal end 336 extends outward in the opposite direction from the second side wall 328, resulting in the inner wall 342 of the second flange member 334 no longer forming the lumen 340 when the electrode cuff 310 is in the fully open position of FIG. 12. As a result, when the electrode cuff 310 is in the fully open position, neither the first flange member 330 nor the second flange member 334 are positioned so as to extend over or near the top wall 322 of the base portion 320 of the electrode cuff 310, the inner side wall 344 of the first flange member 330 is no longer positioned over or near the outer side wall 346 of the second flange member 334, and the inner side wall 341 of the second flange member 334 no longer forms the inner wall 342 of the lumen 340.

[048] In this way, by enabling the electrode cuff 310 to be advanced between the fully engaged position, the intermediate open position, and the fully open position, the electrode cuff 310 can be more easily positioned over a nerve during implantation of the lead 100, using the same method of implantation as described above in FIG. 6, for example. If desired, an adhesive material (not shown) could be added to the distal end 352 of the third flange member 350 in order to make a smoother transition at the distal end 352 and the inner wall 334 of the first flange member 330 during positioning of the electrode cuff 310 abouot the nerve.

[049] As can be seen in FIGS. 10-12, the second flange member 334 according to one embodiment has a first thickness 360 along a proximal end 362 located at the top wall 322 of the base portion 120 along the second side wall 328, and a second thickness, less than the first thickness 360, at the distal end 336 of the second flange member 334, so that the second flange member 334 is tapered in thickness from the proximal end 362 to the distal end 336. Similarly, the third flange member 350 has a first thickness 364 along a proximal end 366 located at the top wall 322 of the base portion 320 along the first side wall 326, and a second thickness, less than the first

thickness 364, at the distal end 352 of the third flange member 350, so that the third flange member 350 is tapered in thickness from the proximal end 366 to the distal end 352. While the inner flange member 334 of FIGS. 8-10 is shown to be tapered, it is understood that both the inner flange member 334 and the outer flange member 332 could be formed without being tapered. In addition, it is understood that the inner flange member 134 of FIGS. 3-5 may also be tapered as described in the embodiment of FIGS. 10-12.

[050] The flange members described above may be formed from polyurethane, silicon or a blend of polyurethane and silicon. Furthermore, according to an embodiment, one of the flange members could be formed of polyurethane while the other is formed of silicon. If formed from silicone, then the durometer of the flange material range would be within a range of approximately 40A – 70A. The thickness of the flange material could be from approximately 0.005 inches to 0.025 inches. Nominally, if the flange is formed of a polyurethane having a durometer of approximately 85A, the flange would be 0.0075 inches thick. In the embodiment of FIGS. 10-12, the inner flange 334 is formed from molded polyurethane and the outer flange 330 is formed from a portion of a polyurethane tubing. In either embodiment, the polyurethane is formed to have a "memory" that enables the flange members to be biased towards the fully engaged positioned. The lumen 140, 340 may have an inner diameter between 0.050 and 0.400 inches, while according to an embodiment, the inner diameter is approximately 0.140 inches in the fully engaged position.

[051] If the inner flange member 134, 334 is tapered, the respective proximal end 135 and 360 may have a thickness of approximately 0.025 to 0.030 inches, and the distal end 136, 336 may have a thickness of approximately 0.001 to 0.010 inches. This provides a strong mechanical connection to the sidewall and also provides the needed thickness to hold and strain relief the electrodes. According to one embodiment, the distal end 136, 336 has a thickness of 0.005 inches. Similarly, the distal end 352 of the third flange member 350 may have a thickness of approximately 0.001 to 0.010 inches, and according to an embodiment in which the distal end 336 of the second flange member 334, the distal end 352 of the third flange member would also have a thickness of approximately 0.005 inches.

[052] FIG. 13 is a front view of an expandable electrode cuff positioned about a nerve in an intermediate open position according to an embodiment. As illustrated in FIG. 13, depending upon the circumference of the nerve 200, once the nerve 200 is positioned over the top wall 322 of the base portion 320 of the electrode cuff 310 and adjacent to the third flange member 350, and the second flange member 334 is positioned about the nerve 200 during the advancement of the electrode cuff 310 from the fully open position of FIG. 10 to the intermediate open position, the distal end 336 of the second flange member 334 may be positioned to be spaced further above the proximal end 331 of the first flange member 330 and the distal end 352 of the third flange member 350 than when the electrode cuff 310 is in the intermediate open position of FIG. 11. As a result, the size of the lumen 340 can be increased relative to when the electrode cuff 310 is in the intermediate open position of FIG. 11 to accommodate the size of the nerve 200 during positioning of the electrode cuff 310.

[053] FIG. 14 is a front view of an expandable electrode cuff positioned about a nerve in a fully engaged position according to an embodiment. Similarly, during the advancement of the electrode cuff 310 from the intermediate open position of FIG. 13 to the fully engaged position during implant of the electrode cuff 310, the distal end 332 of the outer flange member 330 may be positioned along the outer side wall 346 of the second flange member 334 to be spaced further away from the second side wall 328 than when the electrode cuff 310 is in the fully engaged position of FIG. 10, and to be above, rather than below the top wall 332 of the base portion 320. As a result, the diameter of the lumen 340 is increased relative to when the electrode cuff 310 is in the fully engaged position of FIG. 10 prior to being implanted, to accommodate the size of the nerve. Therefore, as illustrated in FIGS. 13 and 14, in order to accommodate the size of the nerve, the first and second flanges 330 and 334 can be advanced or expanded to increase the diameter of the lumen 340.

[054] FIG. 15 is a front view of an expandable electrode cuff positioned around a nerve according to an embodiment of the invention. As illustrated in FIG. 15, according to one embodiment, in order to address the effects of swelling of the hypoglossal nerve 200 that may sometimes occur, particularly after the initial trauma associated with implanting the electrode cuff 310, the first and second flange

members 330 and 334 are expandable so that the circumference of the lumen 340 formed by the electrode cuff 310 can be increased to accommodate increases in the diameter of the nerve 200 that occur subsequent to the initial positioning of the expandable electrode cuff 310 about the nerve 200, as illustrated in FIG. 14. For example, during swelling of the nerve 200 subsequent to implant of the device 100, the first flange member 330 and the second flange member 334 expand so that the distal end 332 of the first flange member 330 becomes positioned to be spaced further away from the second side wall 328 of the base portion 320, and to be even further above, rather than below, the top wall 322 of the base portion 320 than when the electrode cuff 310 was initially positioned about the nerve to the position illustrated in FIG. 14. At the same time, the distal end 336 of the second flange member 334 becomes positioned to be spaced further above the distal end 352 of the third flange member 350, and further away from the first side wall 326 and the top wall 322 of the base portion 320, thereby further increasing the size of the lumen 340 to accommodate the swelling. As the swelling of the nerve 200 subsides, the first and second flange members 330 and 334 return towards the original fully engaged position about the nerve 200 that occurred during positioning of the electrode cuff 310 at the time of implant of the device, such as is illustrated in FIG. 14.

[055] By forming the first and second flange members, described above, to extend over the base member so that each of the flange members extend from a proximal end located on one side of the base member to a distal end located along the other side of the base member, the electrode cuff will continue to be positioned completely around the nerve, thereby preventing open gaps from being formed between the distal ends of the flange members as the nerve swells. Rather, the first and second flange members described above enable the necessary expansion of the flange members to accommodate increasing the diameter of the lumen required for maintaining the nerve to be completely enclosed within the lumen. In this way, using the electrode cuff described above, the opportunity for the nerve to extend and extend out of the lumen is decreased, since the electrode cuff is able to more effectively accommodate such swelling.

[056] FIG. 16 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position. As illustrated in FIG. 16, according to an embodiment, an expandable electrode cuff 410 includes a first flange member 430 and a second flange member 434 extending from a base portion 420, as described above. Ends 432 and 436 of one or both of the first flange member 430 and the second flange member 434, respectively, may include having chamfered corners 435 to prevent the corners 435 from curling during placement of the expandable electrode cuff 410 over the nerve, as described above.

[057] FIG. 17 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position. As illustrated in FIG. 17, according to an embodiment, an expandable electrode cuff 510 includes a first flange member 530 and a second flange member 534 extending from a base portion 520, as described above. Ends 532 and 536 of one or both of the first flange member 530 and the second flange member 534, respectively, may include a suture 537 attached thereto. For example, one or more holes 539 may be formed along the ends or at the respective corners 535 for attaching a suture 537 to the flange member. The suture 537 is utilized to pull one or both of the flange members 530 and 534 through and under the nerve during positioning of the electrode cuff 510 about the nerve while in the fully open position. In addition, the sutures 537 may also be utilized to aid in advancing the electrode cuff from the fully engaged position to the fully open position prior to placement of the electrode cuff 510. Once the expandable electrode cuff 510 is positioned under the nerve, the implanter merely releases the hold on the sutures 537 to allow either of the flange members 530 and 534 to be engaged around the nerve, as described above, and the sutures 537 may then be removed by being cut off from the electrode cuff 510.

[058] According to an embodiment, the sutures 537 may come already attached to the electrode cuff, or the electrode cuff may only include the holes formed at one or more of the ends, so that the implanter merely inserts the sutures in the desired holes prior to positioning of the electrode cuff about the nerve.

[059] FIG. 18 is a top view of an expandable electrode cuff according to an embodiment of the invention in the fully open position. As illustrated in FIG. 18,

according to an embodiment, an expandable electrode cuff 610 includes a first flange member 630 and a second flange member 634 extending from a base portion 620, as described above. One or both corners of ends 632 and 636 of one or both of the first flange member 630 and the second flange member 634, respectively, may include a molded or attached tab 645, that, similar to the sutures of FIG. 17, are utilized pull one or both of the flange members 630 and 634 through and under the nerve during positioning of the electrode cuff 610 about the nerve while in the fully open position. In addition, the tabs 645 may also be utilized to aid is advancing the electrode cuff 610 from the fully engaged position to the fully open position prior to placement of the electrode cuff 610. Once the expandable electrode cuff 610 is positioned under the nerve, the implanter merely releases the hold on the tabs 645 to allow either of the flange members 630 and 634 to be engaged around the nerve, as described above. In addition, an embodiment may include a combination of the tabs 645 and one or more holes 639 formed at the respective corners 635 of the ends 632 and 636 to aid in placement of the electrode cuff about the nerve. If the use of sutures to aid in implant is desired, the implanter may merely inserts a suture in the desired hole 639.

[060] FIGS. 19-21 are front views of an expandable electrode cuff according to embodiments of the invention. As illustrated in FIGS. 19-21, other configurations of the flange members may also be utilized. An electrode cuff 410 according to one embodiment may include a second flange member 434 and a third flange member 450 formed to have any desired lengths to enable the respective ends 436 and 452 to be positioned at any desired location within the lumen 440. For example, as illustrated in FIG. 19, the distal end 436 of the second flange member 434 and the distal end 452 of the third flange member 450 may be positioned further above the first side wall 426 than in the exemplary illustration of FIG. 10. In addition, in another embodiment the length of the first flange member 430 may be increased so that the first flange member 430 extends over the top wall 422 of the base portion 420, around the second flange member 434 and under the bottom wall 424 of the base member 420, with the distal end 432 of the first flange member 430 being positioned below the proximal end 431 of the first flange member 430 along the first side wall 426.

[061] As illustrated in FIG. 20, according to another embodiment, the length of a first flange member 530 may be even further increased so that the first flange member 530 extends over the top wall 522 of the base potion 520, around the second flange member 534, under the bottom wall 524 of the base member 520 and over the first flange member 530 along the proximal end 531 of the first flange member 530, with the distal end 532 of the first flange member 530 being positioned above the proximal end 531 of the first flange member 530 along the first side wall 426.

[062] As illustrated in FIG. 21, according to yet another embodiment, the second flange member 634 and the third flange member 650 may be formed to be symmetrical, with the distal end 636 of the second flange member 634 positioned approximately the same distance above the second side wall 628 of the base portion 620 as the distal end 652 of the third flange member 650 is positioned above the first side wall 626 of the base portion 620. In addition, the length of the first flange member 630 may be increased so that the first flange member 630 extends over the top wall 622 of the base portion 620 a multiple number of times, around the second flange member 434 and under the bottom wall 424 of the base member 420 the multiple number of times, with the distal end 432 of the first flange member 430 being positioned at any location around the electrode cuff 610, such as above the proximal end 431 of the first flange member 430 along the first side wall 426, as shown in FIG. 21.

[063] While at least one exemplary embodiment has been presented in the foregoing detailed description, it should be appreciated that variations exist. It should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope, applicability, or configuration of the invention in any way. Rather, the foregoing detailed description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the invention as set forth in the appended claims and the legal equivalents thereof.

WE CLAIM:

1. An expandable electrode cuff of an implantable stimulation system, comprising:

a base member extending from a first side wall to a second side wall and having a top wall and a bottom wall;

a first flange member extending from a proximal end along the first side wall to a first distal end; and

a second flange member extending from a proximal end along the second side wall to a second distal end, wherein the first flange member extends over both the top wall of the base member and the second flange member, and the second flange member extends over the top wall of the base member to form a lumen.

2. The expandable electrode cuff of claim 1, wherein the electrode cuff is capable of being advanced between a first position and a second position, the first position corresponding to both of the first flange member and the second flange member extending over the top wall of the base member, and the second position corresponding to the first flange member not extending over the top wall of the base member and the second flange member extending over the top wall of the base member.

3. The expandable electrode cuff of claim 2, wherein the electrode cuff is capable of being advanced between the first position, the second position, and a third position, the third position corresponding to both of the first flange member and the second flange member not extending over the top wall of the base member.

4. The expandable electrode cuff of claim 1, wherein the first flange member is capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the first distal end is positioned below the proximal end of the second flange member in the first position, and the first distal end is positioned above the proximal end of the second flange member in the second position.

5. The expandable electrode cuff of claim 1, wherein the second flange member is capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the second distal end is positioned a first distance above the proximal end of the first flange member in the first position, and the second distal end is positioned a second distance, greater than the first distance, above the proximal end of the first flange member in the second position.

6. The expandable electrode cuff of claim 1, wherein the first flange member and the second flange member are capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the first distal end is positioned below the proximal end of the second flange member and the second distal end is positioned a first distance above the proximal end of the first flange member in the first position, and the first distal end is positioned above the proximal end of the second flange member and the second distal end is positioned a second distance, greater than the first distance, above the proximal end of the first flange member in the second position.

7. The expandable electrode cuff of claim 1, wherein the first flange member is capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the first distal end is positioned a first distance above the second side wall of the base member in the first position, and the first distal end is positioned a second distance greater than the first distance above the second side wall of the base member in the second position.

8. The expandable electrode cuff of claim 1, wherein the second flange member is capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the

second distal end is positioned a first distance above the first side wall of the base member in the first position, and the second distal end is positioned a second distance greater than the first distance above the first side wall of the base member in the second position.

9. The expandable electrode cuff of claim 1, wherein the first flange member and the second flange member are capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the first distal end is positioned a first distance above the second side wall of the base member and the second distal end is positioned a second distance above the first side wall of the base member in the first position, and the first distal end is positioned a third distance greater than the first distance above the second side wall of the base member and the second distal end is positioned a fourth distance greater than the second distance above the first side wall of the base member in the second position.

10. The expandable electrode cuff of claim 1, wherein the second flange member has a first thickness at the proximal end of the second flange member and a second thickness, less than the first thickness, at the second distal end.

11. The expandable electrode cuff of claim 1, further comprising means for pulling one or both of the first flange member and the second flange member under a nerve during positioning of the expandable electrode cuff about the nerve.

12. An expandable electrode cuff of an implantable stimulation system, comprising:

a base member extending from a first side wall to a second side wall and having a top wall and a bottom wall;

a first flange member extending from a proximal end along the first side wall to a first distal end positioned above the first side wall;

a second flange member extending from a proximal end along the second side wall to a second distal end; and

a third flange member having a proximal end fixedly engaged against the first flange member and extending to a third distal end, wherein the third flange member extends over both the top wall of the base member and the second flange member, the second flange member extends over the top wall of the base member, and the second distal end is spaced above the first distal end so that the first flange member, the second flange member and the third flange member form a lumen.

13. The expandable electrode cuff of claim 12, wherein the electrode cuff is capable of being advanced between a first position, a second position, and a third position, the first position corresponding to both of the second flange member and the third flange member extending over the top wall of the base member, the second position corresponding to the third flange member not extending over the top wall of the base member and the second flange member extending over the top wall of the base member, and the third position corresponding to both of the second flange member and the third flange member extending over the top wall of the base member.

14. The expandable electrode cuff of claim 12, wherein the third flange member is capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the third distal end is positioned a first distance above the second side wall of the base member in the first position, and the third distal end is positioned a second distance great than the first distance above the second side wall of the base member in the second position.

15. The expandable electrode cuff of claim 12, wherein the second flange member is capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the second distal end is positioned a first distance above the first distal end in the first position, and the second distal end is positioned a second distance, greater than the first distance, above the first distal end in the second position.

16. The expandable electrode cuff of claim 12, wherein the third flange member and the second flange member are capable of being advanced between a first position, prior to positioning of the electrode cuff about a nerve, and a second position subsequent to the positioning of the electrode cuff about the nerve, wherein the third distal end is positioned a first distance above the second side wall of the base member and the second distal end is positioned a second distance above the first distal end in the first position, and the first distal end is positioned a third distance great than the first distance above the second side wall of the base member and the second distal end is positioned a fourth distance, greater than the second distance, above the first distal end in the second position.

17. The expandable electrode cuff of claim 12, wherein the third flange member is capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the third distal end is positioned a first distance above the second side wall of the base member in the first position, and the third distal end is positioned a second distance greater than the first distance above the second side wall of the base member in the second position.

18. The expandable electrode cuff of claim 12, wherein the second flange member is capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the second distal end is positioned a first distance above the first distal end the first position, and the second distal end is positioned a second distance greater than the first distance above the first distal end in the second position.

19. The expandable electrode cuff of claim 12, wherein the third flange member and the second flange member are capable of being advanced between a first position, corresponding to a first diameter of the lumen at initial positioning of the electrode cuff about a nerve, and a second position corresponding to a second

diameter greater than the first diameter subsequent to the initial positioning of the electrode cuff about the nerve, wherein the third distal end is positioned a first distance above the second side wall of the base member and the second distal end is positioned a second distance above the first distal end in the first position, and the third distal end is positioned a third distance greater than the first distance above the second side wall of the base member and the second distal end is positioned a fourth distance greater than the second distance above the first distal end in the second position.

20. The expandable electrode cuff of claim 12, wherein the second flange member has a first thickness at the proximal end of the second flange member and a second thickness, less than the first thickness, at the second distal end.

21. The expandable electrode cuff of claim 12, further comprising means for pulling one or both of the third flange member and the second flange member under a nerve during positioning of the expandable electrode cuff about the nerve.

22. An implantable stimulation system, comprising:

an implantable pulse generator;

a stimulation lead having a lead body extending from a lead body proximal end to a lead body distal end;

a connector positioned at the lead body proximal end for electrically connecting the stimulation lead and the implantable pulse generator; and

an expandable electrode cuff positioned at the lead body distal end, the expandable electrode cuff comprising:

a base member extending from a first side wall to a second side wall and having a top wall and a bottom wall;

a first flange member extending from a proximal end along the first side wall to a first distal end; and

a second flange member extending from a proximal end along the second side wall to a second distal end, wherein the first flange member extends over both the top wall of the base member and the second flange member, and the second flange member extends over the top wall of the base member to form a lumen.

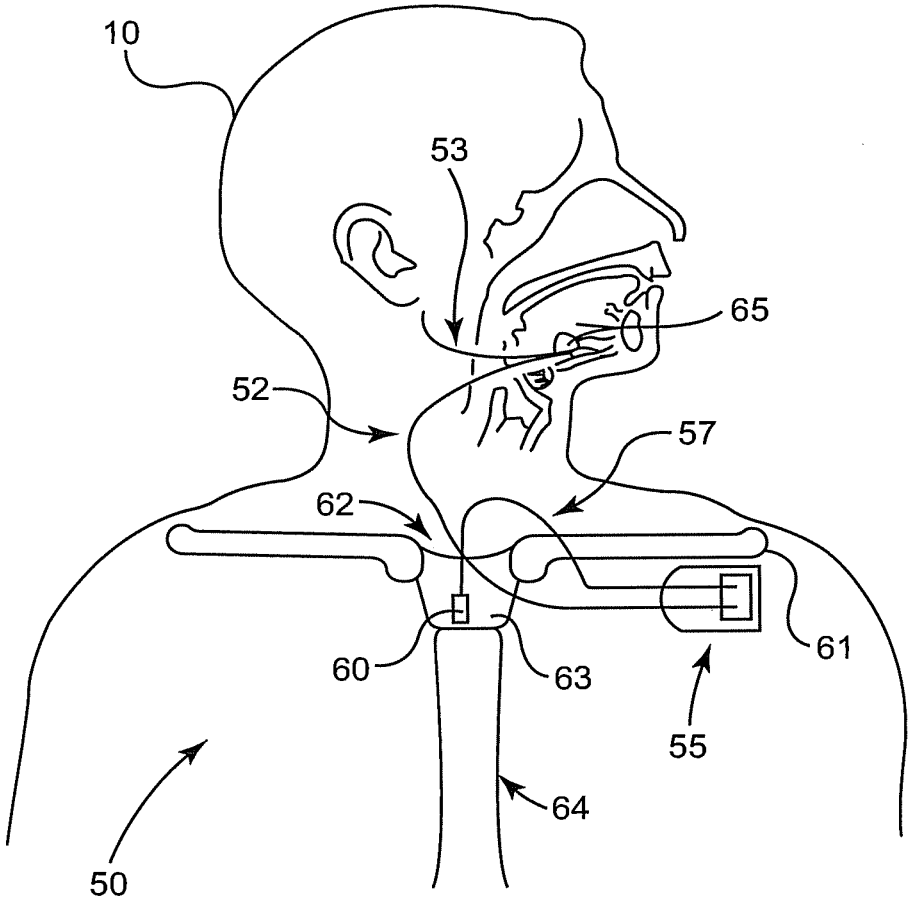


Fig. 1

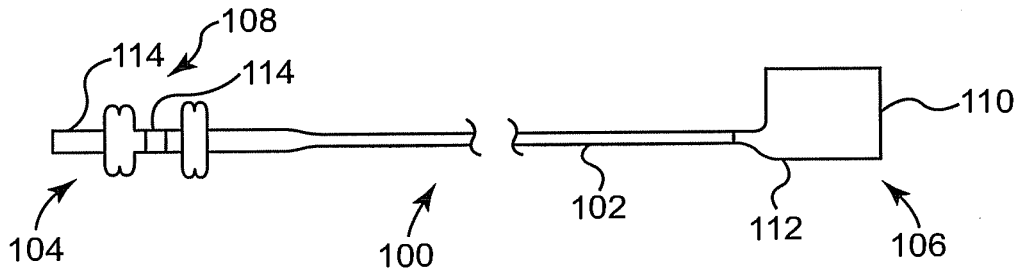

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Fig. 2

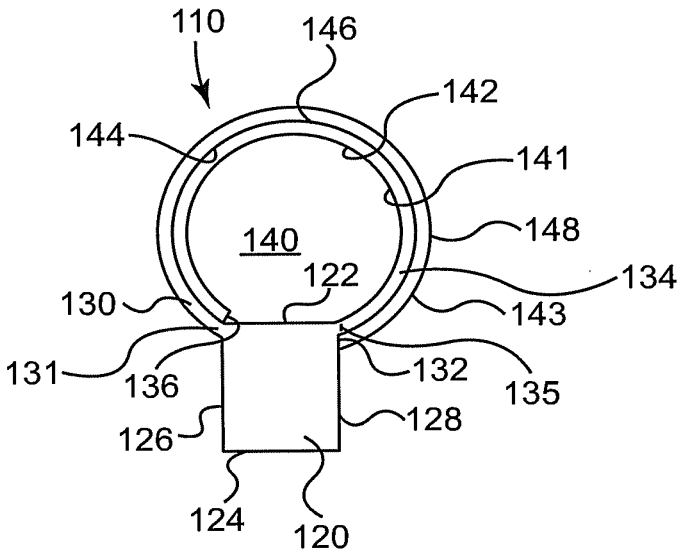

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Fig. 3

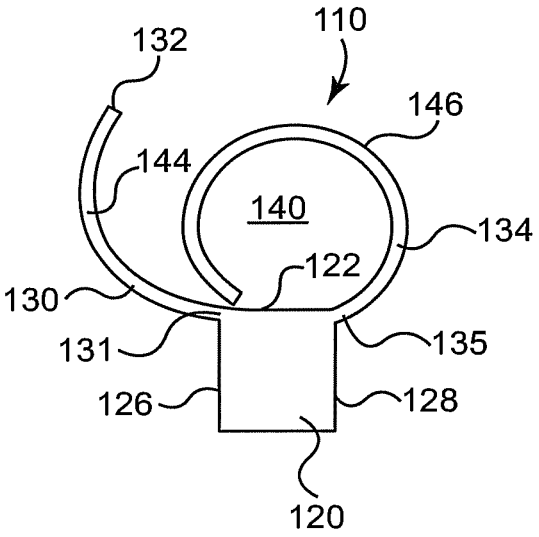

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Fig. 4

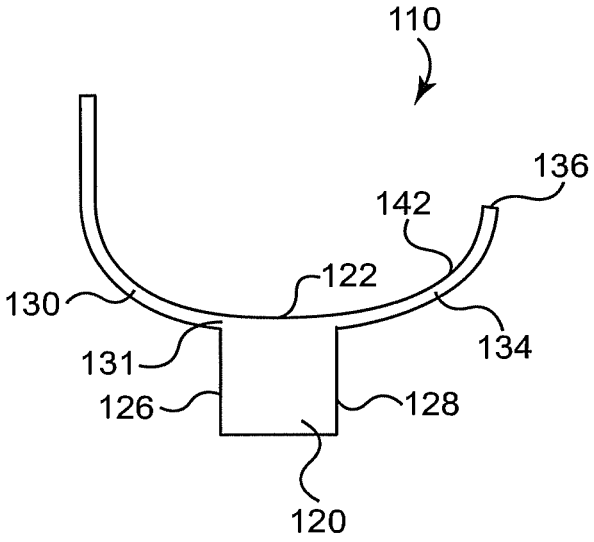

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Fig. 5

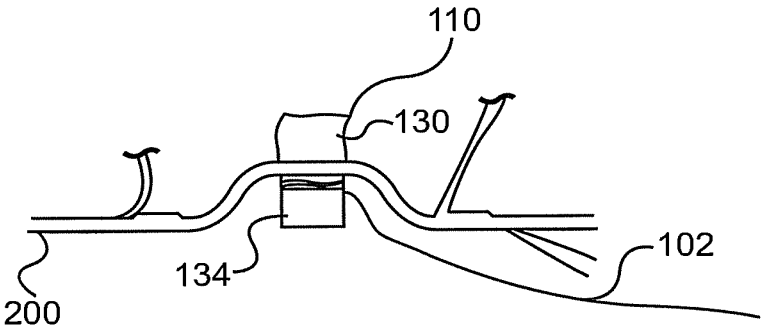


Fig. 6

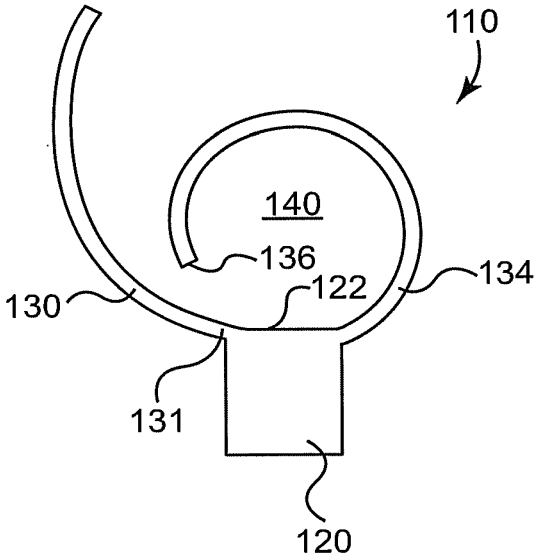


Fig. 7

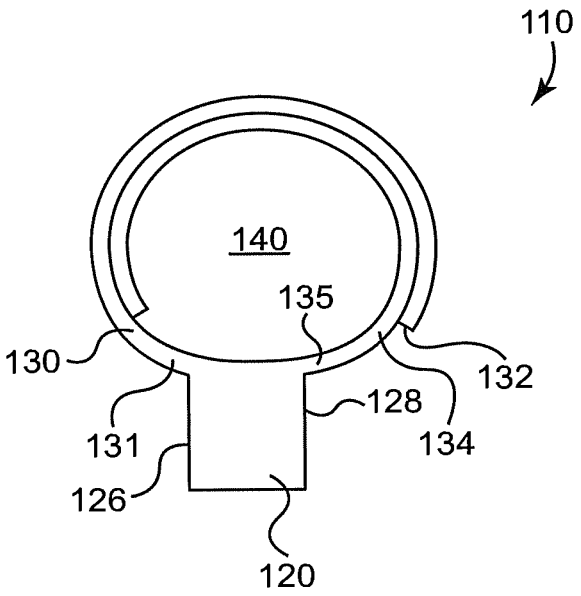

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Fig. 8

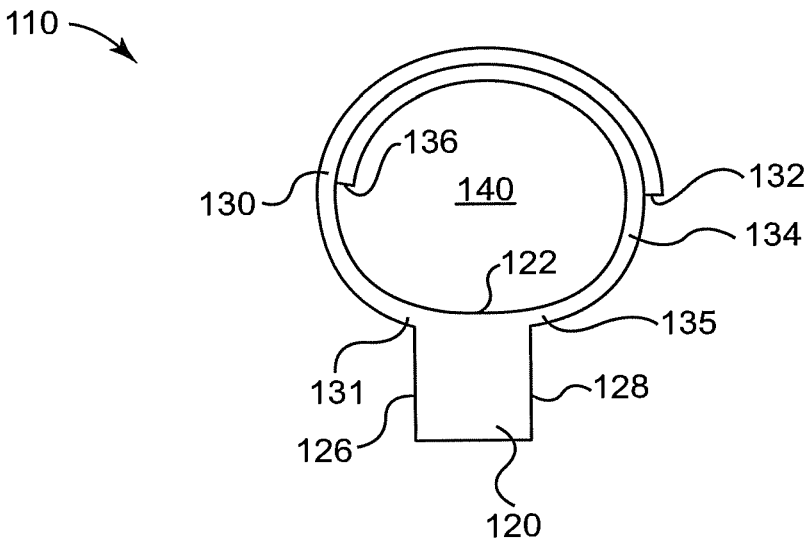

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Fig. 9

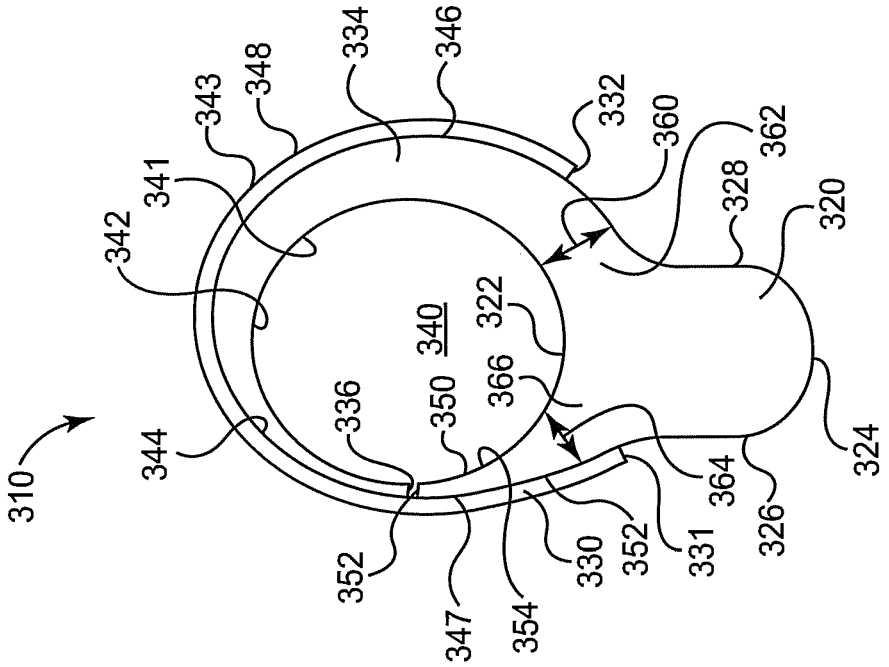

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Fig. 10

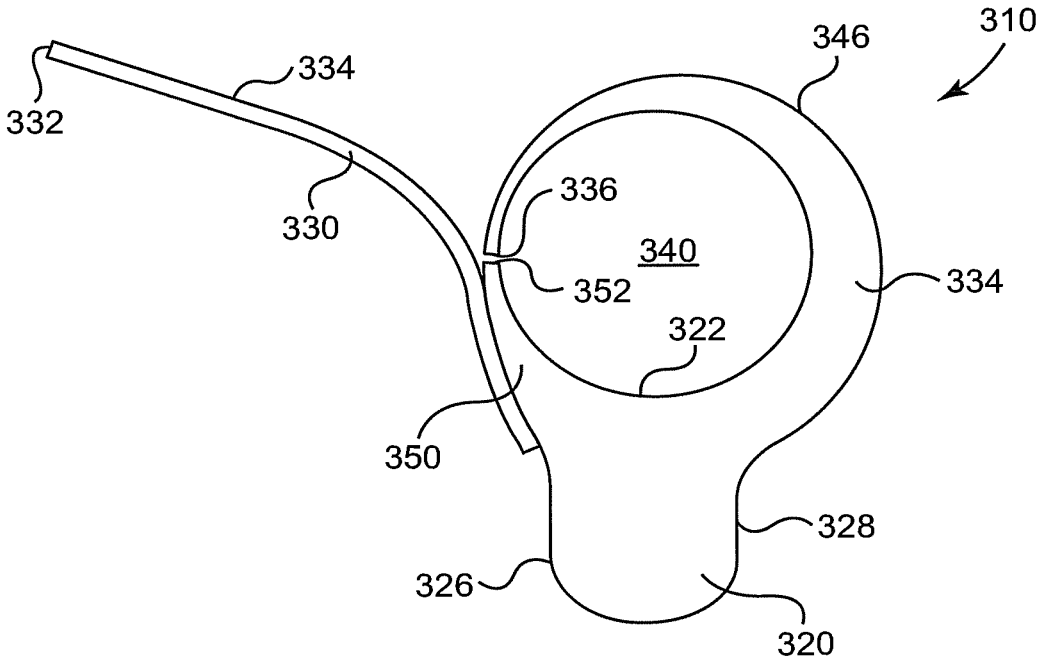

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Fig. 11

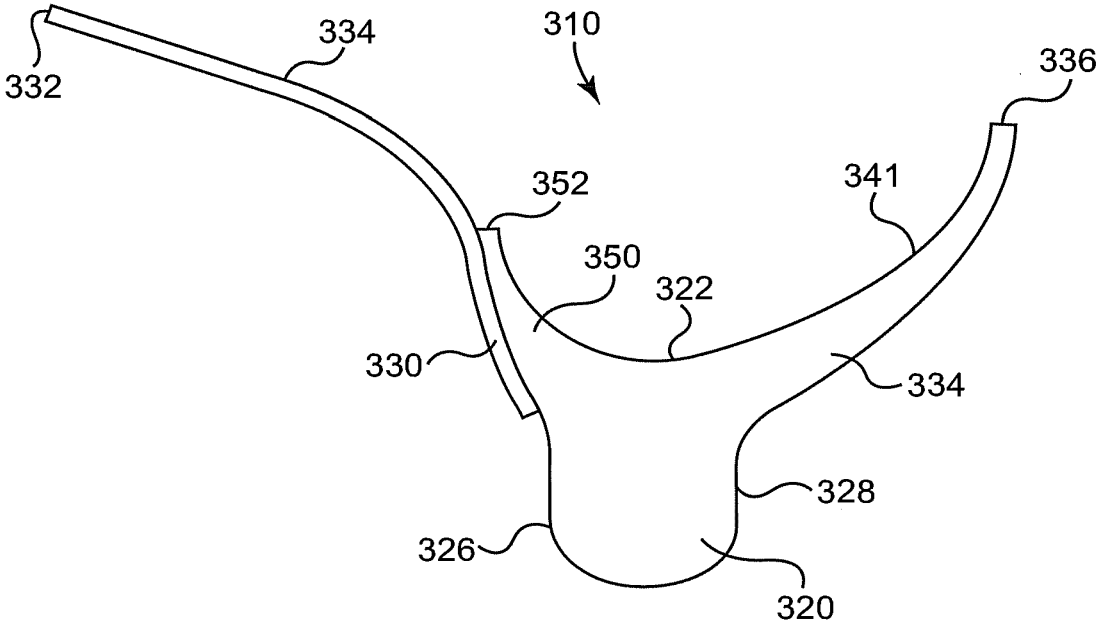

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Fig. 12

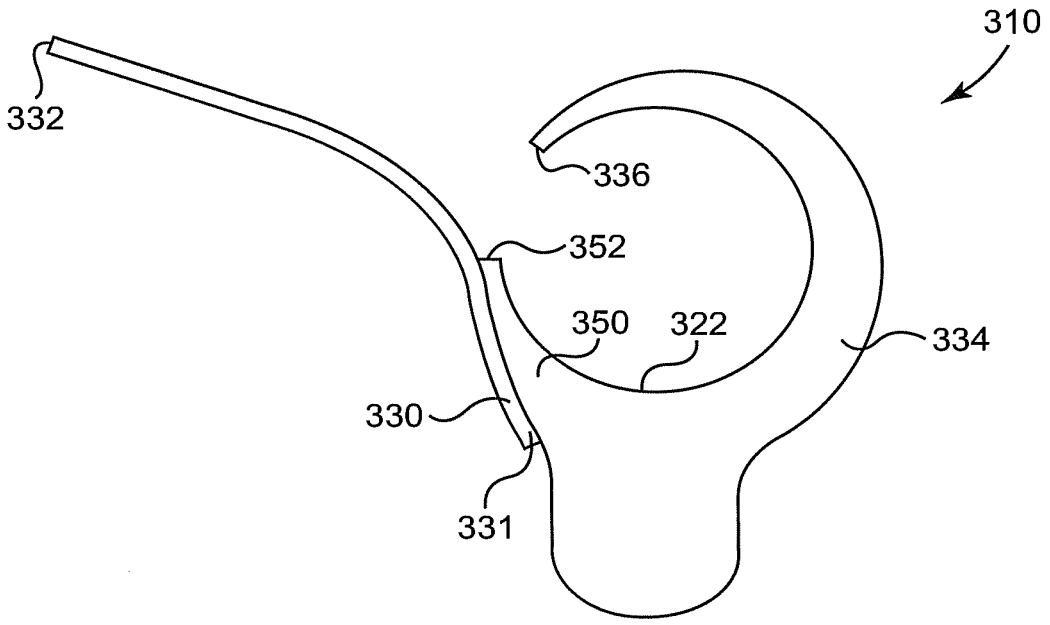


Fig. 13

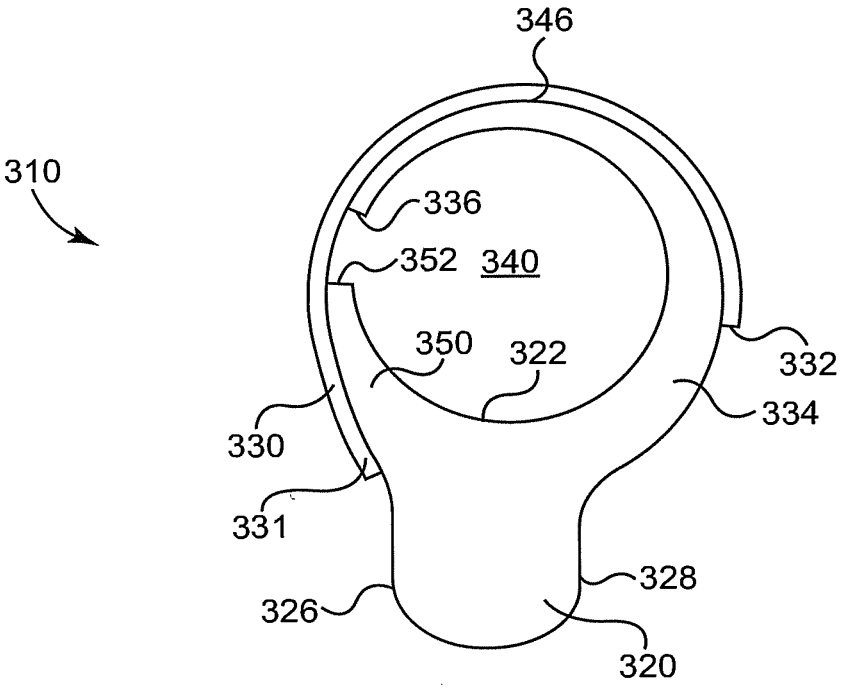

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Fig. 14

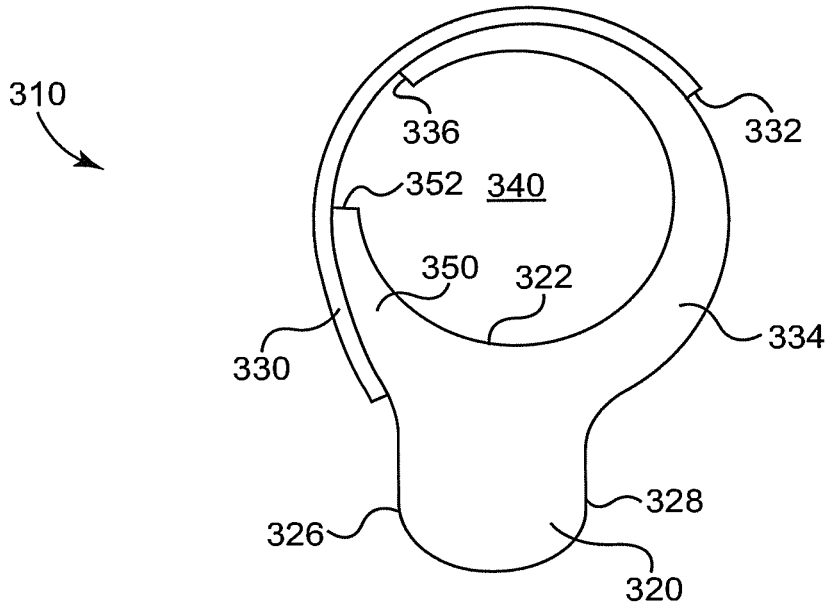

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Fig. 15

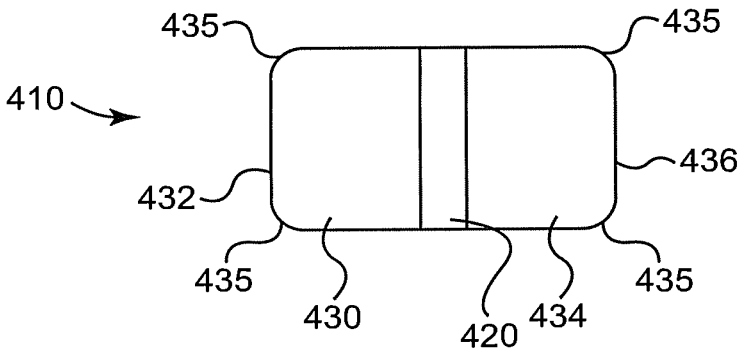


Fig. 16

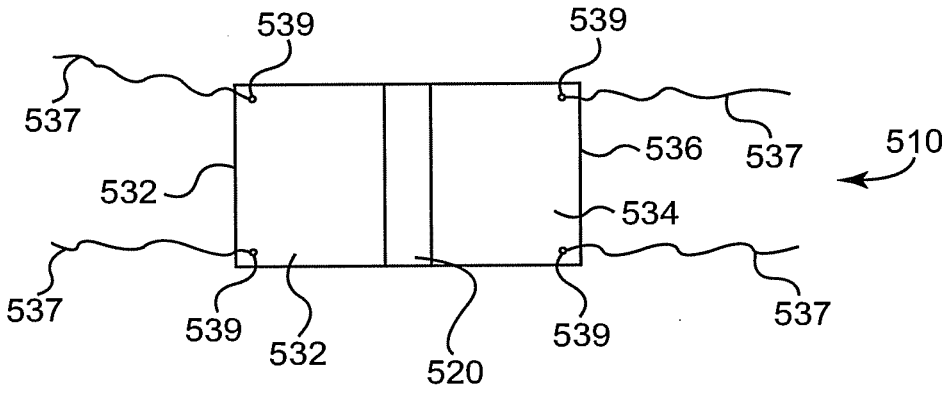


Fig. 17

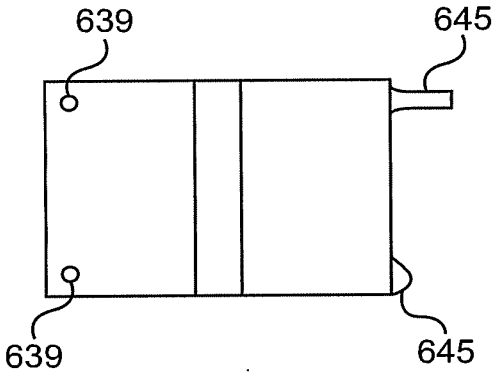


Fig. 18

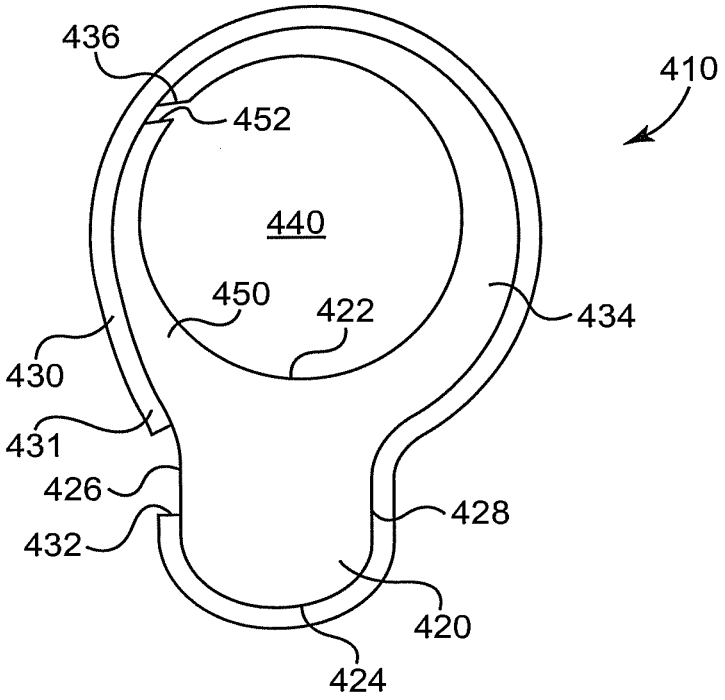

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Fig. 19

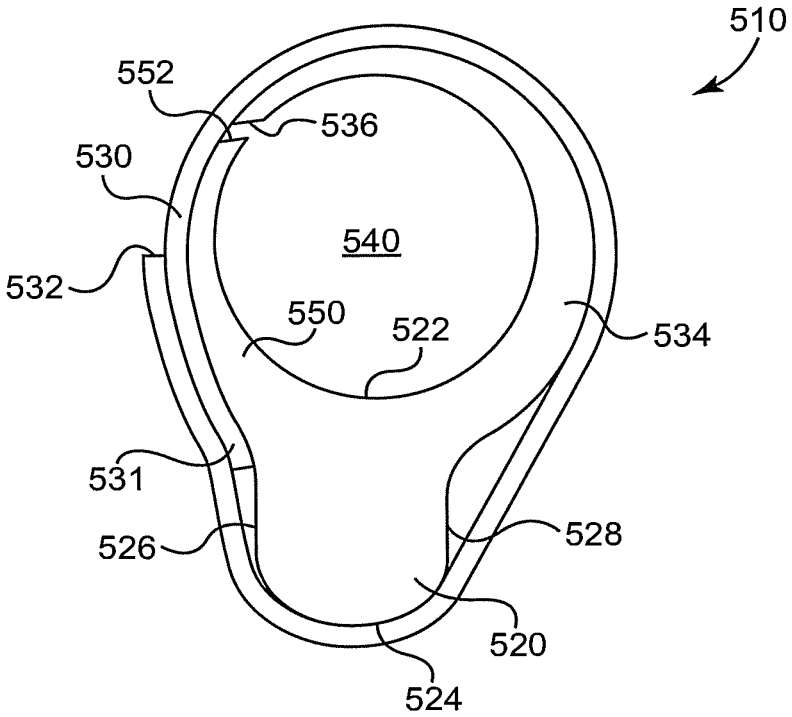

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Fig. 20

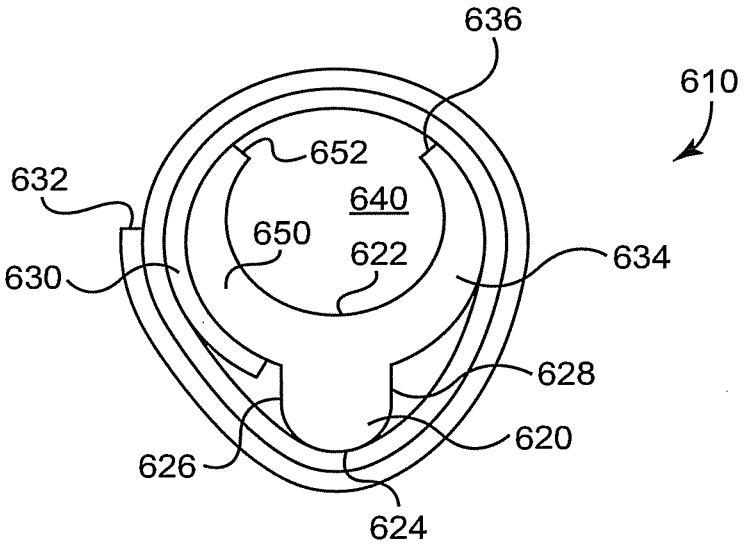


Fig. 21

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/042543

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/05

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/048471 A (APNEX MEDICAL INC [US]; BOLEA STEPHEN L [US]; HOEGH THOMAS B [US]; PER) 24 April 2008 (2008-04-24) paragraphs [0046], [0097], [0098]; figure 1 paragraphs [0065] - [0067]; figure 6 paragraphs [0103] - [0107]; figures 16C,16D,16E,16F paragraph [0109]; figure 18	1-10,22
Y	-----	11,21
X	US 6 093 197 A (BAKULA TOMISLAV [US] ET AL) 25 July 2000 (2000-07-25) column 4, line 30 - column 5, line 47; figures 12-14	1-9,11
Y	-----	11
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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

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"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search	Date of mailing of the international search report
4 August 2009	17/08/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Smit, Jos

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/042543

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 7 248 930 B1 (WOLOSZKO JEAN [US] ET AL) 24 July 2007 (2007-07-24) column 2, lines 42-57; figure 1 column 3, line 30 - column 4, line 31; figures 3,4A,4B,5 column 4, line 54 - column 5, line 12; figures 8-16 column 5, lines 13-26; figures 17A,17B,17C	1,12-22
Y		12,21
Y	US 2006/030919 A1 (MRVA JOSEPH J [US] ET AL) 9 February 2006 (2006-02-09) paragraphs [0032] - [0037]; figures 1,2A,2B paragraphs [0038] - [0040]; figures 3A,3C paragraphs [0043], [0044]; figure 5	12
Y	ELEANOR V GOODALL ET AL: "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 43, no. 8, 1 August 1996 (1996-08-01), XP011006271 ISSN: 0018-9294 pages 851-852	12

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/042543

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008048471 A	24-04-2008	AU 2007313319 A1	24-04-2008
		CA 2666529 A1	24-04-2008
		US 2008103407 A1	01-05-2008
		US 2008103545 A1	01-05-2008
US 6093197 A	25-07-2000	AU 1629999 A	28-06-1999
		WO 9929366 A1	17-06-1999
US 7248930 B1	24-07-2007	DE 69826546 D1	04-11-2004
		DE 69826546 T2	06-10-2005
		EP 0865800 A2	23-09-1998
		US 5938596 A	17-08-1999
US 2006030919 A1	09-02-2006	WO 2006017634 A2	16-02-2006

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 April 2010 (08.04.2010)

PCT

(10) International Publication Number
WO 2010/039853 A1

(51) International Patent Classification:
A61N 1/36 (2006.01) *A61F 2/82* (2006.01)
A61N 1/372 (2006.01)

(21) International Application Number:
PCT/US2009/059060

(22) International Filing Date:
30 September 2009 (30.09.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/101,952 1 October 2008 (01.10.2008) US

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(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **NI, Quan** [US/US]; 5812 Prairie Ridge Drive, Shoreview, Minnesota 55126 (US). **CHRISTOPHERSON, Mark A.** [US/US]; 4100 Reiland Lane, Shoreview, Minnesota 55126 (US). **HERBERT, Timothy P.** [US/US]; 14707 62nd Avenue North, Maple Grove, Minnesota 55311 (US). **RONDONI, John** [US/US]; 2740 Fountain Lane, Plymouth, Minnesota 55447 (US).

(74) Agents: **GRUNZWEIG, Paul S.** et al.; Dicke, Billig & Czaja, PLLC, 100 S. Fifth Street, Suite 2250, Minneapolis, Minnesota 55402 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ,

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(54) Title: TRANSVENOUS METHOD OF TREATING SLEEP APNEA

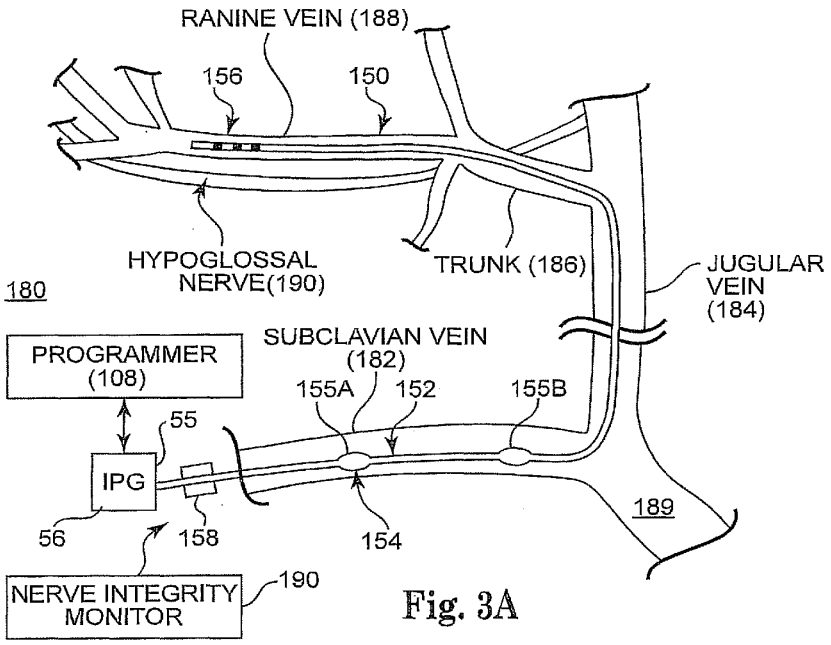


Fig. 3A

(57) Abstract: A system and method for treating sleep apnea includes inserting an implantable pulse generator subcutaneously within a body of a patient and connecting a lead to the pulse generator. The lead is inserted within the vasculature and advanced transvenously through the vasculature until a stimulation portion of the lead becomes positioned in close proximity to the hypoglossal nerve. A nerve-stimulation signal is applied to the hypoglossal nerve via the stimulation portion of the lead.

WO 2010/039853 A1

TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

TRANSVENOUS METHOD OF TREATING SLEEP APNEA

BACKGROUND

[001] The present disclosure relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the present disclosure relates to a method of using a transvenous delivery of a stimulation lead to treat sleep apnea.

[002] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[003] One treatment for obstructive sleep apnea has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a cuff electrode placed around the hypoglossal nerve.

BRIEF DESCRIPTION OF THE DRAWINGS

[004] Aspects and features of the present disclosure will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments of the present disclosure when considered in connection with the accompanying drawings, wherein:

[005] FIG. 1 is a schematic illustration of an implantable stimulation system, according to an embodiment of the present disclosure;

[006] FIG. 2A is a schematic illustration of a block diagram of an implantable stimulation system, according to an embodiment of the present disclosure;

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[007] FIG. 2B is a schematic illustration of a block diagram of a sensing monitor, according to an embodiment of the present disclosure;

[008] FIG. 3A is a schematic illustration of a transvenous placement of a stimulation lead and sensor for treating sleep apnea, according to an embodiment of the present disclosure;

[009] FIG. 3B is a schematic illustration of an array of response evaluation tools and a nerve monitoring system, according to an embodiment of the present disclosure;

[010] FIG. 4A is a schematic illustration of a method of stimulating a nerve via multiple venous pathways and/or via multiple stimulation sites, according to an embodiment of the present disclosure;

[011] FIG. 4B is a schematic illustration of a stimulation lead system including multiple independent stimulation leads, according to an embodiment of the present disclosure;

[012] FIG. 5A is a side plan view of an over-the-wire delivery system for a stimulation lead, according to an embodiment of the present disclosure;

[013] FIG. 5B is a side plan view of an stylet-driven delivery mechanism for a stimulation lead, according to an embodiment of the present disclosure;

[014] FIG. 6 is a schematic illustration of a method of selecting a stimulation site, according to an embodiment of the present disclosure;

[015] FIG. 7 is a schematic illustration of a transvenous placement of a stimulation lead and sensor for treating sleep apnea, according to an embodiment of the present disclosure;

[016] FIG. 8 is a side plan view of a stimulation lead, according to an embodiment of the present disclosure;

[017] FIG. 9 is a side plan view of a stimulation lead including a coiled configuration at a distal portion, according to an embodiment of the present disclosure;

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[018] FIG. 10 is a perspective view of a distal portion of a stimulation lead including an array of ring electrodes, according to an embodiment of the present disclosure;

[019] FIG. 11 is a side plan view of a distal portion of a stimulation lead including a combined stent-electrode configuration, according to an embodiment of the present disclosure;

[020] FIG. 12A is a side plan view of a distal portion of a stimulation lead including an array of selectively deployable tines shown in a deployed configuration, according to an embodiment of the present disclosure;

[021] FIG. 12B is a side plan view of the lead of FIG. 12A with the tines shown in a storage position, according to an embodiment of the present disclosure;

[022] FIG. 13 is a perspective view of a distal portion of a stimulation lead including a programmable array of electrodes mounted circumferentially around the lead, according to an embodiment of the present disclosure;

[023] FIG. 14 is a perspective view of a distal portion of a stimulation lead including an array of programmable ring electrodes, according to an embodiment of the present disclosure;

[024] FIG. 15A is a side plan view schematically illustrating a nerve stimulation system, according to an embodiment of the present disclosure;

[025] FIG. 15B is a schematic illustration of a transvenous placement of a microstimulator of the system of FIG. 15A, according to an embodiment of the present disclosure;

[026] FIG. 15C is a schematic illustration of a garment configured to provide respiratory sensing for the system of FIGS. 15A-15B, according to an embodiment of the present disclosure;

[027] FIG. 16 is a side plan view schematically illustrating an anchoring system of a transvenously delivered microstimulator, according to an embodiment of the present disclosure;

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[028] FIG. 17A is a side plan view schematically illustrating a stent-based anchoring system of a transvenously delivered microstimulator, according to an embodiment of the present disclosure;

[029] FIG. 17B is a sectional view schematically illustrating a microstimulator and a stent of the anchoring system of FIG. 17A, according to an embodiment of the present disclosure; and

[030] FIG. 17C is a side plan view schematically illustrating a microstimulator and a stent of the anchoring system of FIG. 17A, according to an embodiment of the present disclosure.

DESCRIPTION OF EMBODIMENTS

[031] The following detailed description is merely exemplary in nature and is not intended to limit the present disclosure or the application and uses of the present disclosure. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, or the following detailed description.

[032] Embodiments of the present disclosure provide an implantable medical device for treating obstructive sleep apnea wherein stimulation is provided to the hypoglossal nerve (or another target nerve) through a transvenous lead system. The stimulation may be provided synchronous with respiration detected by a sensing lead system. In some embodiments, a single transvenous lead includes both a sensing lead and the stimulation lead, such that the sensing lead is integral with or connected to the stimulation lead. In other embodiments, the sensing lead forms a transvenous lead separate from a transvenous stimulation lead. In still other embodiments, the sensing lead comprises a sensing lead external to the venous system altogether (such as being mounted externally on a patient or subcutaneously implanted) while the stimulation lead comprises a transvenous lead.

[033] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a transvenously placed stimulation electrode, according to an embodiment of the present disclosure. As illustrated in FIG.1, an example of an implantable stimulation system 10 according to one embodiment of the present disclosure

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includes an implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 20, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes a stimulation electrode portion 65 and extends from the IPG 55 so that the stimulation electrode portion 65 is positioned within a portion of the vasculature adjacent a desired nerve, such as the hypoglossal nerve 53 of the patient 10, to enable stimulation of the nerve 53, as described below in detail. An exemplary implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., and which is incorporated herein by reference in its entirety. In one embodiment, the lead 52 further includes an sensor portion 60 (electrically coupled to the IPG 55 and extending from the IPG 55) positioned in the patient 10 for sensing respiratory effort.

[034] In some embodiments, in addition to the IPG 55 being configured to treat obstructive sleep apnea, the IPG 55 is additionally configured as a cardiac therapy device, such as a bradycardia pacemaker, implantable cardiac defibrillator, or cardiac resynchronization therapy device. In one aspect, one or more leads extend from the IPG 55 to access the heart via a transvenous approach in order to apply a cardiac therapy. In one embodiment, one or more of these cardiac therapy configurations of the IPG 55 also have sensors (pressure, impedance) on the cardiac leads which may also provide a respiratory signal for use in delivering an obstructive sleep apnea therapy. Exemplary embodiments of an implantable stimulation system for applying a cardiac therapy via transvenous delivery of a lead is described in Hill et al. U.S. 6,006,134 and Cho et al. U.S. Patent 6,641,542, which are both incorporated by reference herein in their entirety.

[035] In one embodiment in which the IPG 55 is configured to treat both cardiac therapy and sleep apnea, a first lead (or set of leads) extends from the IPG 55 for sensing cardiac activity and detecting cardiac events while a second lead (or set of leads) extends from the IPG 55 to sense respiratory activity and to detect respiratory events. However, in another embodiment, only one set of leads is used to sense both respiratory activity and cardiac activity. Accordingly, in this latter embodiment, in one configuration, a respiratory signal obtained via a cardiac sensing lead is also

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used to trigger application of a stimulation signal when applying an obstructive sleep apnea therapy, and also optionally is used to monitor and detect apneas.

[036] In some embodiments, instead of using a single IPG to apply both cardiac therapies and sleep apnea therapies, a second implantable pulse generator (IPG 55) is implanted (in addition to the first IPG) so that one IPG 55 applies a cardiac therapy while the other IPG 55 applies an obstructive sleep apnea therapy.

[037] Figure 2A is a block diagram schematically illustrating an implantable stimulation system 100, according to one embodiment of the present disclosure. In one embodiment, system 100 comprises at least substantially the same features and attributes as system 10 of Figure 1. As illustrated in Figure 2A, system 100 includes a sensing module 102, a stimulation module 104, a therapy module 106, and a patient management module 108. In one embodiment, the IPG 109 of therapy module 106 comprises at least substantially the same features and attributes as IPG 55 of Figure 1.

[038] Via an array of parameters, the sensing module 102 receives and tracks signals from various physiologic sensors (such as a pressure sensor, blood oxygenation sensor, acoustic sensor, electrocardiogram (ECG) sensor, or impedance sensor) in order to determine a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. Such respiratory detection may be received from either a single sensor or any multiple of sensors, or combination of various physiologic sensors which may provide a more reliable and accurate signal.

[039] For example, in one embodiment, the sensing module 102 comprises a sensing monitor 120, as illustrated in Figure 2B. The sensing monitor 120 includes a body parameter 130, which includes at least one of a position-sensing component 132 or a motion-sensing component 134. In one embodiment, the motion-sensing component 134 tracks sensing of "seismic" activity (via an accelerometer or a piezoelectric transducer) that is indicative of walking, body motion, talking, etc. In another embodiment, the position-sensing component 132 tracks sensing of a body position or posture via an accelerometer or other transducer. In some embodiments,

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body parameter 130 utilizes signals from both the position-sensing component 132 and the motion-sensing component 134.

[040] In some embodiments, sensing monitor 120 additionally comprises one or more of the following parameters: an ECG parameter 136; a time parameter 138; a bio-impedance parameter 140; a pressure parameter 142; and a blood oxygen parameter 144. In one aspect, the pressure parameter 142 includes a respiratory pressure component 143. In one aspect, the time parameter 142 tracks time generally (e.g. time intervals, elapsed time, etc.) while in other aspects, the time parameter 142 tracks the time of day in addition to or instead of the general time parameters. In another aspect, the time parameter 142 can be used to activate or deactivate a therapy regimen according to a time of day.

[041] It is also understood that system 100 (Figure 2A) would include, or be connected to, the analogous physiologic sensor (e.g., LED-type tissue perfusion oxygen saturation) implanted within or attached to the body of the patient to provide data to each one of their respective parameters (e.g., blood oxygenation parameter 144) of the sensing monitor 120. In some embodiments, sensing monitor 120 also includes a target nerve parameter 146 which represents physiologic data regarding the activity of a nerve to be stimulated, such as the hypoglossal nerve, including specification of the trunk and/or one or more branches of the hypoglossal nerve.

[042] In other embodiments, the target nerve comprises another nerve (other than the hypoglossal nerve) that facilitates a therapy regimen to treat obstructive sleep apnea. In yet other embodiments, sensing monitor 120 also includes an acoustic sensing parameter 147 which represents physiologic data from respiratory airflow or cardiac activity that is sensed acoustically and that is indicative of respiratory effort.

[043] In further reference to Figure 2A, therapy manager 106 of system 100 is configured to automatically control initiation, termination, and/or adjustment of a sleep apnea therapy, in accordance with the principles of the present disclosure. Therapy manager 106 also tracks and applies various treatment parameters, such as an amplitude, pulse width, electrode polarity, duration, and/or frequency of a neuro-stimulation signal, in accordance with a treatment protocol programmed into the therapy manager 106.

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[044] In one embodiment, therapy manager 106 comprises one or more processing units and associated memories configured to generate control signals directing the operation of system 100, including at least sensing module 102, therapy manager 106, stimulation module 104, and patient management module 108. In particular, in response to or based upon commands received via an input and/or instructions contained in the memory associated with the controller in response to physiologic data gathered via the sensing module 102, therapy manager 106 generates control signals directing operation of stimulation module 104 to selectively control stimulation of a target nerve, such as the hypoglossal nerve, to restore airway patency and thereby reduce or eliminate apneic events.

[045] With this in mind, therapy manager 106 acts to synthesize respiratory information, to determine suitable stimulation parameters based on that respiratory information, and to direct electrical stimulation to the target nerve. While any number of physiologic parameters can be used with varying success to detect an apnea, in one embodiment of the present disclosure, the sensing module 102 detects apneas via a thoracic bio-impedance parameter. In particular, a measurement of thoracic impedance is used to track the relative amplitude of the respiratory waveform. Physiologically speaking, the bio-impedance of the lungs varies as the lungs fill and empty with air. Accordingly, thoracic impedance increases during inspiration and decreases during expiration. In another aspect, a varying respiratory drive will also cause the amplitude of the bio-impedance to vary, with a larger respiratory drive increasing the signal amplitude of the bio-impedance. In one embodiment, the vector providing the bio-impedance measurement is predominantly lung-volume related, and not due to diaphragm displacement or cardiac displacement during respiration.

[046] Upon obtaining the bio-impedance signal, the bio-impedance signal is further processed to identify an average peak amplitude over time. An apnea is detected by further identifying cyclic amplitude variations that occur for a duration substantially similar to the already known duration of a typical apneic event.

[047] For purposes of this application, the term "processing unit" shall mean a presently developed or future developed processing unit that executes sequences of instructions contained in a memory. Execution of the sequences of instructions

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causes the processing unit to perform steps such as generating control signals. The instructions may be loaded in a random access memory (RAM) for execution by the processing unit from a read only memory (ROM), a mass storage device, or some other persistent storage, as represented by a memory associated with the controller. In other embodiments, hard wired circuitry may be used in place of or in combination with software instructions to implement the functions described. For example, the controller may be embodied as part of one or more application-specific integrated circuits (ASICs). Unless otherwise specifically noted, the controller is not limited to any specific combination of hardware circuitry and software, nor limited to any particular source for the instructions executed by the processing unit.

[048] In general terms, the stimulation module 104 of system 100 is configured to generate and apply a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) 65) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager 106.

[049] In general terms, the patient management module 108 is configured to facilitate communication to and from the IPG 109 in a manner familiar to those skilled in the art. Accordingly, the patient management module 108 is configured to report activities of the IPG 109 (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG 109 from an external source, such as a patient programmer, clinician programmer, etc.

[050] Figure 3A schematically illustrates a lead 150 in one exemplary embodiment of the implantable stimulation system 10 of Figure 1. As shown in Figure 3A, lead 150 is configured to be delivered transvenously and to be positioned within the vasculature. Lead 150 is configured to place a stimulation electrode portion 156 within the ranine vein 188 adjacent the hypoglossal nerve 190 (or another vein adjacent the hypoglossal nerve or another target nerve). In one aspect, the ranine vein is the vena comitans of the hypoglossal nerve, which begins at its distal end at a point below the front of the tongue, travels along the distal portion of the hypoglossal nerve, and then may join the lingual vein, and eventually opens into the internal jugular vein. In another aspect, other veins, such as another branch of the lingual

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vein may also be a candidate for the simulation electrode placement instead of the ranine vein or in addition to the ranine vein.

[051] Accordingly, lead 150 is employable in a method of transvenously delivering a stimulation electrode to stimulate a target nerve. In this method, as illustrated in FIG. 3A, lead 150 is introduced into and through the subclavian vein 182 and then is advanced through the jugular vein 184, through vein trunk 186, and into the ranine vein 190 (otherwise known as the vein comitans of the hypoglossal nerve) until stimulation electrode portion 156 is within a desired position of the ranine vein 180 (or another vein adjacent a target nerve).

[052] In some embodiments, the neuro-stimulation signal is applied at a single stimulation site along the hypoglossal nerve or another target nerve, as illustrated in Figure 3A. However, in other embodiments, the neuro-stimulation signal of a sleep apnea therapy is applied from one or more of multiple locations 230, 232, 234, 240, 242, 244 (represented by the symbol x) within one or more veins to target multiple stimulation sites 190P, 190M, 190D along a target nerve 190, as schematically illustrated in Figure 4A. The electric field applied at each site is represented schematically by the directional arrow extending from the symbol x toward the stimulation site 190M, 190P, 190D on nerve 190. In one aspect, these multiple sites include multiple stimulation locations arranged proximally (e.g., location 230), midway (e.g. location 232), and distally (e.g., location 234) within vein 231 along the hypoglossal nerve 190, one or more stimulation locations on both the right and left hypoglossal nerves, and/or multiple stimulation locations (proximal 240, midportion 242, and distal 244) along another vein 235 adjacent to the hypoglossal nerve 190. While Figure 4A depicts three stimulation sites or regions 190P, 190M, 190P on the target nerve, it is understood that embodiments of the present disclosure are employable to stimulate nerve 190 at any point (or multiple points) between (or distally beyond or proximally beyond) the identified regions 190P, 190M, 190P along nerve 190.

[053] It is understood, as illustrated in Figure 4B, that in some embodiments, a stimulation lead system 275 includes two or more stimulation leads 276,277 that extend from an IPG 55 (Figures 1-2) to enable the separate leads 276,277 to extend down each of the respective different transvenous pathways to enable two or more

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independent stimulation locations on a single target nerve from different veins, such as veins 231 and 235 (Figure 2). In one aspect, each separate lead includes one, two, or more different electrode portions 280, 282, 284 spaced apart from each other along a length of the distal portion 279 of each lead 276, 277, as further illustrated in Figure 4B. In some embodiments, the electrode portions 280, 282, 284 of each lead 276, 277 are arranged with a minimum distance (D1 or D2) therebetween such that the stimulation signal applied at one electrode portion is separate and independent from the stimulation signal applied at the other electrode portions to achieve independent stimulation sites along the same target nerve. Accordingly, the electrode portions of a distal portion of one lead are spaced apart such that when a stimulation signal from a first electrode portion (e.g., electrode portion 280) is applied at one site, the other respective sites are not stimulated by the first electrode portion. Of course, it is also understood that each of the electrode portions 280, 282, 284 can be activated simultaneously to simultaneously apply a signal to each of the spaced apart, independent stimulation sites.

[054] In some embodiments, the spacing D1 and D2 between the electrodes on the first lead 276 is equal to each other and the spacing D3 and D4 between the electrodes on the second lead 277 is equal to each other. In some other embodiments, the spacing D1 and D2 between the electrodes on the first lead 276 (or the spacing D3 and D4 between the electrodes on the second lead 277) is substantially different from each other. In some embodiments, the spacing (D1, D2) between the electrodes on the first lead 276 is the same as the spacing (D3, D4) between the respective electrode portions on the second lead 277. However, in other embodiments, the spacing (D1, D2) between the electrodes on the first lead 276 are the different than the spacing (D3, D4) between the electrode portions on the second lead 277 to account for the different distances traveled transvenously by the respective leads 276, 277 to locate the different respective electrode portions at desired stimulation sites.

[055] It is understood that in other embodiments, the transvenously accessible stimulation sites along one or more nerves are spaced apart from each other by a distance that requires the application of stimulation signals to enable capturing the corresponding portion of the target nerve but wherein the spacing between adjacent

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stimulation sites along the nerve is close enough to allow some overlap between the adjacent stimulation signals.

[056] In some embodiments, the separate stimulation leads 276, 277 of transvenous lead system 275 are positioned transvenously within different veins (e.g., 231 and 235 or a different set of veins) to stimulation different nerves. In this arrangement, one transvenous lead 276 stimulates a first nerve (such as nerve 190) and the other transvenous lead 277 stimulates a second nerve (not shown). In one aspect, each of the first and second nerves are associated with control of the respiratory system such that their selective stimulation relative to a respiratory pattern restores and maintains airway patency to alleviate obstructive sleep apnea.

[057] Referring again to Figure 3A, in some embodiments a nerve integrity monitor (stand alone monitor 190 or integrated into a sleep apnea physician programmer 108, such as programmer 108 in Figure 2) is used to aide the physician in placing the electrode portion 156 of lead 150 in the proper location. In this regard, in one embodiment, the nerve integrity monitor comprises at least substantially the same features and attributes as the nerve integrity monitor described in U.S. Patent 6,334,068, entitled INTRAOPERATIVE NEUROELECTROPHYSIOLOGICAL MONITOR, issued on December 25, 2001, and which is hereby incorporated by reference in its entirety. In other embodiments, other nerve integrity monitors or an equivalent array of instruments (e.g., a stimulation probe and electromyography system) are used to apply the stimulation signal and evaluate the response of the muscle innervated by the target nerve.

[058] In one embodiment, nerve integrity monitor 190 is further illustrated in Figure 3B and comprises stimulation module 192 and a response module 194 that includes electromyography monitoring electronics (EMG) 196.

[059] With this in mind, Figure 3B further illustrates a response evaluation array 300, according to one embodiment of the present disclosure. As shown in Figure 3B, response evaluation array 300 provides one or more mechanisms to evaluate the effectiveness of a target site for stimulating a target nerve. In one embodiment, the array 300 includes: (1) observing or measuring the extent and location (an extension of the base of the tongue is preferred over extension of the tip) of tongue

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motor response 304, such as but not limited to tongue protrusion (indicated by arrow P); (2) observing or measuring the extent of increased cross-sectional area (indicated by arrow W) of an upper respiratory airway 302; (3) measuring the extent of an EMG response 306 (measured via EMG electronics 196 of monitor 190) of one or more muscles upon stimulation applied at a potential target site within a vein; (4) observing or detecting a twitch of the tongue or laryngeal muscle; and/or (5) a substantial reduction in apnea events.

[060] Accordingly, with this in mind, monitor 190 and one or more aspects of the response array 200 is used to evaluate the positioning of a lead within a vein relative to a potential stimulation site on a target nerve. In one aspect, a repetitive stimulation pattern is applied from the stimulation module 192 of nerve integrity monitor 190 to the electrode portion 156 of lead 150 as the lead 150 is advanced distally during navigation of the ranine vein (or other vein). In some embodiments, the applied stimulation pattern is a 1 second burst of stimulation every 3 seconds, a ramping stimulation pattern, and/or a physician controlled burst. In another aspect, electromyography (EMG) monitoring electronics 196 of the nerve integrity monitor 190 enables measuring a muscle response to the nerve stimulation applied during navigation of the target veins. Accordingly, fine wire electrodes 308 (or similar) are connected in electrical communication with the nerve integrity monitor 190 and are used to continuously monitor the muscle activity in response to the stimulation patterns applied via electrode portion 156 during navigation of the lead 150. Using this arrangement, this closed loop feedback will allow the physician to obtain real-time feedback of a position (along the transvenous pathway) of the electrode leads 156 and feedback regarding the ability of the electrode leads 156 to capture the target nerve at a particular position of the electrode leads 156 along the transvenous pathway adjacent the target nerve. It is also understood that the methods described in association with Figures 1-3B for placement of lead 150 are applicable to placement of other leads described in association with Figures 4A-14.

[061] In order to advance and deliver the electrode portion 156 of lead 150 to the target location, one embodiment of the present disclosure employs a delivery mechanism, such as one of the delivery mechanisms illustrated in Figures 5A-5B. In

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most instances, it is expected that the stimulation lead is introduced into a subclavian vein, however, other entry sites are not strictly excluded.

[062] As illustrated in Figure 5A, an over-the-wire lead system 200 includes an implantable lead 202 including at least one lumen (not shown) slidably advancable over a guide wire 204. In use, distal end 206 of steerable guide wire 204 is advanced through the vasculature 180 (Figure 3A) to the target location and then lead 202 is advanced over the proximal portion 205 of guide wire 204 (and along the length of guide wire 204) until electrode portion 208 of lead 202 is located at the target stimulation site. In one aspect, lead 202 is in electrical communication with IPG 55 (Figure 1) to enable IPG 55 to control operation of electrode portion 208 of lead 202. It is also understood that once electrode portion 208 is located optimally along a length of the vein (through which it extends), the lead 202 can be rotated to thereby rotate the electrode portion 208 to apply different stimulation effects to the various fascicles of the target nerve.

[063] In another embodiment, a stylet-driven mechanism is employed to deliver electrode portion 156 of lead 150 to the target location to stimulate the hypoglossal nerve (or another target nerve). With this in mind, Figure 5B illustrates a stylet lead system 220 that includes a lead 222 secured to a guide wire 224. In use, distal end 226 of steerable lead 222 is advanced through the vasculature 180 via advancing and steering guide wire 224 until electrode portion 228 of lead 222 is located at the target stimulation site. In one aspect, lead 202 is in electrical communication with IPG 55 (Figure 1) to enable IPG 55 to control operation of electrode portion 228 of lead 220.

[064] Referring again to Figure 3A, in the one embodiment, lead 150 includes a lead body 152 that supports a respiratory sensor 154 (including first portion 155A and second portion 155B) at a proximal portion of lead body 152. In other words, the respiratory sensor 154 is provided on the same lead body 152 as the electrode portion 156 so that both the respiratory sensor 154 and the electrode portion 156 are placed in the vasculature 180 in a single pass. With this arrangement, as the electrode portion 156 is advanced distally for placement adjacent a target nerve, the respiratory sensor 154 becomes automatically placed within a pectoral region of the patient 20 to enable sensing the respiration pattern of the thorax of the patient. With

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this placement, the sensor 154 detects respiratory features and/or patterns (e.g., inspiration, expiration, respiratory pause, etc.) in order to trigger activation of electrode portion 156 to stimulate a target nerve. Accordingly, with this arrangement, the IPG 55 (Figure 1) receives sensor waveforms from the respiratory sensor 154, thereby enabling the IPG 55 to deliver electrical stimulation synchronously with inspiration, such as with each respiratory breath (or another aspect of the respiratory pattern related to inspiration) according to a therapeutic treatment regimen in accordance with embodiments of the present disclosure. It is also understood that the respiratory sensor 154 is powered by the IPG 55 and the IPG 55 also contains internal circuitry to accept and process the impedance signal from the lead 150.

[065] In some embodiments, a respiratory waveform is monitored and stimulation (generally synchronous with respiration) is not applied until a respiratory feature and/or pattern indicative of an apnea is identified. Stimulation is terminated upon detection that the apneic-indicative feature or pattern is no longer present within the monitored respiratory waveform.

[066] In one embodiment, the respiratory sensor 154 is an impedance sensor. In one aspect, the impedance sensor is configured to sense a bio-impedance signal or pattern whereby the control unit evaluates respiratory patterns within the bio-impedance signal. For bio-impedance sensing, in one embodiment, electric current will be injected through electrode 155B and an electrically conductive portion of case 56 of the IPG 55 (Figure 3A) and voltage will be sensed between electrode 155A and 155B (or also between 155A and the electrically conductive portion of case 56 of IPG 55) to compute the impedance.

[067] In another embodiment of bio-impedance sensing, during the placement of the impedance sensing lead, the impedance waveform can be displayed on the programmer (108) in real time. The location of electrodes 155A and 155B can be interactively (an array of electrodes would be available to select from via a multiplexer switch within the IPG) adjusted to yield the optimal signal to noise ratio in represent the respiratory phase information.

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[068] In another embodiment, the sensor 154 is a pressure sensor. In one aspect, the pressure sensor in this embodiment detects pressure in the thorax of the patient. In another aspect, this pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow). With this configuration, the controller is configured to analyze this pressure sensing information to detect the respiratory patterns of the patient.

[069] In some embodiments, lead 150 includes an anchor 158 that is locatable at a proximal portion of lead body 152. The anchor 158 is configured to ensure that sensor 154 and electrode portion 156 remain in the proper position within the vasculature 180.

[070] The previously introduced Figures 1 and 3A generally depict a stimulation electrode portion 65,156 transvenously delivered into the ranine vein (i.e., the vena comitans of the hypoglossal nerve) to enable stimulating the hypoglossal nerve to treat sleep apnea. In one embodiment of the present disclosure, as illustrated in Figure 6, a method 250 of treating apnea includes identifying an optimal site to locate stimulation electrode portion 156 (Figure 3A) along a length of the ranine vein (or another vein suitable to apply stimulation to the hypoglossal nerve or another target nerve) that will result in a desired stimulation of the hypoglossal nerve. In particular, as illustrated in Figure 6, in a first step 252 the lead 150 is advanced through the vasculature 180 (Figure 3A) to a range of target sites within the ranine vein (or other nearby vein) and a pre-determined electrical stimulus is applied at each potential target site along the ranine vein (at 254). As illustrated at 256, upon the application of the electrical stimulus at each potential target site, the response to the stimulation is identified by: (1) a degree of tongue protrusion; (2) the size of cross-sectional area of the upper airway; (3) a best EMG response indicative of maintaining airway patency; and/or 4) a twitch from either the tongue or laryngeal muscle. As illustrated at 258, using the response data for each potential target site, the method 250 identifies one or more treatment sites (from among the potential target sites along the ranine vein) correlated with the greatest impact on maintaining airway patency during inspiration.

[071] It is also understood that these steps 252-258 can be repeated iteratively, as necessary, until the optimal vein and the optimal stimulation location along that vein

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are identified. With this in mind, in employing method 250, one or more venous pathways might be explored before one or more veins (and a location along that vein(s)) are identified as being an optimal site(s) from which to apply an electrical stimulus. In other words, method 250 is not limited to evaluating target sites within a single vein adjacent a target nerve, but extends to evaluating several different veins adjacent to one or more target nerves. In this regard, method 250 is employed to identify the vein from among a group of veins that enables providing the most efficacious stimulus to a target nerve (e.g., nerves innervating the muscles of the upper airway including the genioglossal, hypoglossus, palatoglossus, etc.), and to identify the best location along one of the those sites to provide the most efficacious stimulus. As previously mentioned, in some embodiments, more than one vein is identified and used so that a stimulation signal is applied from two different veins toward the target nerve.

[072] In one aspect, in evaluating multiple potential stimulation sites along a vein or along multiple veins, at each site the method 250 iteratively applies a stimulation signal with differing values for each signal parameter (e.g., polarity, pulse width, frequency, and amplitude) to determine which combination of values yields the best impact of the stimulation signal upon the target nerve at a potential site. In this way, each potential site is evaluated under conditions in which the stimulation signal would actually be applied were that potential site chosen as an optimal site for stimulation. In one embodiment, this determination of an optimal stimulation site via evaluating each of the stimulation parameters employs therapy module 106 in cooperation with stimulation module 104, a stimulation lead 150, and patient programming module 108, as previously described in association with Figures 1-3A.

[073] Figure 7 illustrates a stimulation lead system 350 to be deployed instead of lead 150, according to one embodiment of the present disclosure. Lead system 350 comprises substantially the same features and attributes as lead 150 (Figure 3) except for providing the sensing portion along a separate lead body 382 from the lead body 352 that supports a stimulation electrode portion (not shown, but similar to electrode portion 156 in Figure 3A). Accordingly, as illustrated in Figure 7, lead system 350 includes a pair of lead bodies 352 and 382 with lead body 352 dedicated to supporting the stimulation electrodes and with lead body 382 dedicated to support

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the sensor 354. The lead body 382 supports sensor 354, including first portion 355A and second portion 355B spaced apart from each other along a length of lead body 382. In one embodiment, the lead body 382 has a length configured to orient both the first portion 355A and the second portion 355B within the subclavian vein 182. However, in other embodiments, the lead body has a length configured to orient one or both of the first portion 355A and the second portion 355B within one or more portions 189 of the vasculature 180 beyond the subclavian vein 182. In any case, sensor 354 is configured to monitor respiratory effort to detect patterns indicative of apneas/hypopneas, and to detect the patterns of inspiration, expiration, and/or respiratory pause, which may be used to trigger a therapeutic stimulation.

[074] In some embodiments, sensor lead 382 of lead system 350 is not placed transvenously but is implanted subcutaneously, either adjacent to the pocket housing the IPG 55 or tunneled within tissue in the pectoral region surrounding the IPG 55. In other embodiments, sensor lead 382 additionally comprises a cardiac lead (epicardial or intra-cardiac) that is also used for a cardiac therapy (for example, therapies such as bradycardia, tachycardia, or heart failure).

[075] While various different shapes and forms of leads can be used in the methods and systems of the present disclosure, Figures 8-14 illustrate several different exemplary embodiments of leads. In at least some of these embodiments, a fixation mechanism provides releasable fixation for a stimulation lead so that transvenous placement of a stimulation lead can be maintained for semi-permanent time period or can be reversed (i.e., removed) if necessary.

[076] Figure 8 is a side plan view schematically illustrating a lead 400 including a lead body 402 having a proximal portion 404 and a distal portion 406, which supports a stimulation electrode array 409. The electrode array 409 includes one or more surface electrodes 410 spaced apart along a length of the distal portion 406 of the lead body 402. In some embodiments, lead 400 includes an anchor 408 at the proximal portion 404 of lead body 402, which is configured to maintain the position of the lead body 402 relative to a length of the vein(s) through which the lead body 402 extends. In one aspect, this anchor 408 facilitates maintaining the position of the stimulation electrode array 409 at a desired site within the vein adjacent a desired stimulation site of the target nerve.

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[077] Once implanted, a transvenous stimulation system for automatically treating obstructive sleep apnea must remain stable and endure the normal activities of the patient. For example, the neck of a patient moves through a wide range of motion through many different positions. To counteract the potential for a stimulation lead to move back and forth within a vein (relative to a desired stimulation site), embodiments of the present disclosure provide an anchoring mechanism to anchor a distal portion of a stimulation lead within a vein at the desired stimulation site relative to a target nerve. These anchoring mechanisms insure that proper placement of the stimulation lead is maintained despite the dynamic motion and varying positions of the neck, which could otherwise cause inadvertent repositioning of the stimulation lead (relative to the target nerve) if the distal anchoring mechanisms were not present. Several embodiments of a distal anchoring mechanism are described and illustrated in association with Figures 9 and 11-14.

[078] Figure 9 is a side plan view schematically illustrating a lead 430 including a distal anchoring mechanism, in accordance with one embodiment of the present disclosure. In this embodiment, a lead 430 includes a lead body 432 having a proximal portion 434 and a distal portion 436, which supports a stimulation electrode array 439, as illustrated in Figure 9. The electrode array 439 includes one or more surface electrodes 440 spaced apart along a length of the distal portion 436 of the lead body 432. In another aspect, distal portion 436 of lead body 432 comprises a distal anchoring mechanism arranged as a coiled configuration 450 and which is configured to maintain the position of the lead body 402 relative to a length of the vein(s) through which the lead body 402 extends. This coiled configuration acts to fix the distal portion 436 of the lead body 432 within the vein at the location at which the electrodes 440 will apply an electrical stimulus. In one aspect, prior to insertion of the lead 430 into the venous system, the distal portion 436 is in the coiled configuration 450. However, in order to install the lead 432 into the venous system, the distal portion 436 is converted from the coiled configuration 450 into a generally straight configuration (i.e., lacking coils) by advancing the guide wire through at least the distal portion 436 of the lead body 432. After maneuvering the guide wire and the lead 430 to the desired location within the venous system, the guide wire is removed proximally from the lead body 432, which allows the distal portion 436 to return to the coiled configuration 450. In one embodiment, this "memory effect" of

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the coiled configuration is achieved via incorporating materials such as Nitonal or thermo-formed polyurethane into the distal portion 436. In other embodiments, other materials having memory behavior, as known by those skilled in the art, are employed to form distal portion 436, thereby enabling the operation of coiled configuration 450.

[079] In another aspect, as previously described in connection with method 250, each of the various stimulation parameters (for example, electrode polarity, amplitude, frequency, pulse width, and duration) are tested at each potential stimulation site as the stimulation lead 430 is maneuvered (through the venous system) adjacent to the target nerve. By evaluating the response at each location along the venous system (in the target nerve region) and noting the particular value or combination of stimulation parameters that yields the best response at that potential location, one can determine the optimal stimulation site for stimulation electrode array 439. As previously described herein, this method of determining a stimulation site (according to an effective group of corresponding values for the stimulation parameters) can be applied to anyone of the different stimulation electrode configurations within this present disclosure.

[080] In another embodiment of the stimulation leads and as previously described in association with Figures 1-4B, two individual branches of the stimulation lead or two independent stimulation leads can be placed transvenously near both left and right side of the hypoglossal nerve. The IPG and programmer can control stimulation delivery to each branches of the stimulation lead either independently or dependently.

[081] Figure 10 is a perspective view illustrating another embodiment of the present disclosure. In this embodiment, a lead 500 includes an array of ring electrodes 502, 504, 506 at a distal portion of the lead 500 and which is configured to apply an electrical stimulus to a target nerve. In one aspect, this array of ring electrodes 502-506 is configured to direct an electrical field to a target nerve (e.g., hypoglossal nerve) spaced apart from the lead 500 within the vein (e.g., ranine vein). It is also understood that the ring electrodes 502-506 can be optionally employed in one or more of the other embodiments described in association with Figures 8-9 and 11-14.

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[082] Figure 11 is a perspective view schematically illustrating a lead 520 including a distal anchoring mechanism, in accordance with one embodiment of the present disclosure. In this embodiment, the lead 520 includes a stent portion 522 at a distal portion of the lead 520, and in which the stent portion 522 includes one or more stimulation electrodes 524, 526, 528 incorporated into (or added onto) the structure (e.g., struts) of the stent. In one aspect, this array of electrodes 524-528 supported by the stent structure 522 is configured to direct an electrical field to a target nerve (e.g., hypoglossal nerve) spaced apart from the lead 500 within the vein (e.g., ranine vein). Moreover, the stent structure 522 provides a mechanism to secure the location of the electrodes 524-528 at a desired placement along a length of the vein (through which the lead 520 extends) corresponding to a desired stimulation site of a target nerve.

[083] In one embodiment, the stent structure 522 is arranged in a collapsed state (having a diameter generally represented by A in Figure 11) during insertion into the venous system and the vein adjacent the target nerve. Once the stent structure 522 and associated stimulation electrodes are located a potential stimulation site, the physician initiates conversion of the stent structure 522 from its collapsed state to an expanded state (having a diameter generally represented by B in Figure 11) to contact the walls of the vein, which in turn, anchors the electrodes in place. In other words, the stent structure 522 acts as a distal fixation mechanism that fixates the distal portion of the lead within the vein at the desired stimulation site. In one aspect, during the process of evaluating different potential stimulation sites, the stent structure is temporarily expanded to test the effectiveness of a stimulation signal at a potential stimulation site and then re-collapsed to enable repositioning the lead 520 along the vein to place the electrodes and stent structure at a different potential stimulation site. This process is repeated as many times as necessary until the optimal stimulation site is determined, where the stent structure 522 is then re-expanded to secure and maintain the distal portion of the lead 520 at the optimal stimulation site. It is understood that the selective expansion, collapse, and final fixation of the stent structure in an expanded state is performed according to techniques known in the art, such as manipulating the stent structure 522 via rotation, pushing, and/or pulling of a guide wire.

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[084] In other embodiments, instead of using the coiled configuration 350 of Figure 9 or the stent structure of Figure 11, fixation of a distal portion of a stimulation lead within a vein is achieved via other mechanisms.

[085] Figures 12A-12B schematically illustrate a transvenous stimulation lead 530 including a distal fixation mechanism, according to one embodiment of the present disclosure. As illustrated in Figure 12A, a distal portion 531 of the stimulation lead 530 includes a distal fixation mechanism provided via an array 532 of deployable tines 534. In Figure 12A, tines 534 are shown in a deployed configuration in which tines 534 extend radially from the body of distal portion 531 of lead 530. In this position, the tines 534 are configured to releasably engage the walls of a vein to thereby anchor the distal portion 531 within the vein. It is understood that the tines are configured in a manner as to not negatively impact the integrity of the walls of the vein.

[086] In one aspect, as the distal portion of the lead is advanced through the venous system, a guidewire is used to position these tines 534 into a storage position generally against an outer wall of the lead, as schematically illustrated in Figure 12B. After a suitable stimulation site has been determined, the tines 534 are deployed (i.e., selectively expanded radially outward away from the outer wall of the lead as shown in Figure 12A) to engage the walls of the vein to thereby anchor the distal portion 531 of the lead at the desired stimulation site along that vein (and adjacent to the desired location along the target nerve). In some embodiments, the deployable tines 534 are made of a polyurethane material and/or a Nitonal spring.

[087] It is understood that the array 532 of tines 534 is located on distal portion 531 of lead 530 at a position sufficiently close to an electrode stimulation portion of lead 530 (such as one of the electrode configurations illustrated throughout this application) to insure that the electrode stimulation portion is generally fixed within a vein at a location corresponding to a desired stimulation site of a target nerve.

[088] Figure 13 is a perspective view illustrating a transvenous stimulation lead 540 configured to apply an electrical stimulus to a target nerve, according to another embodiment of the present disclosure. In this embodiment, the lead 540 includes a series 541 of programmable arrays 542, 544, 546 of electrode portions 548 with the

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respective arrays 542, 544, 546 spaced apart from each other along a length of the distal portion of the lead 540. In one aspect, the respective electrode portions 548 of each array extend circumferentially about an outer surface of lead 540 in a spaced apart relationship to form a general ring-shaped configuration. In one aspect, the programmable arrays 542-546 of electrode portions 548 are configured to direct an electrical field from a location within the vein (e.g., ranine vein) to a target nerve (e.g., hypoglossal nerve) spaced apart from the lead 540. It is also understood that the arrays 542-546 of electrodes can be optionally employed in one or more of the other embodiments described in association with Figures 8-9 and 11-12B.

[089] In one embodiment, each array 542, 544, 546 of electrodes comprises two, three, four or more independent electrode portions 548. In one aspect, the electrode portions 548 are independently programmed to stimulation the target stimulation site. In other words, at any given time, a stimulation signal is applied from zero, one, two, or more electrode portions 548 of each separate array 542-546. In this embodiment, the many varied positions of the electrode portions both along the length of the distal portion of the lead 540 and circumferentially or radially about the lead 540 enables precise activation of selective groups of electrode portions 548 (at their various spaced apart locations) to produce a stimulation signal at virtually any point relative to the distal portion of lead 540. Accordingly, this arrangement enables stimulation of a target nerve (or select portions/fascicles of a target nerve) with little or no rotation of the lead 540 to direct the stimulation to the target stimulation site.

[090] Figure 14 is a perspective view illustrating a transvenous stimulation lead 560 configured to apply an electrical stimulus to a target nerve, according to another embodiment of the present disclosure. In this embodiment, a lead 560 includes a programmable array of ring electrodes 562 mounted at a distal portion 564 of the lead 560. In one aspect, this programmable array of ring electrodes 562 is configured to direct an electrical field from the location of the respective ring electrodes 562 within the vein (e.g., ranine vein) to a target nerve (e.g., hypoglossal nerve) spaced apart from the lead 560. It is also understood that the ring electrodes 562 can be optionally employed in one or more of the other embodiments described in association with Figures 8-9 and 11-12B. In one embodiment, each ring 562 may be independently programmed to stimulate the target stimulation site. In this

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embodiment, the many varied positions of the ring electrodes 562 along the length of the distal portion of the lead 560 enables precise activation one, two, or more ring electrodes 562 (at their various spaced apart locations) to produce a stimulation signal at virtually any point along a length of the distal portion of lead 560. Accordingly, this arrangement enables stimulation of a target nerve with little or no rotation of the lead 560 to direct the stimulation to the target stimulation site. Moreover, once lead 560 is located generally in the region of interest, the lead 560 need not be maneuvered extensively distally or proximally within the vein in order to position an electrode adjacent to a desired stimulation site of a nerve because any one or combination of the ring electrodes 562 along the length of the distal portion of the lead are available for activation to apply a stimulation signal to the target nerve. In one embodiment, the array of electrodes 562 has a length that substantially matches a majority of a length of the hypoglossal nerve, as it extends from a position near the jugular vein toward the genioglossus muscle. In one aspect, this length of the array enables determining which electrodes 562 of the array produce the most efficacious respiratory airway patency without having to reposition the array within the vasculature. In another aspect, an efficacious respiratory airway patency is determined upon identifying which ring electrode 562 or combination of ring electrodes 562 produces a longest duration of increased airway patency, a largest size of increased airway patency, and/or a substantial reduction in apneas.

[091] In this embodiment, the lead does not require rotation of the lead to direct the stimulation to the target stimulation site. Further with multiple rings attached the control unit, minimal positioning of the lead within the vein is required as optimal stimulation settings may be evaluated using multiple combinations of active or inactive electrode rings.

[092] Several different embodiments have been described in association with Figures 1-7, in which an IPG 55 is implanted in a pectoral region and in which a sensor electrode(s) and a stimulation electrode(s) (extending from the IPG 55) are delivered transvenously to sense respiratory patterns and to apply a stimulation signal, respectively. In addition, several embodiments of stimulation electrode arrays (and associated distal fixation mechanisms) have been described in association with Figures 8-14. Moreover, it is understood that in some embodiments, a lead is

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transvenously placed in each side of the body (left and right) such that bilateral (simultaneous or alternating) stimulation takes place on the left and/or right hypoglossal nerve (or other target nerve). With these various embodiments in mind, it is further understood that among those embodiments, several configurations are provided in which at least two electrodes are spaced apart in the body in the vicinity of the upper airway such that an impedance is measurable between the two spaced apart electrodes to provide an indication of airway patency (e.g., opening and/or closing of the upper airway). For example, to measure this impedance, one of the stimulations electrodes is placed transvenously on a first side of the body and the other one of the stimulation electrodes is placed transvenously on a second side of the body. In some embodiments, this bio-impedance is measured as a trans-thoracic bio-impedance, a trans-laryngeal bio-impedance, or a trans-pharyngeal bio-impedance.

[093] In some configurations, the spaced electrodes are both stimulation electrodes, while in other configurations, the spaced apart electrodes comprise one stimulation electrode and one respiratory sensor electrode. In yet other configurations, the two spaced apart electrodes (used for measuring an impedance indicative of airway patency) include one of the electrodes comprising at least one of a stimulation electrode and a respiratory sensor electrode and the other one of the electrodes comprising an electrode formed by an electrically conductive portion of a case 56 or housing of the IPG 55.

[094] Moreover, in some embodiments, the respective electrodes portions provide a dual function in that each electrode provides a respiratory sensing function or a stimulation function as well as acting as a part of a pair of impedance sensing electrodes. On the other hand, in other embodiments, at least one electrode of the pair of impedance sensing electrodes does not also act to sense respiration (e.g. inspiration) or to stimulate but rather is dedicated for use in sensing impedance to detect or indicate a degree of airway patency.

[095] Accordingly, by using a pair of electrodes to sense an impedance that is indicative of airway patency, a system operating according principles of the present disclosure enables detection of apnea event by indicating whether or not a collapse of the airway has taken place. In one embodiment, this impedance-based indication

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of airway patency is used along with other physiologic sensing information (such as the sensing information described at least in association with Figures 2A-2B) to detect an apnea event, and to potentially trigger stimulation of a target nerve to restore airway patency in accordance with the embodiments of the present disclosure.

[096] FIG. 15A is a side plan view schematically illustrating a nerve stimulation system 600 for treating obstructive sleep apnea, according to an embodiment of the present disclosure. In this embodiment, as illustrated in Figure 15A, system 600 provides therapy to a patient 602 reclined on a support 604 (e.g. a bed) and a headrest structure 606 (e.g., pillow), which houses a power source/controller 622 and one or more radiofrequency transmission coils 620. However, it is understood that this embodiment is not strictly limited to a bed 604 and/or pillow, but extends to other furniture configurations in which the patient 602 can remain stationary for an extended period of time. As further illustrated in Figure 15A, system 600 includes a microstimulator 635 which is delivered transvenously into the ranine vein 188 (or other nearby vein) for stimulating the hypoglossal nerve 190 (or other target nerve), as illustrated in Figure 15B. In some embodiments, transvenous delivery of microstimulator 635 is accomplished via techniques substantially similar to those previously described in association with Figures 9, 11, 12A-12B, as well as via transvenous delivery methods to be further described in association with Figures 16-17C.

[097] In one embodiment, microstimulator 635 comprises a generally elongate member including circuitry for generating a neurostimulation signal and at least one electrode 637 arranged on a surface of the micro stimulator 635 for transmitting the signal to nerve 190, as illustrated in Figure 15B. In some embodiments, microstimulator 635 comprises a microminiature electronic device such as that described in Richmond et al. U.S. Patent 6,240,316, and which is hereby incorporated by reference in its entirety. However, it is understood that in the context of the present disclosure, such micro stimulators are delivered transvenously instead of being directly implanted into a target muscle.

[098] In general terms, system 600 applies a treatment regimen for treating obstructive sleep apnea according to sensing methods and stimulation parameters at

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least substantially the same as those previously described in association with Figures 1—14, including the potential use of bilateral stimulation (for simultaneous or alternate stimulation from the left and right sides of the body) via the use of two separate microstimulators.

[099] Referring again to Figure 15A, system 600 includes at least one sensing component configured to provide respiratory sensing suitable for detection of an apnea and for triggering application of the stimulation signal synchronous with respiration, such as with inspiration. In some embodiments, respiratory sensing is provided via an externally securable belt 630 including a respiratory pressure sensor 631. Signals sensed at sensor 631 are transmitted wirelessly to power/controller 622 for use in apnea detection and treatment. In other embodiments, respiratory sensing is provided via an impedance sensor 640 which is secured on an external surface of a chest via a patch or even implanted subcutaneously. Sensor 640 communicates wirelessly with power/controller 622. In some embodiments, belt 630 or the other sensor 640 includes an accelerometer or piezoelectric transducer for detecting body motion/position, with such information also being used by controller 622 and/or microstimulator 635 to determine when to monitor for apneas and/or when to treat apneas.

[0100] In use, as the patient reclines on the support 604, respiratory sensor 631 or 640 provides information about respiratory effort which is monitored via a power/controller 622. Once a treatment threshold is detected, power/controller 622 generates power which is communicated to micro stimulator 635 via radiofrequency/transmission coils 620. It is also understood that in some embodiments, microstimulator 635 stores programmed instructions for applying a stimulation signal according to an obstructive sleep apnea treatment regimen, while in other embodiments micro stimulator 635 receives such programmed instructions from controller 622 via coils 620. In either case, the instructions are also programmable by a clinician or by a patient (within certain physician-authorized constraints). With this in mind, the microstimulator 635, in turn, selectively stimulates nerve 190 (Figure 15B) according to a treatment regimen to restore airway patency, thereby alleviating the obstructive sleep apnea.

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[0101] In some embodiments, as illustrated in Figure 15C, respiratory sensing information is obtained via sensors arranged on a garment 675 configured to be worn by the patient 602 during a time period when apneas might potentially occur (e.g. sleeping, resting). In one embodiment, garment 675 provides a respiration sensing belt 682 similar to belt 630, while in other embodiments garment 675 comprises one or more impedance sensors or other respiratory effort sensors 684 (and/or body motion/position detectors) on a pectoral region 680 of the garment 675.

[0102] FIG. 16 is a side plan view schematically illustrating an anchoring system of a transvenously delivered microstimulator, according to an embodiment of the present disclosure. Accordingly, in some embodiments, as illustrated in Figure 16, a transvenous delivery mechanism 700 includes a steerable catheter/stylet 710 including a proximal portion 714 and a distal portion 712. The micro stimulator 635 is releasably secured at distal portion 712 of steerable catheter/stylet 710 via release mechanism 730. Using techniques known to those skilled in the art, catheter 710 is used to advance and maneuver the microstimulator 635 transvenously until adjacent to a desired stimulation site of a target nerve. At this location, the release mechanism 730 is activated to secure micro stimulator 635 within the vein adjacent the target nerve and the remainder the catheter 710 is then withdrawn from the vein leaving the microstimulator 635 within the vein. While various mechanisms can be used to secure the microstimulator 635 within the vein, in this embodiment, an array of selectively deployable tines 720 (or other selectively deployable anchors) extends radially outward from micro stimulator 635 to secure the microstimulator 635 relative to the vein and, thereby relative to the target nerve.

[0103] FIG. 17A is a side plan view schematically illustrating a stent-based anchoring system of a transvenously delivered microstimulator configured to treat obstructive sleep apnea, according to an embodiment of the present disclosure. In this embodiment, a microstimulator 635 is coupled to a stent 770. A steerable catheter/stylet 760 is adapted to transvenously deliver (using techniques known to those skilled in the art) the combination of the stent 770 (in its collapsed state) and the microstimulator 635 to a location within a vein adjacent a target nerve. Further manipulation of the steerable catheter 760 results in release and expansion of the stent 770 to be secured relative to the walls of the vein and then withdrawal of the

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catheter/stylet 760. With this arrangement, the microstimulator 635 becomes generally fixed relative to a length of the vein and therefore generally fixed relative to a portion of the target nerve.

[0104] In some embodiments, micro stimulator 635 is coupled to extend within an interior 771 of stent 770, as illustrated in Figure 17B. In one embodiment, micro stimulator 635 is coupled relative to the stent 770 via one or more semi- rigid or resilient tethers 772.

[0105] In yet other embodiments, microstimulator 635 is configured to extend distally forward from (or proximally relative to) an end 773 of stent 770 via support 782 (which extends from one or more struts 774), as illustrated in Figure 17C. accordingly, in this arrangement, microstimulator 635 is not located within the interior 771 (Figure 17B) of stent 770, which may lessen any potential interference of the body of stent 770 relative to the stimulation signal from microstimulator 635.

[0106] Embodiments of the transvenously-delivered microstimulator (described herein) enable precise location of a microstimulator adjacent to an optimal neurostimulation site because the transvenous approach enables the surgeon to vary the position of the microstimulator along the length of a vein (using the steerable catheter techniques) and thereby vary the position of the microstimulator along the length of the target nerve. This method allows the surgeon to identify a precise optimal stimulation site that causes contraction of one or more specific muscles (suited to restore airway patency) prior to fixing the location of the micro stimulator relative to the target nerve. Moreover, steerable catheter/stylets or other transvenous delivery instruments enable rotation of the microstimulator within the vein to further adjust the effect of the stimulation on a target nerve or portions of the target nerve.

[0107] Embodiments of the present disclosure provide an implantable system to provide therapeutic solutions for patients diagnosed with obstructive sleep apnea. The system is designed to stimulate the hypoglossal nerve during inspiration thereby preventing occlusions in the upper airway during sleep.

[0108] While at least one exemplary embodiment has been presented in the foregoing detailed description, it should be appreciated that variations exist. It

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should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope, applicability, or configuration of the present disclosure in any way. Rather, the foregoing detailed description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the present disclosure as set forth in the appended claims and the legal equivalents thereof.

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CLAIMS

1. A method of treating sleep apnea, comprising:

inserting an implantable pulse generator subcutaneously within a body of a patient and connecting a lead to the pulse generator;

inserting a lead within the vasculature and advancing the lead transvenously through the vasculature;

positioning a stimulation portion of the lead in close proximity to the hypoglossal nerve; and

applying a nerve-stimulation signal to the hypoglossal nerve via the stimulation portion of the lead.

2. The method of claim 1, wherein applying the nerve-stimulaton signal comprises:

synchronizing the application of the nerve-stimulation signal with respiration.

3. The method of claim 2, wherein synchronizing the application comprises:

applying the nerve-stimulation signal to occur at each respiratory breath.

4. The method of claim 2, comprising at least one of:

sensing the at least one respiratory feature via positioning a first respiration sensor on an exterior surface of a patient's body; or

sensing the at least one respiratory feature via delivering a second respiration sensor subcutaneously within an upper body portion of a patient's body.

5. The method of claim 4, comprising:

coupling at least one of the respective first and second respiration sensors to the implantable pulse generator.

6. The method of claim 4, comprising:

providing the second respiration sensor on a sensor portion of the lead.

7. The method of claim 4, wherein sensing the at least one respiratory feature comprises at least one of:

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measuring a trans-thoracic bio-impedance to track the relative amplitude of the respiratory waveform.

8. The method of claim 4, wherein sensing the at least one respiratory feature including additionally measuring at least one of:

a body motion parameter;

an electrocardiography parameter;

a respiratory flow parameter;

a blood oxygen parameter; and

a time-of-day parameter.

9. The method of claim 7, comprising:

determining an average peak amplitude based on the tracked relative amplitudes; and

detecting, via the at least one respiratory feature, an apneic respiration pattern as cyclic variations of an amplitude of the trans-thoracic bio-impedance relative to the average peak amplitude for a duration corresponding to a nominal apneic duration.

10. The method of claim 1, wherein applying the nerve-stimulation signal comprises:

detecting an apneic-indicative respiratory pattern prior to applying the nerve-stimulation signal;

synchronizing the application of the nerve-stimulation signal with respiration; and

discontinuing application of the nerve-stimulation signal when the apneic-indicative respiratory pattern is no longer detected.

11. The method of claim 1, wherein the lead includes:

a base portion;

a first portion extending from the base portion; and

a second portion extending from the base portion and being separate from the first portion, wherein the second portion includes the stimulation portion.

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12. The method of claim 1, including:

coupling a base portion of the lead to the pulse generator;

arranging a first portion to extend from the base portion; and

arranging a second portion to extend from the base portion and separate from the first portion.

13. The method of claim 12, comprising:

delivering the first portion to a first hypoglossal nerve on a first side of the body and defining the first portion to include a first stimulation electrode structure of the stimulation portion; and

delivering the second portion to a second hypoglossal nerve on a second side of the body and defining the second portion to include a second stimulation electrode structure of the stimulation portion.

14. The method of claim 13, comprising:

applying the stimulation signal in an alternating pattern between the first stimulation electrode on the first side of the body and the second stimulation electrode on the second side of the body.

15. The method of claim 13, comprising:

applying the stimulation signal simultaneously at the first stimulation electrode on the first side of the body and at the second stimulation electrode on the second side of the body.

16. The method of claim 12, comprising:

delivering the first portion within a first vein of vasculature to be in close proximity to a hypoglossal nerve on a first side of the body and defining the first portion to include a first stimulation electrode structure of the stimulation portion; and

delivering the second portion within a second vein of the vasculature to be in close proximity to the hypoglossal nerve on the first side of the body and defining the second portion to include a second stimulation electrode structure of the stimulation portion.

17. The method of claim 12, comprising:

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delivering the first portion within a first vein of vasculature to be in close proximity to a hypoglossal nerve on a first side of the body and defining the first portion to include a first stimulation electrode structure of the stimulation portion; and

delivering the second portion within a second vein of the vasculature to be in close proximity to a second nerve on the first side of the body and defining the second portion to include a second stimulation electrode structure of the stimulation portion, wherein the second nerve innervates a respiration-related muscle.

18. The method of claim 1, comprising:

arranging the stimulation portion to include an array of independently programmable electrode elements spaced apart from each other along a length of the stimulation portion and spaced apart from each other circumferentially on the outer surface of the stimulation portion; and

identifying at least one target site along a length of the hypoglossal nerve via applying a stimulation signal to different combinations of the electrode elements and evaluating which combination of electrode elements achieves an efficacious respiratory airway patency.

19. The method of claim 1, comprising:

arranging the stimulation portion to include an array of electrodes spaced apart from each other along a length of the stimulation portion; and

identifying at least one target site along a length of the hypoglossal nerve via applying a stimulation signal separately to each electrode or electrode combination, on a one-at-a-time basis, and evaluating which electrode or electrode combination achieves an efficacious respiratory airway patency.

20. The method of claim 19, wherein each electrode comprises a ring electrode.

21. The method of claim 19, comprising:

identifying the efficacious respiratory airway patency via identifying, upon application of the test neurostimulation signal, which ring electrode produces at least one of:

a longest duration of increased airway patency;

a largest size of increased airway patency; or

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a substantial reduction in apnea events.

22. The method of claim 19, comprising:

arranging a length of the array to substantially match a majority of a length of the hypoglossal nerve extending from a position near the jugular vein toward the genioglossus muscle; and

determining which electrodes of the array produce the efficacious respiratory airway patency without repositioning the stimulation portion within the vasculature after the stimulation is first positioned in close proximity to the hypoglossal nerve.

23. The method of claim 19, wherein identifying the at least one target portion comprises determining the most efficacious response for each potential target site via at least one of:

determining a degree of tongue motor response;

determining an increased cross-sectional area of an upper respiratory airway;

determining a degree of electromyography response of one or more tongue-protrusion related muscles;

detecting a twitch from either the tongue or laryngeal muscle; or

detecting a reduction in apnea events.

24. The method of claim 19, comprising:

determining, at each potential target site of the hypoglossal nerve, a therapeutic neurostimulation signal via applying a test neurostimulation signal while iteratively varying a value for each signal parameter of a plurality of signal parameters, wherein the signal parameters include at least one of an amplitude, a pulse width, an electrode polarity, a duration, and/or a frequency.

25. The method of claim 1, comprising:

arranging the stimulation portion to include an array of ring electrodes spaced apart from each other along a length of the stimulation portion; and

identifying a target portion of the hypoglossal nerve via applying a stimulation signal different combinations of the respective ring electrodes to determine which selectable combination of ring electrode produces a highest degree of respiratory airway patency.

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26. The method of claim 25, comprising:

applying the stimulation signal simultaneously from the selected combination of ring electrodes.

27. The method of claim 1, wherein positioning the stimulation portion comprising:

providing the lead as single lead and arranging the stimulation portion on a distal portion of the single lead and arranging a respiratory sensing portion on a proximal portion of the single lead; and

distally advancing the single lead within the vasculature to simultaneously cause:

positioning the stimulation portion within first vein in close proximity to the hypoglossal nerve and within a neck region of the patient; and

positioning the respiratory sensing portion within a second vein within a pectoral region of the patient, the second vein in fluid communication with the first vein.

28. The method of claim 27, wherein the first vein comprises a ranine vein and the second vein comprises a subclavian vein.

29. The method of claim 27, comprising:

arranging the sensing portion as a first sensing element and a second sensing element spaced apart from the first sensing element along a length of the single lead.

30. The method of claim 29, comprising:

performing sensing a trans-thoracic bio-impedance relating to respiratory patterns via measuring a voltage across at least one of:

the first sensing element relative to the second sensing element; or

one of the respective first and second sensing elements relative to a conductive case of the pulse generator.

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31. The method of claim 1, comprising:

maintaining the stimulation portion in close proximity to the hypoglossal nerve by anchoring the stimulation portion relative to the vasculature via at least one of:

arranging the stimulation portion as at least part of a coil structure movable between a generally straight state during advancement through the vasculature and an expanded, coiled state at the position for stimulating the hypoglossal nerve; or

arranging the stimulation portion as at least part of a stent structure movable between a generally collapsed state during advancement through the vasculature and an expanded state at the position for stimulating the hypoglossal nerve.

32. The method of claim 1, wherein positioning the stimulation portion comprises:

providing the stimulation portion as at least part of an anchoring mechanism;

advancing the stimulation portion within the vasculature, with the anchoring mechanism in a generally collapsed state, to a first test stimulation site along the hypoglossal nerve;

manipulating the anchoring mechanism into an expanded state to engage a side wall of the vasculature at the first test stimulation site and applying a first neurostimulation test signal, via the stimulation portion, to the hypoglossal nerve;

manipulating the anchoring mechanism into the generally collapsed state to disengage the anchoring mechanism from the side wall of the vasculature and advancing the stimulation portion to a second test stimulation site spaced apart along the length of the hypoglossal nerve from the first test stimulation site; and

manipulating the anchoring mechanism into the expanded state to re-engage the side wall of the vasculature and applying a second neurostimulation test signal, via the stimulation portion, the hypoglossal nerve.

33. The method of claim 32, comprising providing the anchor mechanism at a distal portion of the lead as a stent structure including a generally tubular member, wherein the collapsed state corresponds to a first diameter of the stent structure and the expanded state corresponds to a second diameter substantially larger than the first diameter and sized to engage the side wall of the vasculature.

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34. The method of claim 32, comprising providing the anchor mechanism at a distal portion of the lead as a coil configuration, wherein the collapsed state corresponds to a generally straight shape achieved via insertion of a guide wire through the distal portion of the lead and the expanded state corresponds to radial expansion of distal portion from the generally straight shape into the coil configuration with the radially expanded coil configuration sized to engage the side wall of the vasculature.

35. The method of claim 32, comprising providing the anchor mechanism at a distal portion of the lead as an array of tines located radially about an outer surface of the lead, and when in the generally collapsed state, the tines lay generally flat against the outer surface of the lead and when in the expanded state, the tines protrude generally outward and away from the outer surface of the lead.

36. A method of treating sleep apnea, comprising:

inserting an implantable pulse generator subcutaneously within a body of a patient and connecting a lead to the pulse generator;

inserting a lead within the vasculature and advancing the lead through the vasculature;

positioning an electrode portion of the lead in close proximity to the hypoglossal nerve; and

monitoring respiratory patterns via changes in bio-impedance measured via the electrode portion;

applying, via the electrode portion, a nerve-stimulation signal to the hypoglossal nerve.

37. The method of claim 36, comprising:

synchronizing the application of the nerve-stimulation signal with each respiration breath based on the monitored respiratory patterns.

38. The method of claim 36, wherein applying the nerve-stimulation signal comprises:

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detecting, within the monitored respiratory pattern, an apneic-indicative pattern prior to applying the nerve-stimulation signal;

synchronizing the application of the nerve-stimulation signal with respiration; and

discontinuing application of the nerve-stimulation signal when the apneic-indicative pattern is no longer detected within the monitored respiratory pattern.

39. The method of claim 38, comprising arranging the lead to include a first portion and a second portion, and wherein positioning the electrode portion comprises:

providing the lead as a first arm and a second arm and arranging the electrode portion as a first electrode structure on the first arm and a second electrode structure on the second arm of the lead;

advancing the first arm of the lead within the vasculature on a first side of the body to position the first electrode structure in close proximity to the hypoglossal nerve on the first side of the body; and

advancing the second arm of the lead within the vasculature on a second side of the body to position the second electrode structure in close proximity to the hypoglossal nerve on the second side of the body.

40. The method of claim 39, wherein monitoring the respiratory pattern comprises:

measuring a bioimpedance with the first electrode structure on the first side of the body and the second electrode structure on the second side of the body.

41. The method of claim 40, comprising measuring the bioimpedance as at least one of a trans-laryngeal bio-impedance or a trans-pharyngeal bio-impedance.

42. A method of treating obstructive sleep apnea, comprising:

removably supporting a microstimulator on a distal portion of a catheter;

inserting and advancing the catheter through the vasculature to position the microstimulator in close proximity to a hypoglossal nerve;

anchoring the microstimulator within the vasculature in close proximity to the hypoglossal nerve and removing the catheter from the vasculature;

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applying, via the microstimulator, a nerve-stimulation signal to the hypoglossal nerve.

43. The method of claim 42, comprising monitoring a respiration pattern via at least one of:

a sensing portion of a lead positioned within an upper body portion of a patient; or

a respiration sensor externally attached to the body.

44. The method of claim 43, comprising:

synchronizing application of the nerve-stimulation signal with respiration.

45. The method of claim 43, wherein applying the nerve-stimulation signal comprises:

detecting, within the monitored respiratory pattern, an apneic-indicative pattern prior to applying the nerve-stimulation signal;

synchronizing the application of the nerve-stimulation signal with respiration; and

discontinuing application of the nerve-stimulation signal when the apneic-indicative pattern is no longer detected within the monitored respiratory pattern.

46. The method of claim 42, comprising:

removably supporting a tine structure at the distal portion of the catheter, including securing the microstimulator relative to the tine structure,

wherein advancing the catheter includes maintaining the tine structure in a deactivated state, in which a plurality of tines extend generally parallel to a longitudinal axis of the catheter,

wherein anchoring the microstimulator includes deploying the tine structure into an activated state, in which the tines protrude generally outward to engage a side wall of the vasculature.

47. The method of claim 42, comprising:

removably supporting a stent at the distal portion of the catheter, including securing the microstimulator relative to the stent,

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wherein advancing the catheter includes maintaining the tine structure in a deactivated state, in which the stent has a compressed, first diameter sized less than a diameter of the vasculature at which the stimulation portion is positioned in close proximity to the hypoglossal nerve,

wherein anchoring the microstimulator includes deploying the tine structure into an activated state, in which the stent has an expanded, second diameter sized greater than the diameter of the vasculature at which the stimulation portion is positioned in close proximity to the hypoglossal nerve.

48. The method of claim 47, comprising:

providing the stent as an array of struts assembled into a generally tubular structure with the microstimulator secured to an outer surface of the generally tubular structure.

49. The method of claim 47, comprising:

providing the stent as an array of struts assembled into a generally tubular structure with the microstimulator suspended within an interior of the generally tubular structure.

50. The method of claim 42, comprising:

removably securing a respiratory sensor on an external surface of a patient's body; and

detecting the apneic-type respiration pattern via the externally secured respiratory sensor.

51. The method of claim 42, comprising:

providing a power supply, a controller, and a power transmission mechanism in a first portion of a patient support;

placing the patient's body on a first portion and a second portion of the patient support while positioning the microstimulator in the patient's body in close proximity to the power transmission mechanism of the patient support; and

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employing the power supply and controller to wirelessly transmit power, via the power transmission mechanism, to the microstimulator.

52. The method of claim 51, comprising:

providing the first portion of the patient support as a headrest structure; and

positioning the power transmission mechanism at an upper portion of the headrest structure.

53. An obstructive sleep apnea treatment system comprising:

a respiratory sensor removably securable to an exterior of a patient's body;

a microstimulator configured to be transvenously delivered proximate to a hypoglossal nerve and including:

an anchor mechanism configured to anchor the microstimulator within the vasculature proximate the hypoglossal nerve; and

circuitry configured to generate a neurostimulation signal; and

a patient support housing a power supply, a controller, and a transmission mechanism configured to wirelessly transmit power to the microstimulator upon positioning of the patient support in close proximity to the microstimulator.

54. The system of claim 53, wherein the anchor mechanism comprises:

a tine structure including a base portion and a plurality of tines extending from the base portion, wherein the microstimulator is secured to base portion,

wherein the tine structure is movable between:

a deactivated state, in which the respective tines extend generally parallel to a longitudinal axis of the microstimulator; and

an activated state, in which the tines protrude generally outward from the microstimulator to engage a side wall of the vasculature.

55. The system of claim 53, wherein the anchor mechanism comprises:

a stent, wherein the stent is movable between:

a deactivated state, in which the stent has a compressed, first diameter sized less than a diameter of the vasculature at which the microstimulator is positioned in close proximity to the hypoglossal nerve; and

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an activated state, in which the stent has an expanded, second diameter sized greater than the diameter of the vasculature at which the stimulation portion is positioned in close proximity to the hypoglossal nerve.

56. The system of claim 55, wherein the stent comprises an array of struts defining a generally tubular structure, and wherein the microstimulator is secured to an outer surface of the generally tubular structure.

57. The system of claim 55, wherein the stent comprises an array of struts defining a generally tubular structure, and wherein the microstimulator is secured via a tether to one or more respective struts to be suspended in at a position within an interior of the generally tubular structure.

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01145

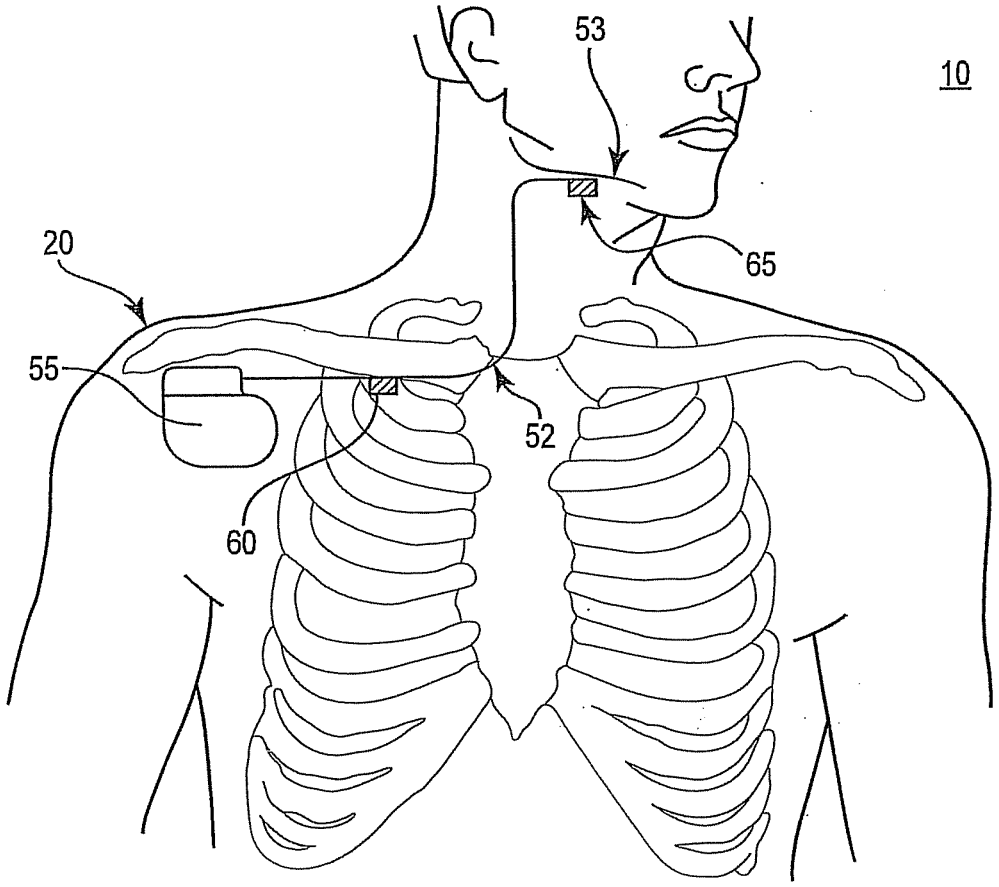


Fig. 1

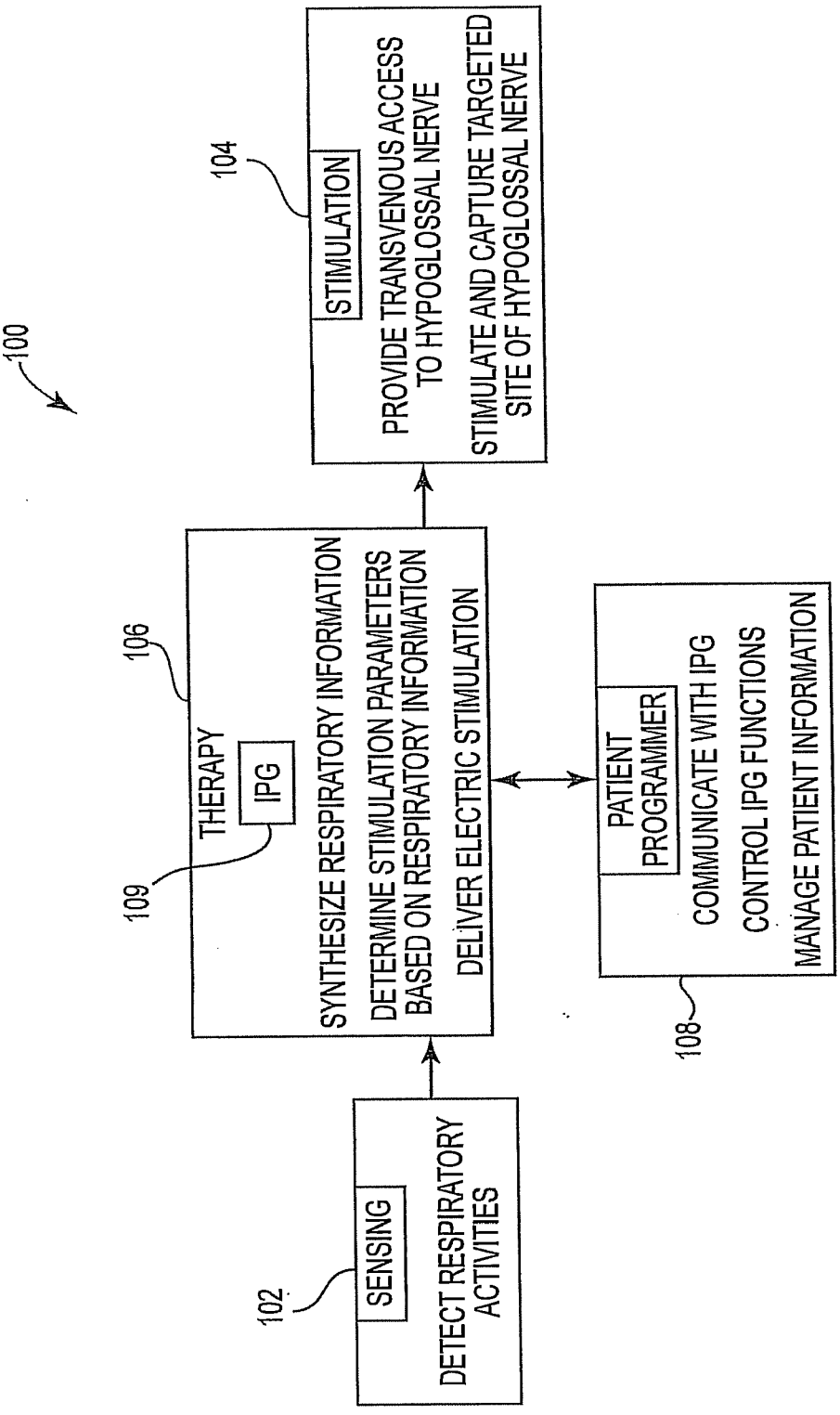

100
102
SENSING
DETECT RESPIRATORY ACTIVITIES
106
109
THERAPY
IPG
SYNTHESIZE RESPIRATORY INFORMATION
DETERMINE STIMULATION PARAMETERS BASED ON RESPIRATORY INFORMATION
DELIVER ELECTRIC STIMULATION
104
STIMULATION
PROVIDE TRANSVENOUS ACCESS TO HYPOGLOSSAL NERVE
STIMULATE AND CAPTURE TARGETED SITE OF HYPOGLOSSAL NERVE
108
PATIENT PROGRAMMER
COMMUNICATE WITH IPG
CONTROL IPG FUNCTIONS
MANAGE PATIENT INFORMATION

Fig. 2A

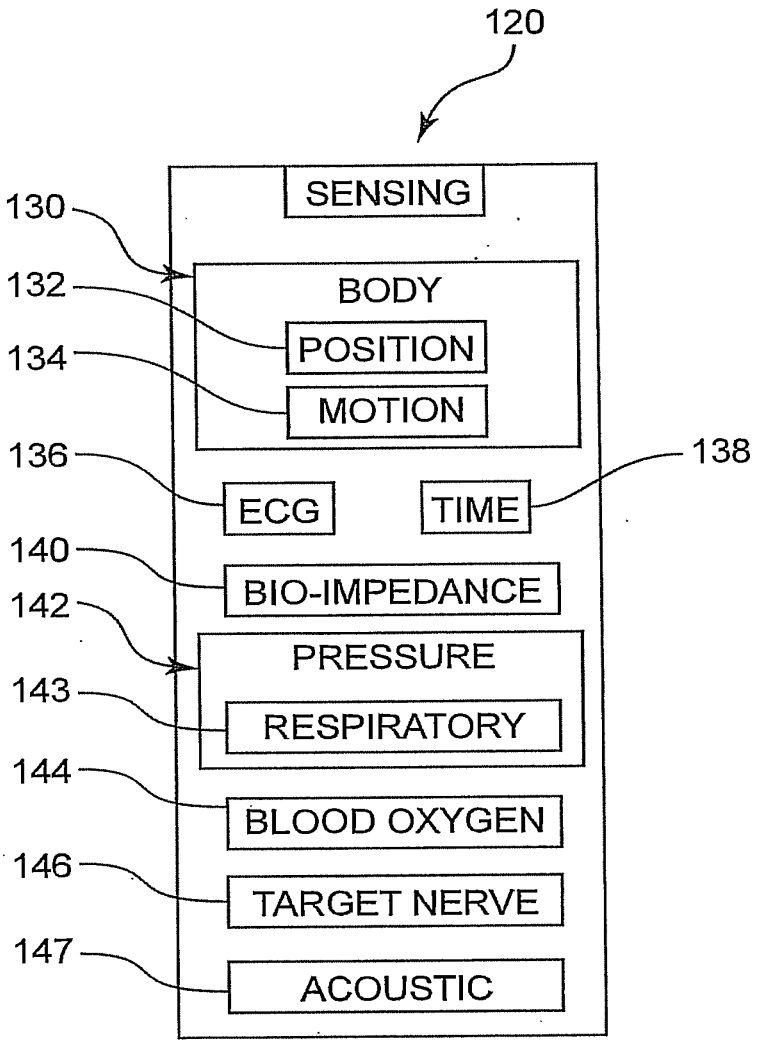

120
SENSING
130
132
BODY
POSITION
134
MOTION
136
138
ECG
TIME
140
BIO-IMPEDANCE
142
PRESSURE
143
RESPIRATORY
144
BLOOD OXYGEN
146
TARGET NERVE
147
ACOUSTIC

Fig. 2B

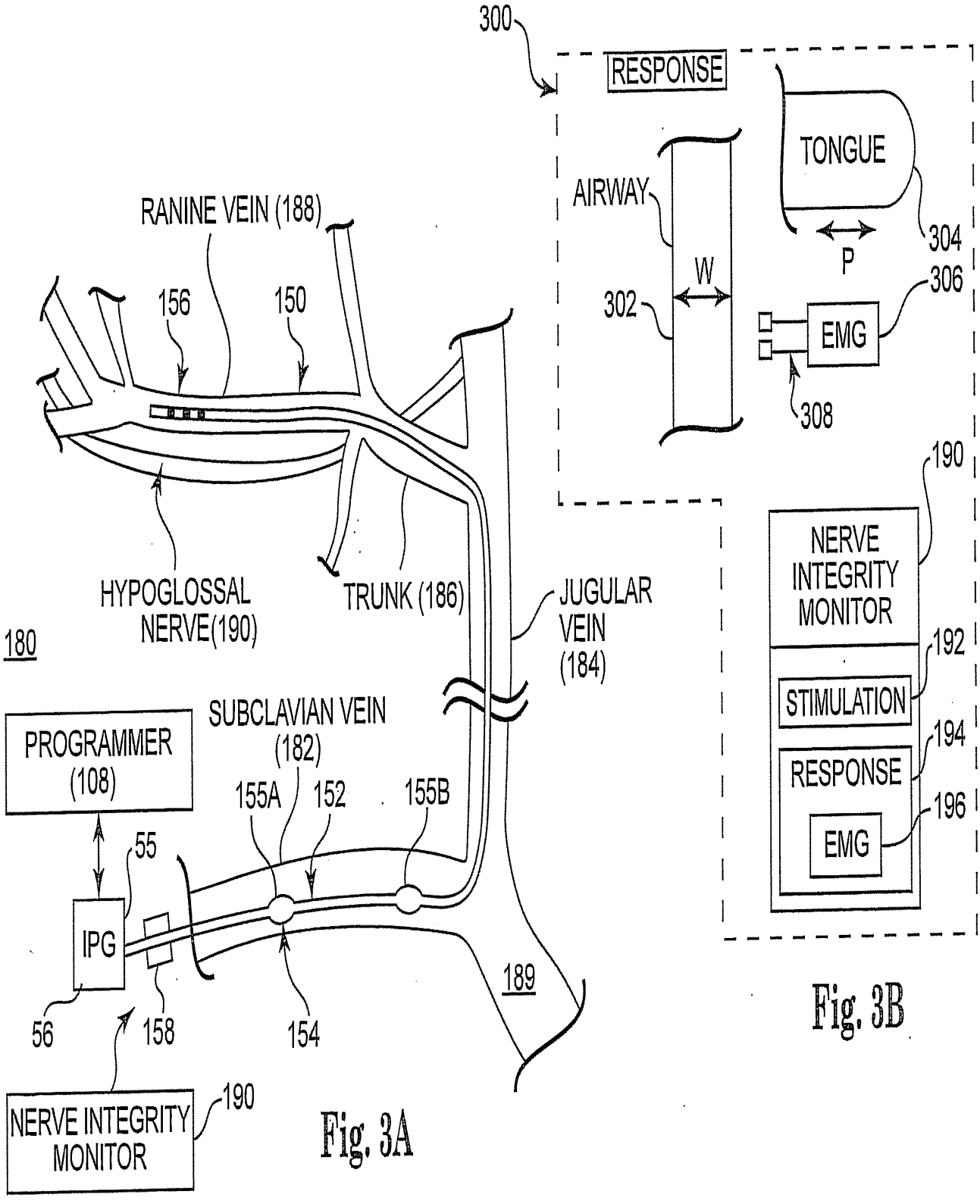

300
RESPONSE
TONGUE
AIRWAY
304
P
W
306
302
EMG
308
190
NERVE INTEGRITY MONITOR
192
STIMULATION
194
RESPONSE
196
EMG
RANINE VEIN (188)
156
150
HYPOGLOSSAL NERVE(190)
TRUNK (186)
JUGULAR VEIN (184)
180
SUBCLAVIAN VEIN (182)
PROGRAMMER (108)
155A
152
155B
55
IPG
189
56
158
154
NERVE INTEGRITY MONITOR
190

Fig. 3B

Fig. 3A

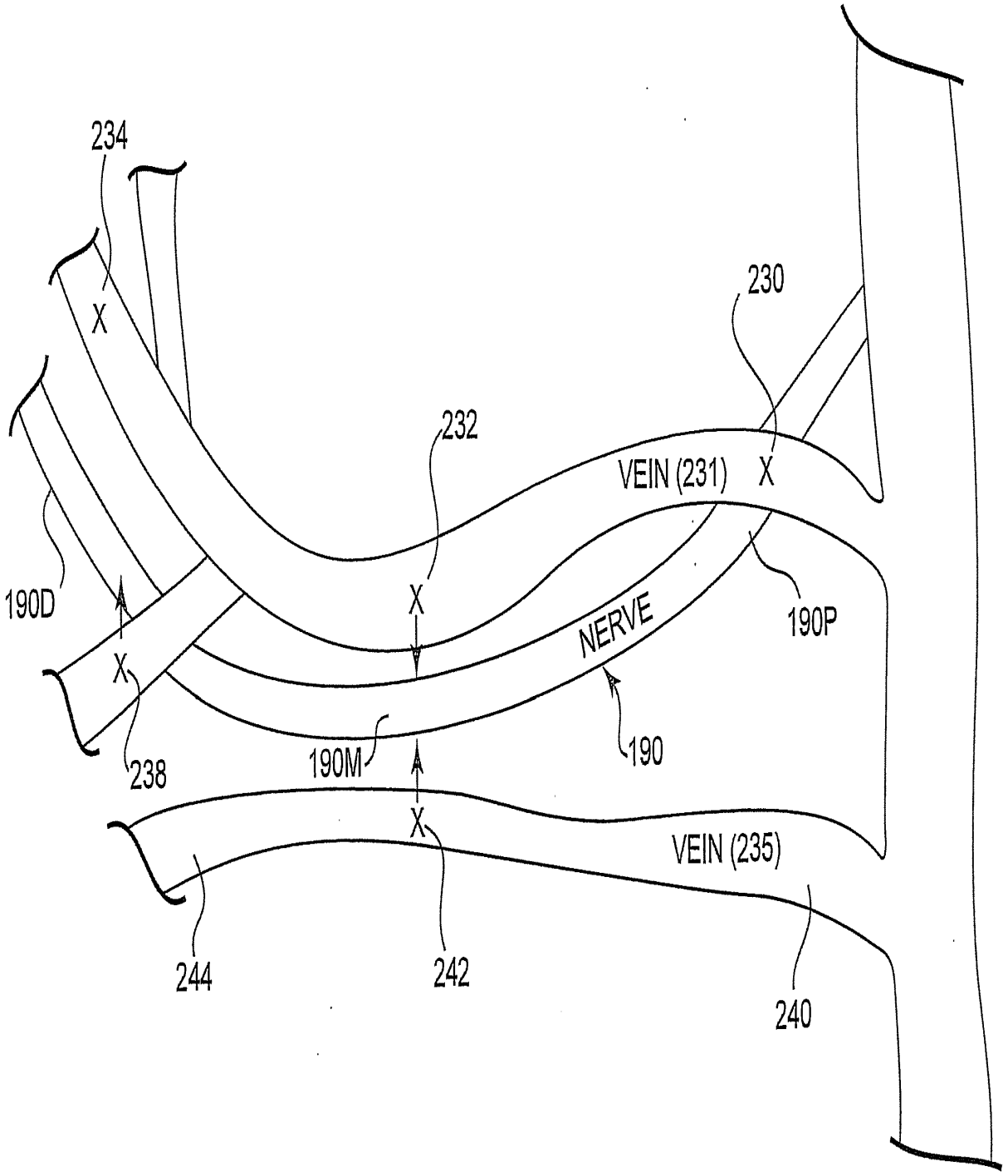

234
X
230
232
VEIN (231)
X
190D
X
X
NERVE
190P
238
190M
190
X
VEIN (235)
244
242
240

Fig. 4A

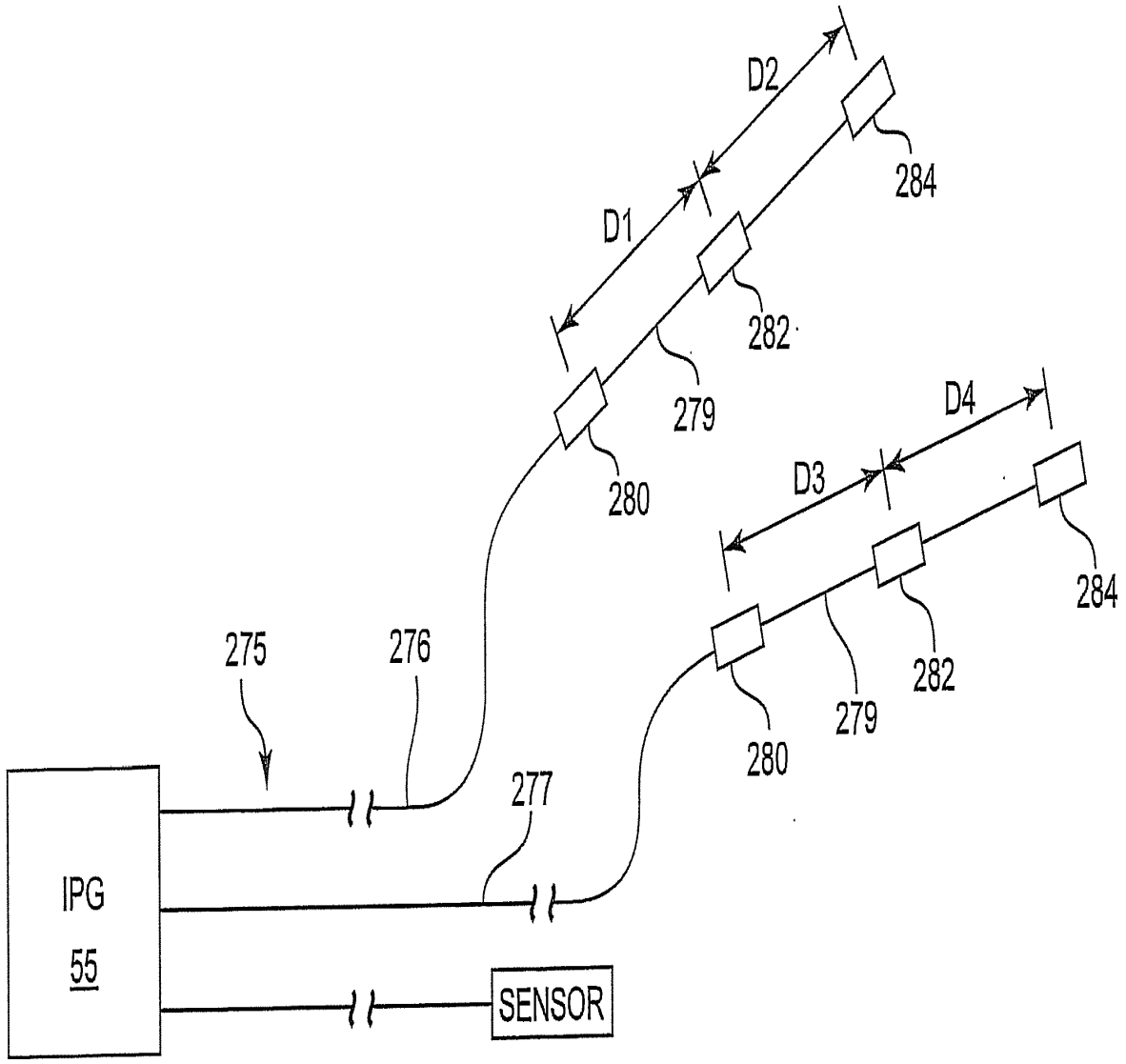

D2
284
D1
282
279
280
D4
D3
284
275
276
282
279
280
277
IPG
55
SENSOR

Fig. 4B

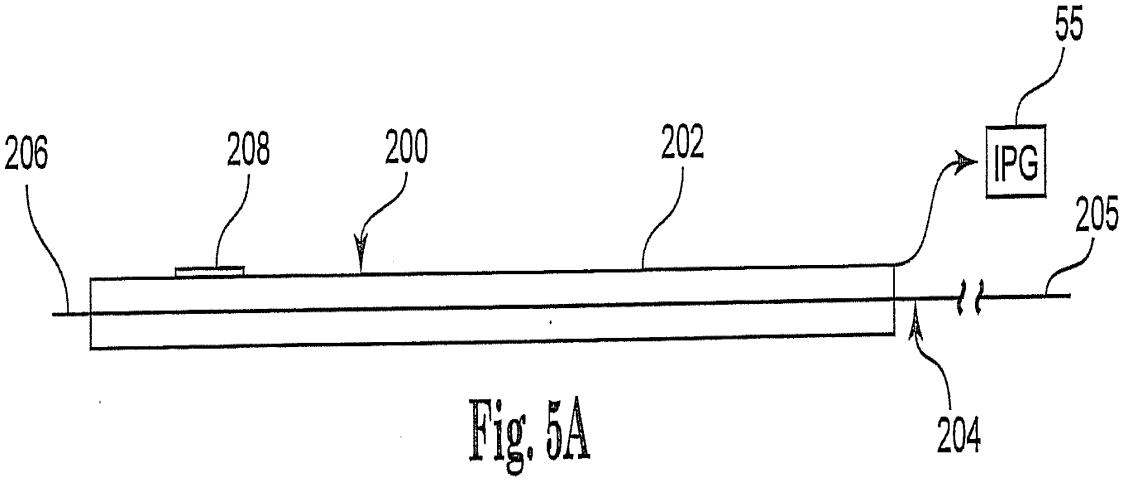


Fig. 5A

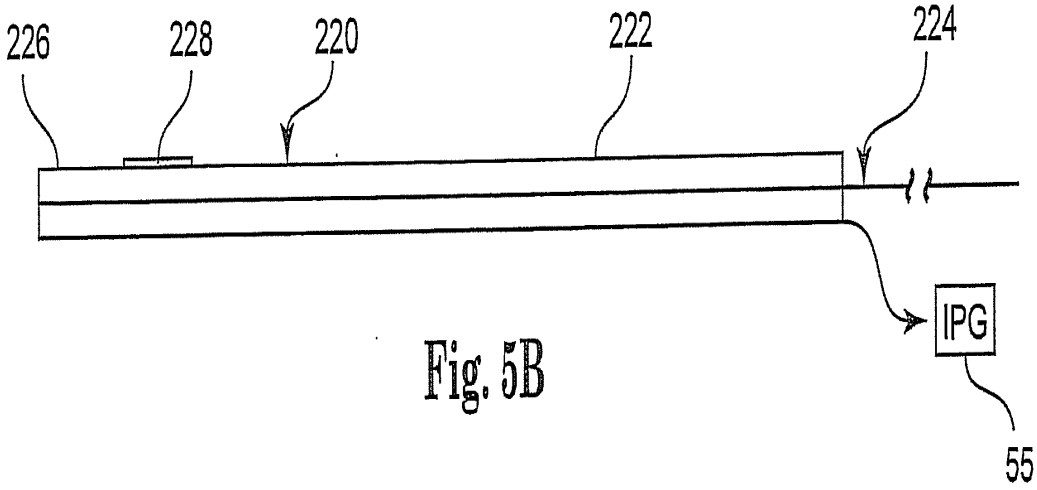


Fig. 5B

Exhibit 1002
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01152

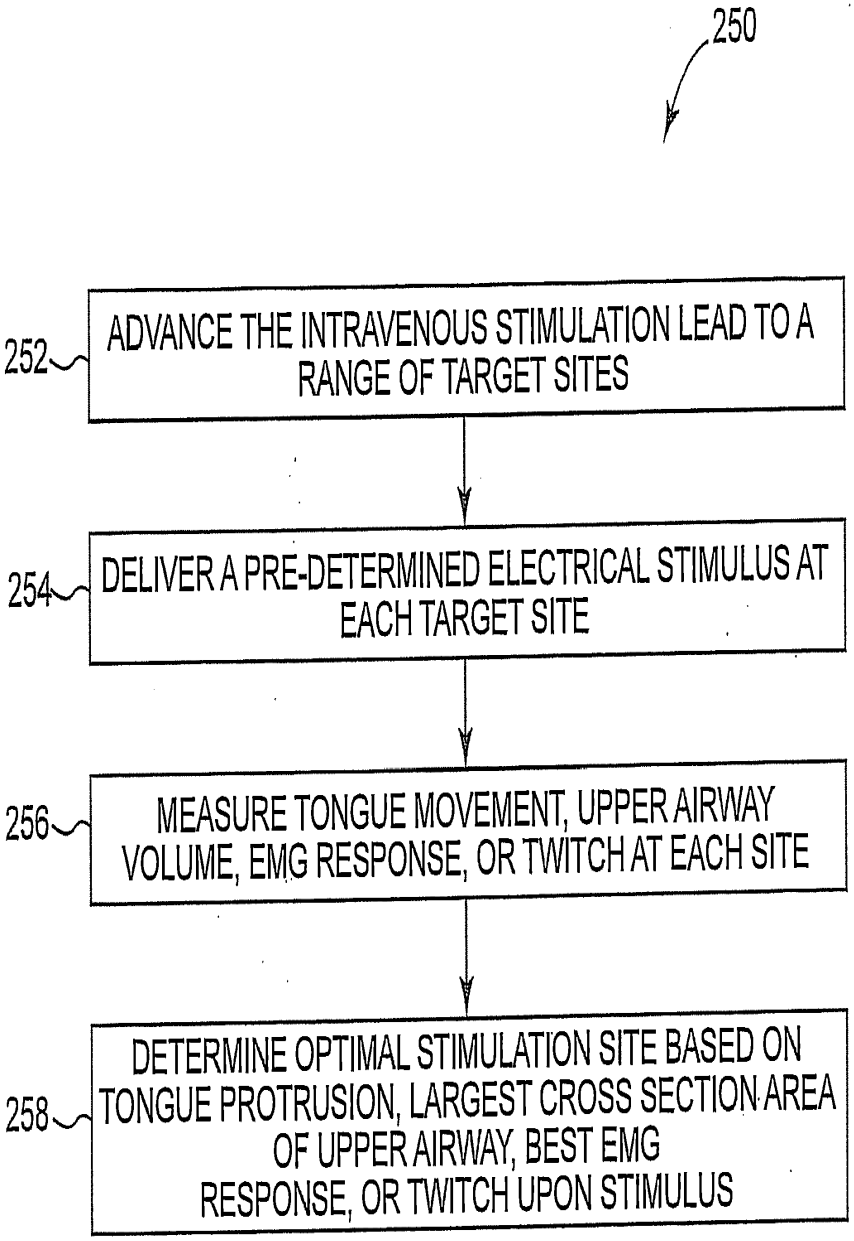

250
252
ADVANCE THE INTRAVENOUS STIMULATION LEAD TO A RANGE OF TARGET SITES
254
DELIVER A PRE-DETERMINED ELECTRICAL STIMULUS AT EACH TARGET SITE
256
MEASURE TONGUE MOVEMENT, UPPER AIRWAY VOLUME, EMG RESPONSE, OR TWITCH AT EACH SITE
258
DETERMINE OPTIMAL STIMULATION SITE BASED ON TONGUE PROTRUSION, LARGEST CROSS SECTION AREA OF UPPER AIRWAY, BEST EMG RESPONSE, OR TWITCH UPON STIMULUS

Fig. 6

SUBCLAVIAN (182)
VEIN
JUGULAR
VEIN
(184)
350
352
IPG
189
55
382
354
355A
355B

Fig. 7

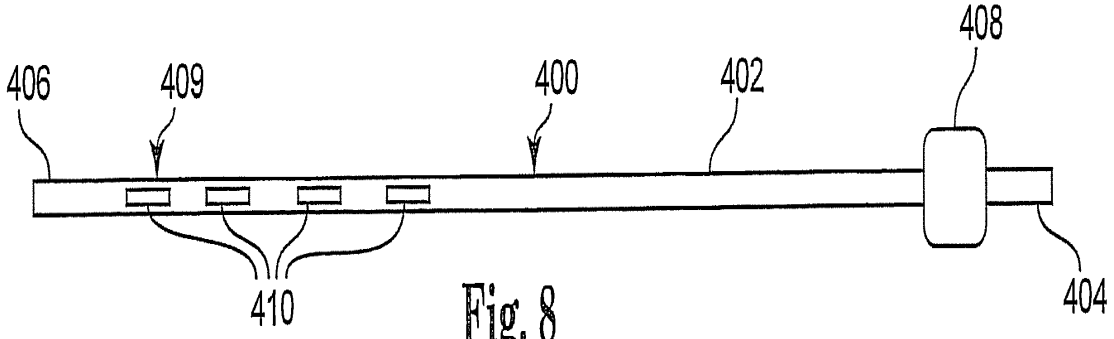


Fig. 8

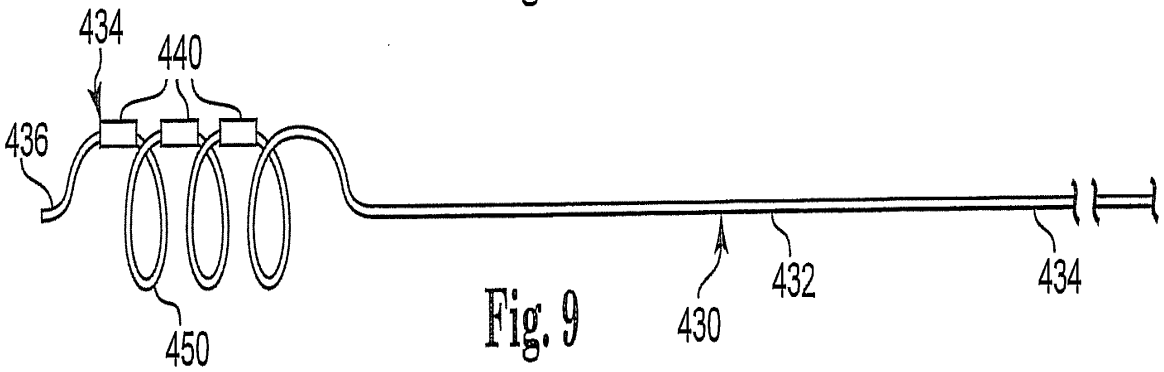


Fig. 9

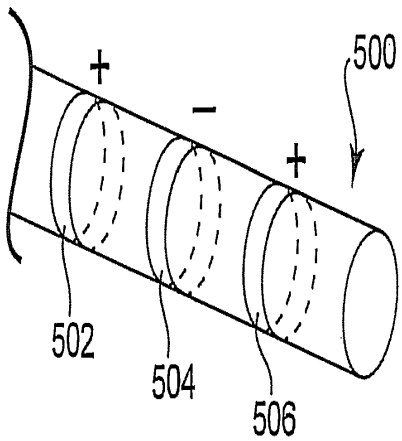


Fig. 10

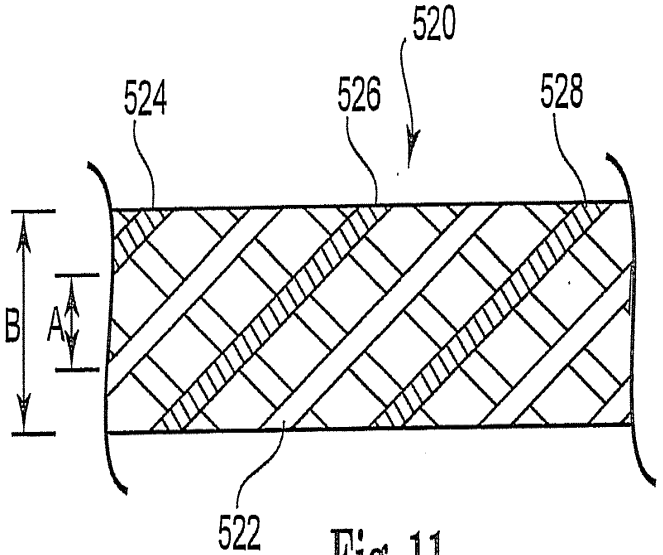


Fig. 11

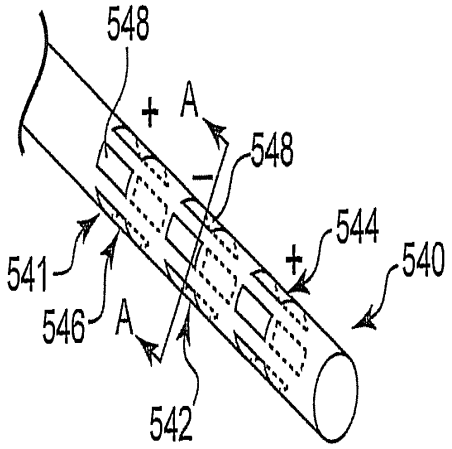
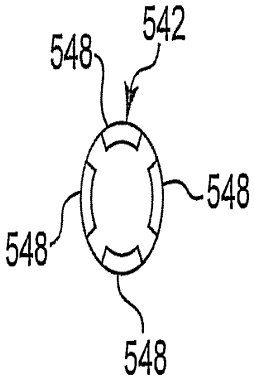


Fig. 13A



VIEW A - A

Fig. 13B

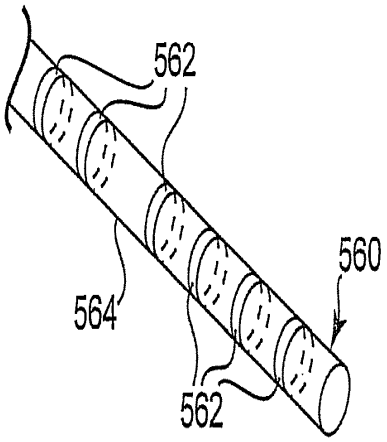


Fig. 14

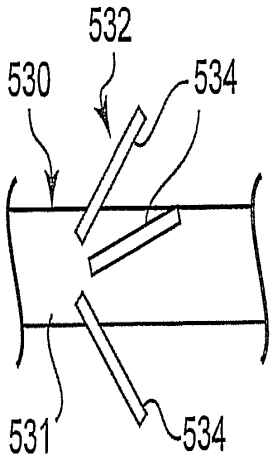


Fig. 12A

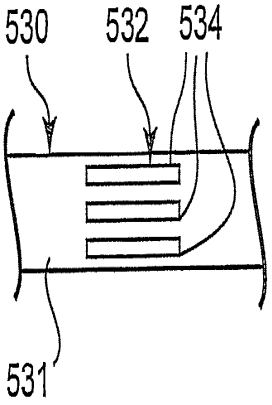


Fig. 12B

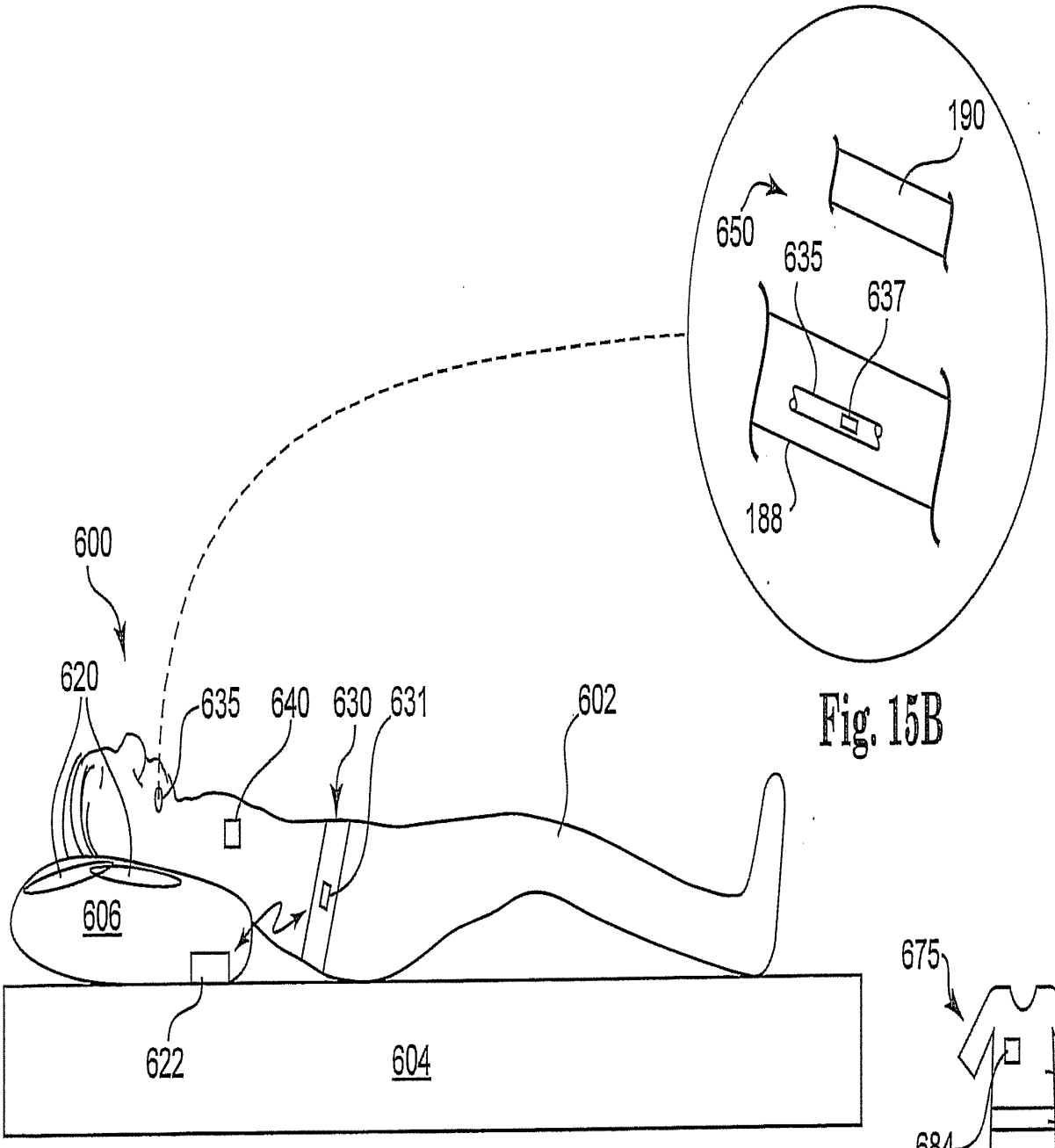


Fig. 15A

Fig. 15B

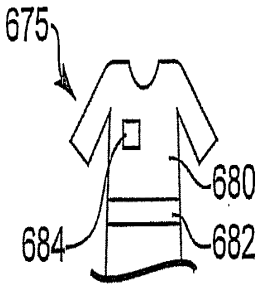


Fig. 15C

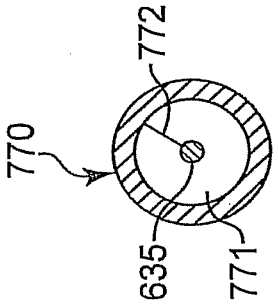


Fig. 17B

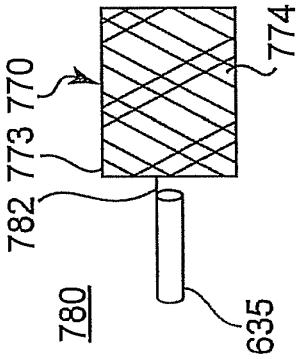


Fig. 17C

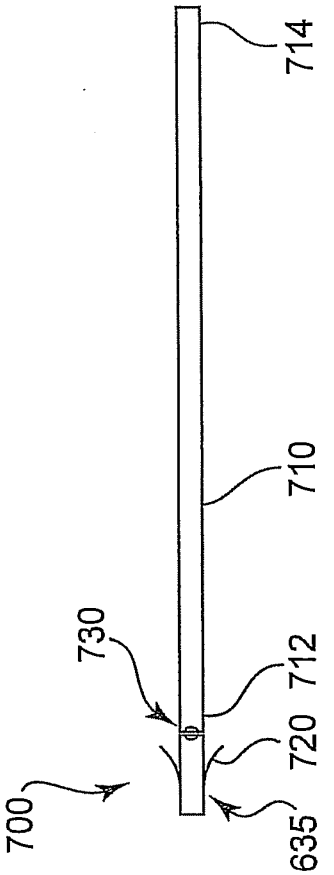


Fig. 16

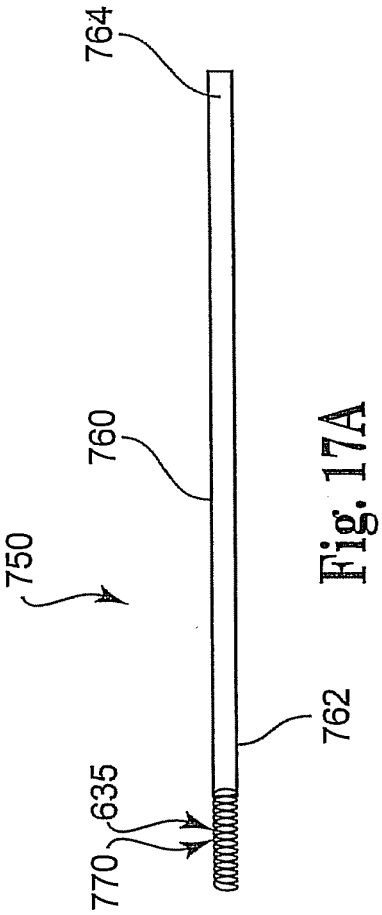


Fig. 17A

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/059060

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/36
ADD. A61N1/372 A61F2/82

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2008/039904 A1 (BULKES CHERIK [US] ET AL) 14 February 2008 (2008-02-14) paragraphs [0137], [0263], [0264], [0266] figures 1,2	53-57
Y	EP 1 175 919 A1 (MEDTRONIC INC [US]) 30 January 2002 (2002-01-30) figures 33,34	53,55-56
Y	WO 2007/068284 A1 (SYNERGIO AG [CH]; SOLEM JAN OTTO [CH]) 21 June 2007 (2007-06-21) figure 11	54
Y	US 2005/080472 A1 (ATKINSON ROBERT EMMETT [US] ET AL) 14 April 2005 (2005-04-14) figures 3-5,9	57

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 February 2010	11/03/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Worms, Georg

1

Form PCT/ISA/210 (second sheet) (April 2005)

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01159

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/059060

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2008/103545 A1 (BOLEA STEPHEN L [US] ET AL) 1 May 2008 (2008-05-01) figures 1,2,32,33	53

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01160

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 1-52

The present application does not meet the criteria of Article 17(2)(a)(i) and Rule 39.1(iv) PCT, because the subject-matter of independent claims 1, 36, and 42 discloses steps of methods of treatment using surgical and therapeutic steps (see also PCT Guidelines 9.10) for the following reasons: Steps like "inserting an implantable pulse generator", "inserting a lead", "positioning a stimulation portion of a lead" are surgical steps carried out on the patient whereas the application of nerve stimulation entails the therapeutic step. All these steps are not allowable and should therefore be removed from the application.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/059060

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-52
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
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01162

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/059060

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2008039904 A1	14-02-2008	WO 2008019384 A1	14-02-2008
EP 1175919 A1	30-01-2002	NONE	
WO 2007068284 A1	21-06-2007	EP 1968698 A1	17-09-2008
		US 2009171408 A1	02-07-2009
US 2005080472 A1	14-04-2005	EP 1722847 A2	22-11-2006
		US 2006009830 A1	12-01-2006
		WO 2005053784 A2	16-06-2005
US 2008103545 A1	01-05-2008	AU 2007313319 A1	24-04-2008
		CA 2666529 A1	24-04-2008
		EP 2116274 A2	11-11-2009
		US 2008103407 A1	01-05-2008
		WO 2008048471 A2	24-04-2008

Exhibit 1002
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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 May 2010 (27.05.2010)

PCT

(10) International Publication Number
WO 2010/057286 A1

(51) International Patent Classification:
A61B 5/04 (2006.01) *A61N 1/36* (2006.01)
A61F 5/56 (2006.01) *A61N 1/372* (2006.01)

(21) International Application Number:
PCT/CA2008/002036

(22) International Filing Date:
18 November 2008 (18.11.2008)

(25) Filing Language: English

(26) Publication Language: English

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI

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(54) Title: DEVICE AND METHOD FOR DETECTING SLEEP APNEA EVENTS BY MONITORING THE INTERNAL BRANCH OF THE SUPERIOR LARYNGEAL NERVE

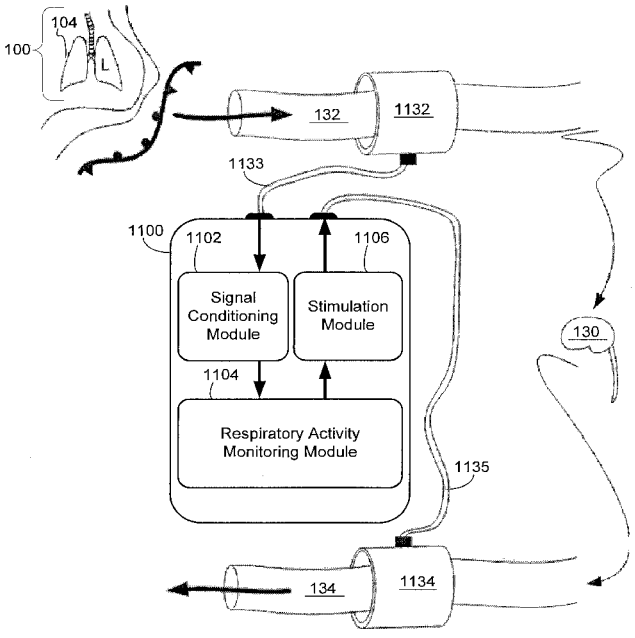


Figure 15

(57) Abstract: A method and device for treating sleep apnea and sleep hypopnea by monitoring respiratory-related activity from the internal branch of the superior laryngeal nerve, interpreting these internal signals to detect and classify apnea events, and stimulating nerves or muscles to elicit appropriate corrective responses to adverse respiratory events.

WO 2010/057286 A1

(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

Device and method for detecting sleep apnea events by monitoring the internal branch of the superior laryngeal nerve

TECHNICAL FIELD

[0001] The present invention relates to a method and device for the detection, identification and treatment of sleep apnea/hypopnea.

BACKGROUND

[0002] Sleep apnea/hypopnea affects around 5% of the adult U.S. population. Its short-term effects consist of complete (apnea) or partial (hypopnea) termination of airflow, decreased oxygen in the blood, increased CO_2 in the blood, interrupted sleep, and excessive daytime sleepiness. Long-term effects may include hypertension, diabetes, heart attack, stroke, arrhythmia and brain damage.

[0003] The principal forms of sleep apnea are: 1) obstructive sleep apnea (OSA), characterized by a physical blockage of the upper airway during sleep, 2) central sleep apnea (CSA), caused by a decreased central respiratory drive during sleep, and 3) mixed sleep apnea, which includes components of both OSA and CSA. OSA is the most common and dangerous of all sleep-related breathing disorders. While CSA is uncommon in its pure form, it is prevalent in patients with congestive heart failure, as a component of Cheyne-Stokes respiration.

[0004] The obstructive component in OSA is related to decreased tone in the upper airway as the muscles relax during sleep. During normal respiration, upper airway patency is maintained by the negative pressure reflex, which activates pharyngeal dilators in response to negative transthoracic pressure during inspiration. In apneic patients, the negative pressure reflex is insufficient to maintain patency during sleep. Here, the negative pressure created during inspiration is sufficient to constrict or collapse the lumen of the flaccid airway.

[0005] The treatment of choice for sleep apnea is continuous positive air pressure (CPAP). Basically, CPAP maintains an open airway by inflating it with pressurized air through a nose or face mask. Used properly, CPAP is 100% effective for treating OSA. Although CSA has a neurological origin, it has also

been successfully treated with positive air pressure. Despite its efficacy, however, CPAP treatment is poorly tolerated by sleep apnea patients. In one recent survey, CPAP non-compliance (less than 4h/night) was reported in between 46% and 83% of patients **[1]**. Reasons for non-compliance include discomfort, claustrophobia, pressure sores, dry nose or mouth, and machine noise.

[0006] The most common alternative to CPAP is a surgical removal of the uvula, caudal soft palate, and tonsils. This procedure has a success rate of about 50%. Other surgical treatments, such as tongue reduction, advancement of the tongue, tracheostomy, or implants to stiffen the soft palate have limited benefit relative to their invasiveness, risk, and irreversibility. Non-surgical approaches such as weight loss, medication, changes in sleeping position or dental appliances also suffer from limited effectiveness or compliance.

[0007] Implantable medical devices are currently under investigation as a method to detect and/or treat sleep apnea. Such devices are similar in their general design to cardiac pacemakers and share in many of the advantages of this mature technology.

[0008] With regard to detection, implantable devices have been described that detect apnea by monitoring the bioelectric activity of the diaphragm, intercostal muscles, or their efferent nerves. Other devices monitor the bioelectric activity of upper airway muscles or their efferent nerves. Still others monitor implanted sensors for indications of, for example, thoracic pressure or blood oxygenation.

[0009] With regard to treatment, implantable devices have been described that terminate apnea using drug delivery, atrial overdrive pacing or electrical stimulation of the nerves or muscles that control respiratory activities. For OSA, electrical stimulation has been described that maintains patency by activating upper airway muscles or the efferent nerves controlling them. For CSA, treatments that elicit breathing by electrically stimulating the diaphragm, intercostal muscles, or their efferent nerves have been described.

SUMMARY

[0010] According to an illustrative embodiment of the present invention, there is provided a method for monitoring the respiratory activity of a subject, comprising the steps of:

recording an electroneurogram signal from the internal branch of the superior laryngeal nerve of the subject;

conditioning the electroneurogram signal;

computing an index of respiratory activity of the conditioned electroneurogram signal; and

reporting an occurrence of an apneic event when the index of respiratory activity meets at least one apnea criteria.

[0011] According to another illustrative embodiment of the present invention, the method further comprising the step of generating a stimulation signal which acts to increase airway patency or stimulate breathing following the reporting of the apneic event.

[0012] According to yet another illustrative embodiment of the present invention, the index of respiratory activity is computed by applying a rectification and bin-integrated algorithm to the conditioned electroneurogram signal.

[0013] According to a further illustrative embodiment of the present invention, the at least one apnea criteria includes a first criteria associated with obstructive sleep apnea and a second criteria associated with central sleep apnea, and wherein the reporting step includes reporting the apneic event as an obstructive sleep apnea event when the index of respiratory activity meets the first criteria and as a central sleep apnea event when the index of respiratory activity meets the second criteria.

[0014] According to a further still illustrative embodiment of the present invention, the method further comprises the step of reporting an occurrence of an obstructive sleep hypopnea event when the index of respiratory activity meets a third criteria associated with obstructive sleep hypopnea and reporting an

occurrence of a central sleep hypopnea event when the index of respiratory activity meets a fourth criteria associated with central sleep hypopnea.

[0015] According to another illustrative embodiment of the present invention, there is provided a method for treating sleep apnea and/or hypopnea of a subject, comprising eliciting a reflexive pattern activity from the central nervous system of the subject following the detection of the sleep apnea event.

[0016] According to a further illustrative embodiment of the present invention, the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve or the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

[0017] According to a another illustrative embodiment of the present invention, the is provided a system implementing the above described methods.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Non-limitative illustrative embodiments of the invention will now be described by way of example only with reference to the accompanying drawings, in which:

[0019] Figure 1 is a schematic representation of the human airway relevant to upper airway pressure as measured at the larynx during normal respiration;

[0020] Figure 2 is a graph of airway pressure measured at the larynx during the normal breathing process;

[0021] Figure 3 is a schematic representation of the human airway relevant to upper airway pressure as measured at the larynx during an obstructive sleep apnea (OSA) event;

[0022] Figure 4 is a graph of airway pressure measured at the larynx at the outset of an OSA event;

[0023] Figure 5 is a schematic representation of the human airway relevant to upper airway pressure as measured at the larynx during a central sleep apnea (CSA) event;

[0024] Figure 6 is a graph of airway pressure measured at the larynx at the outset of a CSA event;

[0025] Figure 7 is a graph of an index of respiratory activity (IRA) computed from the rectified and bin-integrated (RBI) electroneurogram of the iSLN during normal respiration;

[0026] Figure 8 is a graph of an index of respiratory activity (IRA) computed from an RBI electroneurogram of the ISLN at the outset of an OSA event;

[0027] Figure 9 is a graph of an alternative index of respiratory activity (IRA) computed from the duration of peaks in an RBI electroneurogram of the ISLN at the outset of an OSA event;

[0028] Figure 10 is a graph of a further alternative index of respiratory activity (IRA) computed from the interval between peaks in an RBI electroneurogram of the ISLN at the outset of an OSA event;

[0029] Figure 11 is a graph of an index of respiratory activity (IRA) computed from an RBI electroneurogram of the iSLN at the outset of a CSA event;

[0030] Figure 12 is a graph of an index of respiratory activity (IRA) computed from the rectified and bin-integrated (RBI) electroneurogram of the iSLN during normal respiration showing multiple apnea severity levels;

[0031] Figure 13 is a flow diagram depicting the detection, identification and treatment of sleep apnea process in accordance with a first illustrative embodiment of the present invention;

[0032] Figure 14 is a flow diagram depicting the detection, identification and treatment of sleep apnea and hypopnea process in accordance with a second illustrative embodiment of the present invention;

[0033] Figure 15 is a block diagram of an example of a neuromodulator for the detection, identification and treatment of sleep apnea.

DETAILED DESCRIPTION

[0034] Generally stated, the non-limitative illustrative embodiment of the present invention provides a method and device for treating sleep dysfunctions such as sleep apnea/hypopnea by monitoring respiratory-related activity from nerve or muscle, interpreting these internal signals to detect and classify adverse events in the airway, and stimulating nerves or muscles to elicit appropriate corrective responses to adverse respiratory events.

[0035] In the detailed description, unless specified otherwise, reference to the term "apnea" is defined to mean either an obstructive, central, mixed, or complex episode of apnea or hypopnea, occurring during sleep or awake as in Cheynne-Strokes respiration.

Normal respiration

[0036] Referring to Figure 1, there is shown a schematic representation of the human airway 100 relevant to upper airway 110 pressure as measured at the larynx 102 during normal respiration. During normal inspiration, the diaphragm and intercostal muscles 120 contract 122, creating a negative pressure in the airway 100 and drawing air into the lungs 104. Expiration is typically passive, resulting from relaxation of the diaphragm and intercostal muscles 120 back to their resting position 124, and elastic recoil of the lungs 104. The amount of air flow produced by changing airway 100 pressure is influenced by resistance from the structures of the upper airway 110, including the soft palate 112, tongue 114, pharynx 116, and epiglottis 118.

[0037] Figure 2 shows a graph 200 of airway pressure 201 measured at the larynx 102 (see Figure 1) during the normal breathing process, comprising regular inspiration 202 and expiration 204 peaks of similar amplitude and frequency. Airway pressure at larynx 102 is transduced by mucosal mechanoreceptors that are sensitive to pressure and is communicated to the central nervous system via the internal branch of the superior laryngeal nerve (iSLN).

Respiration during an OSA event

[0038] Referring to Figure 3 there is shown a schematic representation of the human airway 100 relevant to upper airway pressure as measured at the

larynx during an OSA event. Here, a lack of muscle tone in the upper airway 110 allows pharyngeal structures 116 to partially or completely block the lumen 119 of the airway 100, particularly when subjects sleep on their back. Respiratory drive continues during the OSA event, the diaphragm and intercostal muscles 120 contract 122, creating a negative pressure in the airway 100 drawing flaccid pharyngeal structures 116 into the airway lumen 119.

[0039] Figure 4 shows a graph 400 of airway pressure 401 measured at the larynx 102 (see Figure 3) at the outset of an OSA event, comprising normal breathing process inspiration 402a and expiration 404a peaks before the OSA event and then inspiration 402b and expiration 404b peaks of a greater amplitude during the OSA event. This increase in the amplitude of the airway pressure 401 reflects continuing attempts on the part of the subject to breathe after airway obstruction, generating greater than normal airway pressures 401. The outset of the OSA event 403 can then be identified by the sudden increase in amplitude of the inspiration 402 and expiration 404 peaks of the airway pressure 401.

Respiration during a CSA event

[0040] Referring to Figure 5, there is shown a schematic representation of the human airway 100 relevant to upper airway pressure as measured at the larynx during a CSA event. Here, the upper airway 110 remains open, but diminished central respiratory drive reduces or eliminates diaphragm 120 movement, and thus air flow during the CSA event.

[0041] Figure 6 shows a graph 600 of airway pressure 601 measured at the larynx 102 (see Figure 5) at the outset of a CSA event, comprising normal breathing process inspiration 602 and expiration 604 peaks before the CSA event and then an absence of, or very low amplitude, inspiration and expiration peaks 606 during the CSA event. Despite a patent upper airway 110, upper airway pressure 601 is not fully modulated after the onset of the CSA event and diminution of diaphragm movement. The outset of the CSA event 603 can then be identified by the sudden drop 606 in the amplitude of the inspiration 602 and expiration 604 peaks of the airway pressure 601.

Detection and classification of apnea events

[0042] It has been discovered that the electroneurogram (ENG) of the internal branch of the superior laryngeal nerve (iSLN) is correlated with pressure in the upper airway 110 (see Figure 1). This relationship can be demonstrated by calculating an index of respiratory activity (IRA) that is indicative of the amplitude and timing of the ENG signal. For example, the IRA may be calculated by applying a rectification and bin-integration (RBI) algorithm to the amplified iSLN signal. Referring to Figure 7, during normal breathing, each peak 702 of the IRA 701 calculated using this method corresponds to a regular inspiration peak 202 of the airway pressure 201 measured at the larynx 102, as illustrated in Figure 2.

[0043] The amplitude of peaks in the IRA during each breath occurs within a normal range of amplitudes which may be determined using a calibration process during normal respiration of a given subject either empirically or using, for example, polysomnographic techniques. This range of amplitudes can be used to set upper 707 and lower 705 thresholds for apnea event detection. Peaks 702 outside of this normal range can be detected using simple fixed-level thresholds and defined as apneic events.

[0044] The upper 707 and lower 705 thresholds can further be used to classify, in real-time, a detected apneic event as being either an OSA event or a CSA event.

[0045] It is to be understood that although the above the IRA is calculated by applying a rectification and bin-integration (RBI) algorithm to the amplified iSLN signal, other signal processing algorithms may also be applied including: high pass filter, low pass filter, bandpass filter, notch filter, FIR filter, IIR filter, smoothing, moving average, Weiner (optimal) filter, rectification, bin-integration, multichannel noise reduction, principal components analysis, independent components analysis, wavelet analysis, Fourier transformation, matched filtering, variance/variance ratio calculations, or some combination of the above. The raw iSLN ENG waveform may also be used directly. IRAs based on neural network analyses, cluster analysis in multidimensional feature space, cluster cutting using k-means,

Bayesian expectation-maximization, closest centers, or manual cluster cutting methods may also be used.

[0046] It is to be also understood that an IRA could be computed from any number of other iSLN ENG signal features that vary with respiratory state such as event or waveform timing, interval, amplitude, duration, rise time, fall time, slope, presence, absence, pattern, 1st derivative, 2nd derivative, 3rd derivative, root mean square amplitude, peak-to-peak amplitude, variance, statistical probability or probability relative to baseline or running average.

OSA event

[0047] Referring to Figure 8, there is shown an example of peaks 802 of the IRA 801 at the outset of an OSA event, comprising normal breathing process inspiration related peaks 802a within the upper 707 and lower 705 thresholds before the OSA event and then inspiration related peaks 802b of an amplitude greater than the upper 707 threshold during the OSA event. The outset of the OSA event 803 can then be identified by the first crossing of the upper 707 threshold by the inspiration related peaks 802.

[0048] Alternatively, referring to Figure 9, it may be observed that at the outset of the OSA event 803 the durations 805b of the peaks 802b of the RBI ENG measured at a fixed level, for example threshold 705, are greater than the peak durations 805a of the peaks 802a measured during the normal breathing process. Accordingly, the peak durations of the RBI ENG may be used to calculate an IRA and identify the outset of an OSA event by setting an appropriate threshold.

[0049] Similarly, referring to Figure 10, it may be observed that at the outset of the OSA event 803 the intervals 807b between the peaks 802b of the RBI ENG measured at a fixed level, for example threshold 705, are smaller than the interpeak intervals 807a between the peaks 802a measured during the normal breathing process. Accordingly, the interpeak intervals of the RBI ENG may be used to calculate an IRA to identify the outset of an OSA event by setting an appropriate threshold.

CSA event

[0050] Referring to Figure 11, there is shown an example of peaks 902 of the IRA 901 at the outset of a CSA event, comprising normal breathing process inspiration related peaks 902 within the upper 707 and lower 705 thresholds before the CSA event and then inspiration related peaks 906 of an amplitude lower than the lower 705 threshold (or absence of peaks) during the CSA event. The outset of the CSA event 903 can then be identified by the first absence of crossing of the lower 705 threshold by the inspiration related peaks 902 for a set time period. This period of time may be set to represent the average time between one or more respiration cycle.

[0051] As is the case with OSA events (see Figures 9 and 10), other IRAs may be calculated in order to identify CSA events, such as the peak durations and interpeak intervals of the RBI ENG by setting appropriate levels and thresholds. It is to be understood that the absence of measurements at a specified level will indicate a CSA event.

[0052] It is also to be understood that detection of respiratory events in the IRA using methods other than fixed-level thresholding may be used, for example noise-tracking or other adaptive thresholds, energy or non-linear energy thresholds, or any variety of other detection operations on the raw or processed data.

Apnea event severity

[0053] In an alternative embodiment, the severity of the apnea event may be determined by comparing the amplitude of the apneic IRA 801, 901 to that observed during normal breathing 701. More severe apnea is characterized by IRA peaks 802, 902 having amplitudes far from the upper 707 and lower 705 thresholds, while less severe apnea or hypopnea is characterized by IRA peaks 802, 902 having amplitudes just above or below the upper 707 and lower 705 thresholds. The level of apnea thus determined can be used to adjust the parameters and characteristics of the applied neurostimulation treatment. This may include changing the stimulation waveform, increasing or decreasing the stimulus amplitude, increasing or decreasing the number of stimuli delivered,

selecting electrodes in specific locations or changing the number of stimulation electrodes used.

[0054] For example, referring to Figure 12, various OSA 707, 709 and CSA 705, 703 severity levels may be assigned corresponding thresholds. It is to be understood that the number of OSA and CSA severity levels may vary depending on the precision of the circuitry and/or algorithm used.

Hypopnea

[0055] In a further alternative embodiment, apneic events may be further identified as OSA or obstructive sleep hypopnea (OSH) as well as CSA or central sleep hypopnea (CSH). For example, referring still to Figure 12, threshold 708 may be associated with OSH while threshold 707 may be associated with OSA, meaning that IRA peaks between thresholds 708 and 707 are identified as OSH while IRA peaks above threshold 707 are identified as OSA. Conversely, threshold 704 may be associated with CSH while threshold 705 may be associated with CSA, meaning that IRA peaks between thresholds 704 and 705 are identified as CSH while IRA peaks below threshold 705 are identified as CSA. The range of values for which IRA peaks are defined as OSH as opposed to OSA, as well as CSH as opposed to CSA, may be determined using a calibration process during abnormal respiration of a given subject using, for example, polysomnographic techniques.

[0056] It is to be understood that OSH, OSA, CSH and CSA may be subdivided into multiple severity levels depending on the precision of the circuitry and/or algorithm used.

[0057] As described above for the OSA and CSA event detection, the variation in IRAs calculated using algorithms other than RBI ENG may also be used to determine the severity of the apneic event.

[0058] Although peaks in the IRA coincident with negative pressure receptor activity are described above, it is to be understood that receptors sensitive to other stimuli and modalities, respiratory events, phases or features, and with afferents carried by other nerves may also used. This is meant to include mechanoreceptors

sensitive to positive airway pressure, stretch, position, shear or slip, vibration, texture, touch, touch and pressure, muscle stretch, muscle "drive", air flow, blood pressure or osmolarity, chemoreceptors sensitive to CO_2, O_2, or pH, thermoreceptors sensitive to temperature or airflow, nociceptors sensitive to polymodal pain, or some combination of the above.

Apneic event detection, identification and treatment

[0059] Referring to Figure 13, there is shown in a flow diagram a process 1000 for the detection and classification of apnea events in accordance with a first illustrative embodiment of the present invention. The steps composing the process are indicated by blocks 1002 to 1020.

[0060] The process 1000 starts at block 1002, where the iSLN ENG signal is recorded, after which, at block 1004, the iSLN ENG signal is conditioned (for example amplified).

[0061] At block 1006, an index of respiratory activity (IRA) is computed. The IRA is a measure of the iSLN ENG signal which varies with the respiratory activity of the subject and may be used to detect sleep apnea events through comparison with thresholds associated with normal respiratory activity. For example, the IRA may be the amplitude envelope computed by applying an RBI algorithm to the filtered and amplified iSLN ENG signal. This algorithm first rectifies the iSLN ENG signal and then sums the result in bins, essentially applying a low pass filter to the rectified signal. Alternatively, the IRA may be the root-mean-square or peak-to-peak amplitude of the iSLN ENG signal, the duration of peaks in the RBI iSLN ENG signal measured at a fixed level or the interval between peaks of the RBI iSLN ENG signal measured at a fixed level. It should be noted that the interpeak intervals are complimentary to the peak durations and as such an IRA based on interpeak interval values should be expressed as the inverse of the measured values.

[0062] Optionally, a moving average filter may then be applied to the IRA, for example a moving average filter spanning one second of data, and the result optimized using, for example, the solution to the Wiener-Hopf equation. The

moving average filter helps to reduce the influence of variability inherent to iSLN ENG signals and its total length may be selected so as to be near the smallest feature (peak width) to be detected.

[0063] At block 1008, the process 1000 verifies if the IRA meets the criteria defining OSA. For example, in the case where the IRA is the RBI ENG of the iSLN signal, OSA is defined as peak values exceeding the upper threshold 707 of the range of amplitudes observed during normal respiration as illustrated in Figure 7. It is to be understood that the criteria defining OSA will vary depending on the IRA used.

[0064] If the IRA meets the criteria of OSA, the process 1000 proceeds to block 1010 where an OSA event is reported. Then, optionally, at block 1012, airway opening stimulation may be triggered in response to the detection of the OSA event.

[0065] The airway opening stimulation may act to replace or augment the negative pressure reflex in response to the OSA event, by artificially improving airway patency during inspiration. The stimulation may take a number of different forms and is designed to remain below the arousal threshold of the sleeping subject. Possible targets for stimulation include specific nerves that control upper airway patency such as, for example, the hypoglossal or glossopharyngeal nerves, or their combination. Likewise, direct stimulation of specific muscles that control upper airway patency such as, for example, genioglossus, tensor palatini, or sternohyoid muscles, or their combination, can also be used. Treatment can be accomplished by applying stimulation individually to some or all of the muscles involved in airway patency, or individually to the nerves efferent to these muscles, or some combination of the thereof. Stimulation of activities or muscles or nerves that increases upper airway patency can be delivered phasically, in synchrony with inspiration or tonically, throughout the entire respiratory cycle.

[0066] In an alternative embodiment, the stimulation may be aimed at eliciting reflexive and pre-programmed coordinated activity from swallow-related central pattern generators in the central nervous system. For example, the iSLN

can be electrically stimulated at a rate of about 20 Hz to 50 Hz in order to provoke a swallowing reflex. Similar stimulus protocols give rise to one or more complete sequences of pharyngeal swallow. During pharyngeal swallow, upper airway pressure increases from negative values up to atmospheric pressure, the muscles of larynx and pharynx are activated, and the pharynx and larynx close and then open. The entire coordinated pattern of pharyngeal muscle activation ends with an open pharynx. Stimulation of this pattern is designed to open a collapsed upper airway and restore airway patency. Stimulation of other patterned activities may also be used to increase airway patency, such as cough, yawn, gag, etc., as well as some combination of stimulated patterned activities. Stimulation of the swallow sequence may also be accomplished using other nerves, for example the glossopharyngeal nerve.

[0067] The process 1000 then proceeds back to block 1002 where the recording of the iSLN ENG signal continues.

[0068] At block 1014, the process 1000 verifies if the IRA meets the criteria defining CSA. For example, in the case where the IRA is the RBI ENG of the iSLN signal, CSA may be defined as peak values remaining below the lower threshold 705 of the range of amplitudes observed during normal respiration as illustrated in Figure 7. It is to be understood that the definition of CSA will vary depending on the IRA used.

[0069] If the IRA meets the criteria of CSA, the process 1000 proceeds to block 1016 where a CSA event is reported. Then, optionally, at block 1018, breathing stimulation may be triggered in response to the detection of the CSA event.

[0070] The breathing stimulation acts to replace or augment respiratory drive in response to the CSA event. The stimulation may take a number of different forms and is designed to remain below the arousal threshold of the sleeping subject. Possible targets for stimulation include specific nerves that control respiratory muscles such as, for example, phrenic or intercostal nerves, or their combination. Likewise, direct stimulation of specific muscles that control

respiration such as, for example, diaphragm or intercostal respiratory muscles, or their combination, can also used. Treatment can be accomplished by applying stimulation to some or all of the muscles involved in respiration, or to some or all the nerves efferent to these muscles, or some combination of the above. Stimulation of activities of muscles or nerves that increase respiration could be delivered in synchrony with remaining or previous inspiratory activity.

[0071] In an alternative embodiment, the stimulation may be aimed at eliciting reflexive and pre-programmed coordinated activity from swallow-related central pattern generators in the central nervous system as previously described at block 1012.

[0072] The process 1000 then proceeds back to block 1002 where the recording of the iSLN ENG signal continues.

[0073] Optionally, at block 1020, the IRA signal corresponding to normal respiration, the process 1000 terminates any ongoing treatment.

[0074] The process 1000 then proceeds back to block 1002 where the recording of the iSLN ENG signal continues.

[0075] Referring to Figure 14, there is shown in a flow diagram a process 2000 for the detection and classification of apnea and hypopnea events in accordance with a second illustrative embodiment of the present invention. The steps composing the process are indicated by blocks 2002 to 2032.

[0076] The process 2000 starts at block 2002, where the iSLN ENG signal is recorded, after which, at block 2004, the iSLN ENG signal is conditioned (for example amplified).

[0077] At block 2006, an index of respiratory activity (IRA) is computed as previously described (see block 1006 of process 1000 from Figure 13).

[0078] At block 2008, the process 2000 verifies if the IRA meets the criteria defining OSA. For example, in the case where the IRA is the RBI ENG of the iSLN signal, the process 2000 verifies if peak values exceed threshold 708 associated with OSA (see Figure 12).

[0079] If the IRA meets the criteria defining OSA, the process 2000 proceeds to block 2010 where an OSA event is reported. Then, optionally, at block 2012, airway opening stimulation as previously described (see block 1012 of process 1000 from Figure 13) may be triggered in response to the detection of the OSA event.

[0080] The process 2000 then proceeds back to block 2002 where the recording of the iSLN ENG signal continues.

[0081] At block 2014, the process 2000 verifies if the IRA meets the criteria defining OSH. For example, in the case where the IRA is the RBI ENG of the iSLN signal, the process 2000 verifies if peak values are situated between thresholds 707 and 708 associated with OSH (see Figure 12).

[0082] If the IRA meets the criteria defining OSH, the process 2000 proceeds to block 2016 where an OSH event is reported. Then, optionally, at block 2018, airway opening stimulation as previously described (see block 1012 of process 1000 from Figure 13), but with adjusted parameters, may be triggered in response to the detection of the OSH event.

[0083] The process 2000 then proceeds back to block 2002 where the recording of the iSLN ENG signal continues.

[0084] At block 2020, the process 2000 verifies if the IRA meets the criteria defining CSA. For example, in the case where the IRA is the RBI ENG of the iSLN signal, the process 2000 verifies if peak values remain under the threshold 704 associated with CSA (see Figure 12).

[0085] If the IRA meets the criteria defining CSA, the process 2000 proceeds to block 2022 where a CSA event is reported. Then, optionally, at block 2024, breathing stimulation as previously described (see block 1018 of process 1000 from Figure 13) may be triggered in response to the detection of the CSA event.

[0086] The process 2000 then proceeds back to block 2002 where the recording of the iSLN ENG signal continues.

[0087] At block 2026, the process 2000 verifies if the IRA meets the criteria defining CSH. For example, in the case where the IRA is the RBI ENG of the iSLN signal, the process 2000 verifies if peak values are situated between thresholds 704 and 705 associated with CSH (see Figure 12).

[0088] If the IRA meets the criteria of CSH, the process 2000 proceeds to block 2028 where a CSH event is reported. Then, optionally, at block 2030, breathing stimulation as previously described (see block 1018 of process 1000 from Figure 13), but with adjusted parameters, may be triggered in response to the detection of the CSH event.

[0089] The process 2000 then proceeds back to block 2002 where the recording of the iSLN ENG signal continues.

[0090] It is to be understood that in other alternative embodiments, the detection and classification algorithm may further subdivide the OSH, OSA, CSH and CSA events into multiple severity levels, each level having associated stimulation parameter adjustments.

Neuromodulator for the detection, identification and treatment of sleep apnea

[0091] Referring to Figure 15, there is shown a block diagram of an example of a neuromodulator 1100 for detection, identification and treatment of sleep apnea by monitoring respiratory-related activity from nerve or muscle, interpreting these internal signals to detect and classify adverse events in the airway, and stimulating nerves or muscles to elicit appropriate corrective responses to adverse respiratory events.

[0092] In the illustrated example, apnea is detected and identified by monitoring respiratory-related activity from the internal branch of the superior laryngeal nerve (iSLN) 132. The iSLN carries afferents from receptors in the laryngeal mucosa toward the central nervous system 130. Other peripheral nerves carrying afferents modulated by respiratory condition may also be monitored, including the recurrent laryngeal nerve, the main branch of the SLN, the vagus nerve, the phrenic nerve, each nerve alone, or in combination with the other(s).

Respiratory activity may also be monitored from nerves carrying efferent signals to muscles of the upper airway, diaphragm, or intercostal muscles, or by monitoring the activity of these respiratory muscles themselves, alone, or in some combination with other nerves or muscles modulated by respiratory activity.

[0093] The neuromodulator 1100 includes a signal conditioning module 1102, a respiratory activity monitoring module 1104 and a stimulation module 1106.

[0094] A recording electrode 1132 is placed in, around, or near a peripheral nerve that carries afferent neural activity from receptors in the upper airway 110 (see Figure 1) toward the central nervous system 130. One particular nerve that may be used is the iSLN 132. A lead 1133 connects the electrode 1132 to the signal conditioning module 1102.

[0095] It is to be understood that depending on the application there maybe multiple recording electrodes 1132 to simultaneously or sequentially monitor multiple signal sources. The recording electrode 1132 may also target other peripheral receptors that exhibit modulations of bioelectric potential correlated with respiration. Other receptors that may be monitored to determine respiratory condition include: mechanoreceptors sensitive to positive airway pressure, stretch, position, shear or slip, vibration, texture, touch, touch and pressure, muscle stretch, muscle "drive", air flow, blood pressure or osmolarity, chemoreceptors sensitive to CO_2, O_2, or pH, thermoreceptors sensitive to temperature or airflow, nociceptors sensitive to polymodal pain, or some combination of the above.

[0096] A stimulation electrode 1134 is placed in, around, or near, a target nerve or muscle depending on the type of stimulation used. A lead 1135 connects the stimulation electrode 1134 to the stimulation module 1106. The stimulation electrode 1134 may contain additional features allowing for enhanced current carrying capacity, selective stimulation using current steering, directionally selective stimulation of efferent or afferent fibers, or selectivity for stimulating axons of a particular diameter.

[0097] It is to be understood that there may be multiple targets for stimulation and that their selection may vary depending on the identified apneic event and the type of stimulation used. Furthermore, the stimulation may target the central nervous system 130 when the stimulation is aimed at eliciting reflexive and pre-programmed coordinated activity such as swallowing. It is further to be understood that in some alternative embodiment, a single electrode may be used both for the recording 1132 and the stimulation 1134 electrodes, for example when the iSLN is used for both recording and stimulation. Furthermore, multiple electrodes may be use, some or all of them being used both as recording 1132 and stimulation 1134 electrodes while others only as recording 1132 or stimulation 1134 electrodes.

[0098] In an alternative embodiment, iSLN ENG signals may be passed from electrode 1132 to the signal conditioning module 1102 wirelessly. Similarly, the stimulation signals from the stimulation module 1106 may be passed to the electrode 1134 wirelessly.

[0099] The electrodes 1132 and 1134 may be, for example, cuff electrodes. An example of a cuff electrode that may be used as electrodes 1132 and 1134 is disclosed in U.S. Patent No. 5,824,027 entitled "NERVE CUFF HAVING ONE OR MORE ISOLATED CHAMBERS", issued October 20, 1998, to Hoffer et al. It is to be understood that other types of electrodes, leads, probes, cuff-electrodes, etc., may be used as well. Other examples of cuff electrodes that may be used are disclosed in U.S. Patent Application Publication No. 2008/0065184 entitled "NERVE CUFF, METHOD AND APPARATUS FOR MANUFACTURING SAME", published March 13, 2008, by Hoffer et al. and PCT Patent Application Publication No. WO 2008/025155 entitled "NERVE CUFF INJECTION MOLD AND METHOD OF MAKING A NERVE CUFF", filed August 29, 2007, by Imbeau et al.

[00100] The signal conditioning module 1102 conditions the iSLN ENG signal, for example amplifying it, recorded by the first electrode 1132 and provides the conditioned iSLN ENG signal to the respiratory activity monitoring module 1104, which includes an algorithm that uses the conditioned iSLN ENG signal to

monitor respiratory activity, detect apnea events before they result in arousal from sleep and identify the type of apnea event.

[00101] The signal conditioning module 1102 may include, without limiting the illustrative embodiment to these components, a signal amplifier and a rectifier circuit. Examples of amplifiers and rectifier circuit that may be used are respectively disclosed in U.S. Patent Application Publication No. 2006/0189881 entitled "IMPLANTABLE SIGNAL AMPLIFYING CIRCUIT FOR ELECTRONEUROGRAPHIC RECORDING", published August 24, 2006, by Baru Fassio and U.S. Patent No. 7,282,980 entitled "PRECISION RECTIFIER CIRCUIT FOR HIGH-DENSITY, LOW-POWER IMPLANTABLE MEDICAL DEVICE", issued October 16, 2007, to Baru Fassio.

[00102] The algorithm executed by the respiratory activity monitoring module 1104 implements blocks 1006 to 1010, 1014 and 1016 of process 1000 shown in Figure 13 or blocks 2006 to 2011 and 2014 to 2017 of process 2000 shown in Figure 14. Upon the detection of an apnea event, the respiratory activity monitoring module 1104 sends a trigger to the stimulation module 1106 along with an identification of the type of apnea event, i.e. OSH, OSA, CSH or CSA depending on the implemented algorithm, which generates a stimulation appropriate for the type of apnea event. Optionally, the respiratory activity monitoring module 1104 may also send an indication of the severity level of the apnea event, as well as timing information of previous or continuing respiration patterns, to the stimulation module 1106.

[00103] The respiratory activity monitoring module 1104 may optionally provide information about the respiratory activity of the subject, report sleep apnea events and/or allow remote modification of various criteria/thresholds through a communication link such as, for example, a radio frequency (RF) or infrared (IR) link (not shown).

[00104] The stimulation module 1106 implements the various stimulation strategies disclosed in blocks 1012 and 1018 of process 1000 and in blocks 2012, 2018, 2024 and 2030 of process 2000, shown in Figures 13 and 14, respectively.

The produced stimulation signals may be square pulses or arbitrary waveforms, constant voltage or constant current. Stimulation location, amplitude, and/or waveform may be adjusted in a closed-loop based on current respiratory conditions or conditions relayed by the respiratory activity monitoring module 1104 in response to previous stimulation. Stimulation waveforms may also contain features allowing for selective stimulation using current steering, directionally selective stimulation of efferent or afferent fibers, selectivity for stimulating axons of a particular diameter, or features designed to block transmission of undesired bioelectric activity.

[00105] The stimulation module 1106 may optionally allow remote selection and/or modification of the stimulation strategies and stimulation parameters through a communication link such as, for example, a radio frequency (RF) or infrared (IR) link (not shown).

[00106] The stimulation module 1106 may include, without limiting the illustrative embodiment to this component, a pulse generator for providing current and/or voltage stimulation signals to muscles, nerves or tissue. Examples of pulse generators that may be used are disclosed in U.S. Patent Application No. 11/920,814 entitled "IMPLANTABLE PULSE GENERATOR", filed on October 9, 2007, by Roy et al.

[00107] Finally, the neuromodulator 1100 may include an internal power supply (not shown) or use a transcutaneous energy transfer system (not shown).

[00108] Other applications of the invention will be apparent to those skilled in the art. For example, the device has the capacity to detect respiration rate, phase, and timing. This provides for general monitoring of vital signs, aside from apnea detection, and could provide respiration-related parameters to other devices such as external monitoring equipment, or implanted devices such as pacemakers or implantable defibrillators.

[00109] Further, apneas occurring during sleep or waking, as in cases of Cheyne-Stokes respiration or Charcot-Marie-Tooth disease could be effectively treated with the invention described herein. Other adverse respiratory conditions or

types of sleep disordered breathing could be detected by monitoring naturally occurring receptors in the airway, such as narrowing or obstruction of the airway, snoring, presence of solids or fluids in the airway, respiratory difficulty in congestive heart failure, presence of reflux in the airway, or inappropriate magnitude or timing of airway muscle activity. Detection of these events might be applied to the detection and treatment of respiratory disorders such as asthma, dysphagia, aspiration pneumonia, or SIDS. Stimulation treatments could result in bronchodilation or bronchoconstriction, change in breathing pattern, swallow, cough, gag, muscle or sphincter activation or inhibition, change in mucus or other secretion, or other activity of the airway.

[00110] It is to be understood that the various units, modules and sub-modules and algorithms may be implemented using, for example one or more electronic circuit, microcontroller or DSP.

[00111] It is also to be understood that the detection, identification and treatment of sleep apnea processes 1000 (see Figure 13) and 2000 (see Figure 14) as well as the neuromodulator 1100 (see Figure 15) may be selectively activated, for example when a subject is sleeping. The activation may be user initiated, optionally with a delay, according to a given schedule, by monitoring the heart rate of the subject, the orientation of the subject, etc.

[00112] Although the present invention has been described by way of illustrative embodiments and examples thereof, it should be noted that it will be apparent to persons skilled in the art that modifications may be applied to the present particular embodiment without departing from the scope of the present invention.

REFERENCE

[1] Chamberlin, N.L., Eikermann, M., Fassbender, P., White, D.P., and Malhotra, A., (2007) "Genioglossus premotoneurons and the negative pressure reflex in rats." J. Physiol. 579: 515-526.

WHAT IS CLAIMED IS:

1. A method for monitoring the respiratory activity of a subject, comprising the steps of:

recording an electroneurogram signal from the internal branch of the superior laryngeal nerve of the subject;

conditioning the electroneurogram signal;

computing an index of respiratory activity of the conditioned electroneurogram signal; and

reporting an occurrence of an apneic event when the index of respiratory activity meets at least one apnea criteria.

2. A method according to claim 1, further comprising the step of generating a stimulation signal which acts to increase airway patency or stimulate breathing following the reporting of the apneic event.

3. A method according to claim 2, wherein parameters of the stimulation signal are selected in accordance with the index of respiratory activity.

4. A method according to claim 2, wherein the stimulation signal is selected so as to elicit a reflexive pattern activity from the central nervous system of the subject.

5. A method according to claim 4, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

6. A method according to claim 5, wherein the swallowing reflexive pattern activity is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

7. A method according to claim 5, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

8. A method according to claim 1, wherein the at least one apnea criteria includes a first criteria associated with obstructive sleep apnea and a second criteria associated with central sleep apnea, and wherein the reporting step includes reporting the apneic event as an obstructive sleep apnea event when the index of respiratory activity meets the first criteria and as a central sleep apnea event when the index of respiratory activity meets the second criteria.

9. A method according to claim 8, further comprising the step of generating a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event or stimulate breathing following the reporting of the central sleep apnea event.

10. A method according to claim 8, further comprising the step of reporting an occurrence of an obstructive sleep hypopnea event when the index of respiratory activity meets a third criteria associated with obstructive sleep hypopnea and reporting an occurrence of a central sleep hypopnea event when the index of respiratory activity meets a fourth criteria associated with central sleep hypopnea.

11. A method according to claim 10, further comprising the step of generating a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep hypopnea event or of the obstructive sleep apnea event, or stimulate breathing following the reporting of the central sleep hypopnea event or of the central sleep apnea event, parameters of the stimulation signal being selected according to whether the obstructive sleep hypopnea event, the obstructive sleep apnea event, the central sleep hypopnea event or the central sleep apnea event was reported.

12. A method according to claim 1, wherein the index of respiratory activity is indicative of the amplitude and timing of the electroneurogram signal.

13. A method according to claim 12, wherein the index of respiratory activity is selected from a group consisting of the peaks of the electroneurogram signal, the root-mean-square of the electroneurogram signal, the peak-to-

peak amplitude of the electroneurogram signal, the duration of peaks of the electroneurogram signal, the interpeak intervals of the electroneurogram signal and any combination thereof.

14. A method according to claim 1, wherein the index of respiratory activity is computed by applying a rectification and bin-integration algorithm to the conditioned electroneurogram signal.

15. A method according to claim 14, wherein the step of conditioning the electroneurogram signal includes amplification and band-pass filtering.

16. A method according to claim 14, wherein the step of computing the index of respiratory activity further includes applying a moving average filter to the rectified and bin-integrated amplified electroneurogram signal and optimizing the result.

17. A method according to claim 14, wherein the reporting step includes reporting the apneic event as an obstructive sleep apnea event when the index of respiratory activity exceeding a first threshold.

18. A method according to claim 17, wherein the first threshold is set according to calibration during the normal respiration of the subject during sleep using polysomnographic techniques.

19. A method according to claim 17, further comprising the step of generating a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event.

20. A method according to claim 19, wherein a target of the stimulation signal is selected from a group consisting of the hypoglossal nerve, the glossopharyngeal nerve, the genioglossus muscle, the tensor palatini muscle, the sternohyoid muscle and any combination thereof.

21. A method according to claim 19, wherein a target of the stimulation signal is selected so as to elicit a reflexive pattern activity from the central nervous system of the subject.

22. A method according to claim 21, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

23. A method according to claim 22, wherein the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

24. A method according to claim 22, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

25. A method according to claim 14, wherein the apneic event reporting step includes reporting the apneic event as an obstructive sleep hypopnea event when the index of respiratory activity is between a first and a second thresholds and as an obstructive sleep apnea event when the index of respiratory activity exceeds the second threshold.

26. A method according to claim 25, wherein the first and second thresholds are set according to calibration during the normal and abnormal respiration of the subject during sleep using polysomnographic techniques.

27. A method according to claim 25, further comprising the step of generating a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event or of the obstructive sleep hypopnea event, parameters of the stimulation signal being selected according to whether the obstructive sleep apnea event or the obstructive sleep hypopnea event was reported.

28. A method according to claim 27, wherein a target of the stimulation signal is selected from a group consisting of the hypoglossal nerve, the glossopharyngeal nerve, the genioglossus muscle, the tensor palatini muscle, the sternohyoid muscle and any combination thereof.

29. A method according to claim 27, wherein a target of the stimulation signal is selected so as to elicit a reflexive pattern activity from the central nervous system of the subject.

30. A method according to claim 29, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

31. A method according to claim 30, wherein the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

32. A method according to claim 30, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

33. A method according to claim 14, wherein the reporting step includes reporting the apneic event as a central sleep apnea event when the index of respiratory activity remains below a third threshold.

34. A method according to claim 33, wherein the third threshold is set according to calibration during the normal respiration of the subject during sleep using polysomnographic techniques.

35. A method according to claim 33, further comprising the step of generating a stimulation signal which acts to stimulate breathing following the reporting of the central sleep apnea event.

36. A method according to claim 35, wherein a target of the stimulation signal is selected from a group consisting of the phrenic nerve, the intercostal nerve, the diaphragm muscle, the intercostal respiratory muscle and any combination thereof.

37. A method according to claim 35, wherein a target of the stimulation signal is selected so as to elicit a reflexive pattern activity from the central nervous system of the subject.

38. A method according to claim 37, wherein the reflexive pattern activity is selected from a group consisting of negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

39. A method according to claim 38, wherein the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

40. A method according to claim 38, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

41. A method according to claim 14, wherein the apneic event reporting step includes reporting the apneic event as a central sleep hypopnea event when the index of respiratory activity is between a third and a fourth thresholds and as a central sleep apnea event when the index of respiratory activity remains under the fourth threshold.

42. A method according to claim 41, wherein the third and fourth thresholds are set according to calibration during the normal and abnormal respiration of the subject during sleep using polysomnographic techniques.

43. A method according to claim 41, further comprising the step of generating a stimulation signal which acts to stimulate breathing following the reporting of the central sleep apnea event or of the central sleep hypopnea event, parameters of the stimulation signal being selected according to whether the central sleep apnea event or the central sleep hypopnea event was reported.

44. A method according to claim 43, wherein a target of the stimulation signal is selected from a group consisting of the phrenic nerve, the intercostal nerve, the diaphragm muscle, the intercostal respiratory muscle and any combination thereof.

45. A method according to claim 43, wherein a target of the stimulation signal is selected so as to elicit a reflexive pattern activity from the central nervous system of the subject.

46. A method according to claim 45, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

47. A method according to claim 46, wherein the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

48. A method according to claim 46, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

49. A method for treating a sleep-related breathing disorder of a subject, comprising eliciting a reflexive pattern activity from the central nervous system of the subject following the detection of the sleep-related breathing disorder.

50. A method according to claim 49, wherein the sleep-related breathing disorder is sleep apnea.

51. A method according to claim 49, wherein the sleep-related breathing disorder is sleep hypopnea.

52. A method according to claim 49, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

53. A method according to claim 52, wherein the reflexive pattern activity is swallowing and is elicited by stimulating the internal branch of the superior laryngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

54. A method according to claim 52, wherein the swallowing reflexive pattern activity is elicited by stimulating the glossopharyngeal nerve with an electrical signal at a rate of about 20 Hz to 50 Hz.

55. A system for monitoring the respiratory activity of a subject, comprising:

an electrode configured to be positioned in contact with the internal branch of the superior laryngeal nerve of the subject;

a control unit operatively connected to the electrode, the implantable control unit including:

a signal conditioning module for conditioning an electroneurogram signal recorded by the electrode;

a monitoring and detection module for computing an index of respiratory activity from the electroneurogram signal and for reporting an occurrence of an apneic event when the index of respiratory activity meets at least one apnea criteria.

56. A system according to claim 55, wherein the system is fully implantable.

57. A system according to claim 55, wherein the electrode includes a cuff electrode assembly adapted to surround part of the internal branch of the superior laryngeal nerve of the subject.

58. A system according to claim 57, wherein the cuff electrode assembly is provided with multiple chambers having electrodes therein.

59. A system according to claim 55, wherein the index of respiratory activity is indicative of the amplitude and timing of the electroneurogram signal.

60. A system according to claim 59, wherein the index of respiratory activity is selected from a group consisting of the peaks of the electroneurogram signal, the root-mean-square of the electroneurogram signal, the peak-to-peak amplitude of the electroneurogram signal, the duration of peaks of the electroneurogram signal, the interpeak intervals of the electroneurogram signal and any combination thereof.

61. A system according to claim 55, wherein the index of respiratory activity is computed by applying a rectification and bin-integration algorithm to the conditioned electroneurogram signal.

62. A system according to claim 61, wherein the conditioning module includes an amplifier and a band-pass filter.

63. A system according to claim 61, wherein the monitoring and reporting module reports the apneic event as an obstructive sleep apnea event when the index of respiratory activity exceeding a first threshold.

64. A system according to claim 63, wherein the first threshold is set according to calibration during the normal respiration of the subject during sleep using polysomnographic techniques.

65. A system according to claim 63, further comprising a stimulation electrode and wherein the control unit further includes a stimulation module operatively connected to the monitoring and detection module and to the stimulation electrode, the stimulation module generating through the stimulation electrode a stimulation signal which acts to increase airway patency following the reporting the obstructive sleep apnea event.

66. A system according to claim 61, wherein the monitoring and reporting module reports the apneic event as an obstructive sleep hypopnea event when the index of respiratory activity is between a first and a second thresholds and as an obstructive sleep apnea event when the index of respiratory activity exceeds the second threshold.

67. A system according to claim 66, wherein the first and second thresholds are set according to calibration during the normal and abnormal respiration of the subject during sleep using polysomnographic techniques.

68. A system according to claim 66, further comprising a stimulation electrode and wherein the control unit further includes a stimulation module operatively connected to the monitoring and detection module and to the stimulation electrode, the stimulation module generating through the stimulation electrode a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event or of the obstructive sleep hypopnea event, parameters of the stimulation signal

being selected according to whether the obstructive sleep apnea event or the obstructive sleep hypopnea event was reported.

69. A system according to claim 61, wherein the monitoring and reporting module reports the apneic event as a central sleep apnea event when the index of respiratory activity remains below a third threshold.

70. A system according to claim 69, wherein the third threshold is set according to calibration during the normal respiration of the subject during sleep using polysomnographic techniques.

71. A system according to claim 69, further comprising a stimulation electrode and wherein the control unit further includes a stimulation module operatively connected to the monitoring and detection module and to the stimulation electrode, the stimulation module generating through the stimulation electrode a stimulation signal which acts to stimulate breathing following the reporting of the central sleep apnea event.

72. A system according to claim 61, wherein the monitoring and reporting module reports the apneic event as a central sleep hypopnea event when the index of respiratory activity is between a third and a fourth thresholds and as a central sleep apnea event when the index of respiratory activity remains under the fourth threshold.

73. A system according to claim 72, wherein the third and fourth thresholds are set according to calibration during the normal and abnormal respiration of the subject during sleep using polysomnographic techniques.

74. A system according to claim 72, further comprising a stimulation electrode and wherein the control unit further includes a stimulation module operatively connected to the monitoring and detection module and to the stimulation electrode, the stimulation module generating through the stimulation electrode a stimulation signal which acts to stimulate breathing following the reporting of the central sleep apnea event or of the central sleep hypopnea event, parameters of the stimulation signal being selected

according to whether the central sleep apnea event or the central sleep hypopnea event was reported.

75. A system according to claim 55, wherein the control unit further includes a stimulation module operatively connected to the monitoring and detection module, the stimulation module generating through the electrode a stimulation signal which acts to increase airway patency or stimulate breathing following the reporting of the apneic event.

76. A system according to claim 75, wherein parameters of the stimulation signal are selected by the stimulation module in accordance with the index of respiratory activity.

77. A system according to claim 75, wherein the stimulation signal is generated by the stimulation module so as to elicit a reflexive pattern activity from the central nervous system of the subject.

78. A system according to claim 77, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

79. A system according to claim 78, wherein the swallowing reflexive pattern activity is elicited by generating an electrical signal at a rate of about 20 Hz to 50 Hz.

80. A system according to claim 75, wherein the at least one apnea criteria includes a first criteria associated with obstructive sleep apnea and a second criteria associated with central sleep apnea, and wherein the monitoring and detection module reports the apneic event as an obstructive sleep apnea event when the index of respiratory activity meets the first criteria and as a central sleep apnea event when the index of respiratory activity meets the second criteria.

81. A system according to claim 80, wherein the stimulation module generates through the electrode a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event.

82. A system according to claim 80, wherein the monitoring and detection module reports an occurrence of an obstructive sleep hypopnea event when the index of respiratory activity meets a third criteria associated with obstructive sleep hypopnea and an occurrence of a central sleep hypopnea event when the index of respiratory activity meets a fourth criteria associated with central sleep hypopnea.

83. A system according to claim 82, wherein the stimulation module generates through the electrode a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep hypopnea event or of the obstructive sleep apnea event, parameters of the stimulation signal being selected according to whether the obstructive sleep hypopnea event or the obstructive sleep apnea event was reported.

84. A system according to claim 75, further comprising a stimulation electrode operatively connected to the stimulation module, and wherein the stimulation signal is generated through the stimulation electrode.

85. A system according to claim 84, wherein parameters of the stimulation signal are selected by the stimulation module in accordance with the index of respiratory activity.

86. A system according to claim 84, wherein the stimulation signal is generated by the stimulation module so as to elicit a reflexive pattern activity from the central nervous system of the subject.

87. A system according to claim 86, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

88. A system according to claim 87, wherein the swallowing reflexive pattern activity is elicited by generating an electrical signal at a rate of about 20 Hz to 50 Hz.

89. A system according to claim 84, wherein the at least one apnea criteria includes a first criteria associated with obstructive sleep apnea and a

second criteria associated with central sleep apnea, and wherein the monitoring and detection module reports the apneic event as an obstructive sleep apnea event when the index of respiratory activity meets the first criteria and as a central sleep apnea event when the index of respiratory activity meets the second criteria.

90. A system according to claim 89, wherein the stimulation module generates through the stimulation electrode a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep apnea event or stimulate breathing following the reporting of the central sleep apnea event.

91. A system according to claim 84, wherein the monitoring and detection module reports an occurrence of an obstructive sleep hypopnea event when the index of respiratory activity meets a third criteria associated with obstructive sleep hypopnea and an occurrence of a central sleep hypopnea event when the index of respiratory activity meets a fourth criteria associated with central sleep hypopnea.

92. A system according to claim 91, wherein the stimulation module generates through the stimulation electrode a stimulation signal which acts to increase airway patency following the reporting of the obstructive sleep hypopnea event or of the obstructive sleep apnea event, or stimulate breathing following the reporting of the central sleep hypopnea event or of the central sleep apnea event, parameters of the stimulation signal being selected according to whether the obstructive sleep hypopnea event, the obstructive sleep apnea event, the central sleep hypopnea event or the central sleep apnea event was reported.

93. A system according to claim 84, wherein the stimulation electrode is configured to be positioned in contact with the glossopharyngeal nerve of the subject.

94. A system according to claim 93, wherein the stimulation electrode includes a cuff electrode assembly adapted to surround part of the glossopharyngeal nerve of the subject.

95. A system according to claim 93, wherein the stimulation signal is generated by the stimulation module so as to elicit a reflexive pattern activity from the central nervous system of the subject.

96. A system according to claim 95, wherein the reflexive pattern activity is selected from a group consisting of the negative pressure reflex, coughing, yawning, gagging, swallowing and any combination thereof.

97. A system according to claim 96, wherein the swallowing reflexive pattern activity is elicited by generating an electrical signal at a rate of about 20 Hz to 50 Hz.

98. A system for treating a sleep apnea event, comprising:

a sleep apnea event detection module;

an stimulation electrode configured to be positioned in contact with the internal branch of the superior laryngeal nerve or the glossopharyngeal nerve of the subject; and

a stimulation module operatively connected to the detection module and to the electrode;

wherein following the detection of the sleep apnea event by the detection module, the stimulation module generates through the electrode a stimulation signal having a rate of about 20 Hz to 50 Hz in order to elicit a swallowing reflexive pattern activity.

99. A system according to claim 98, wherein the system is fully implantable.

100. A system according to claim 98, wherein the stimulation electrode includes a cuff electrode assembly adapted to surround part of internal branch of the superior laryngeal nerve or the glossopharyngeal nerve of the subject.

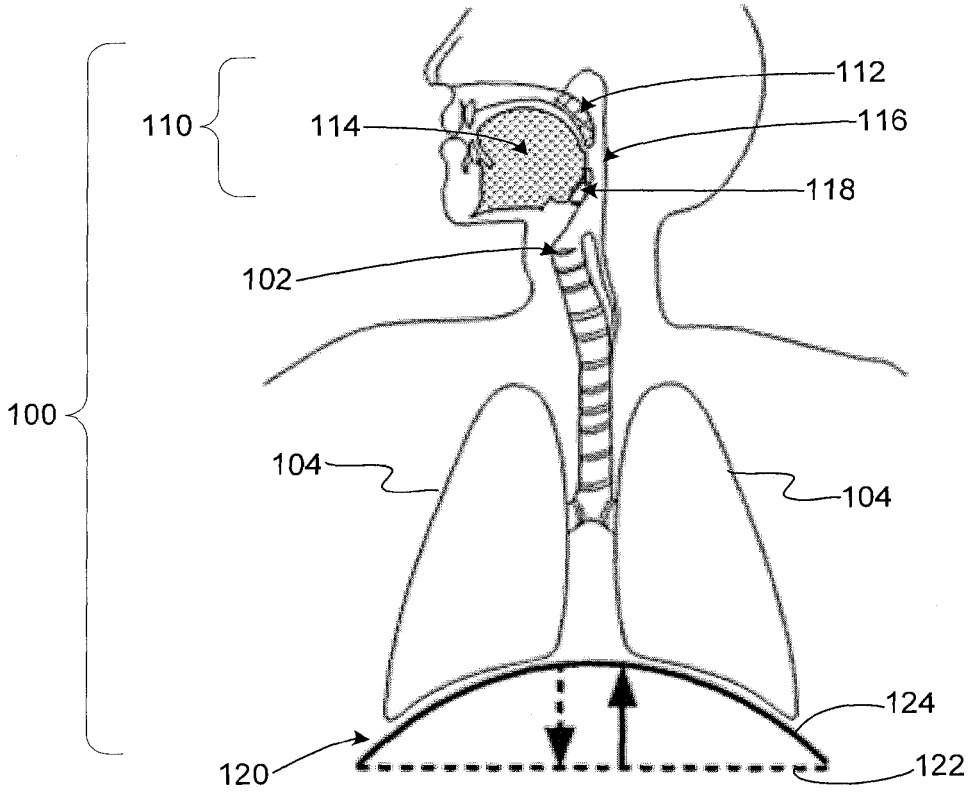


Figure 1

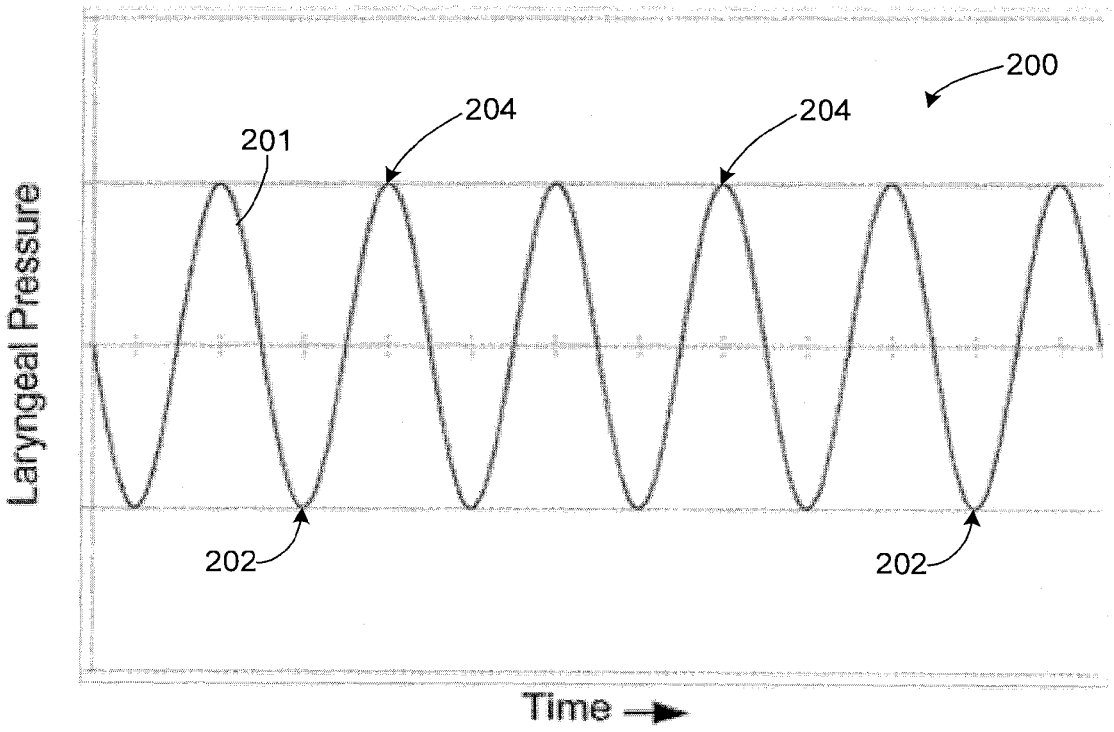


Figure 2

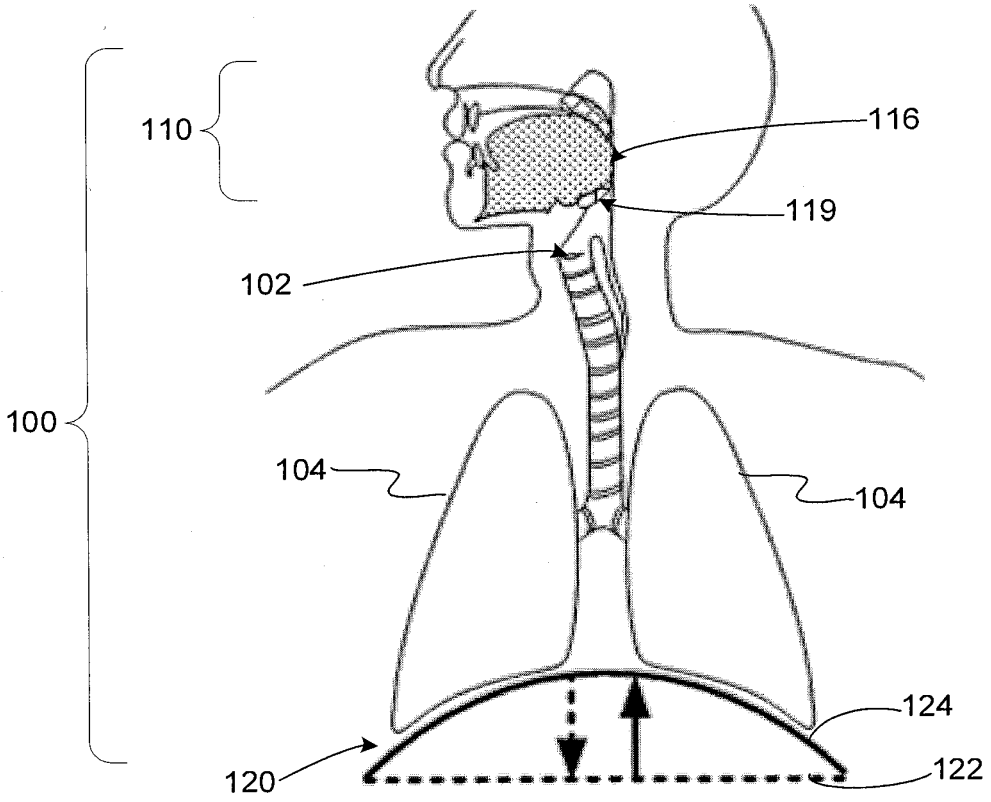


Figure 3

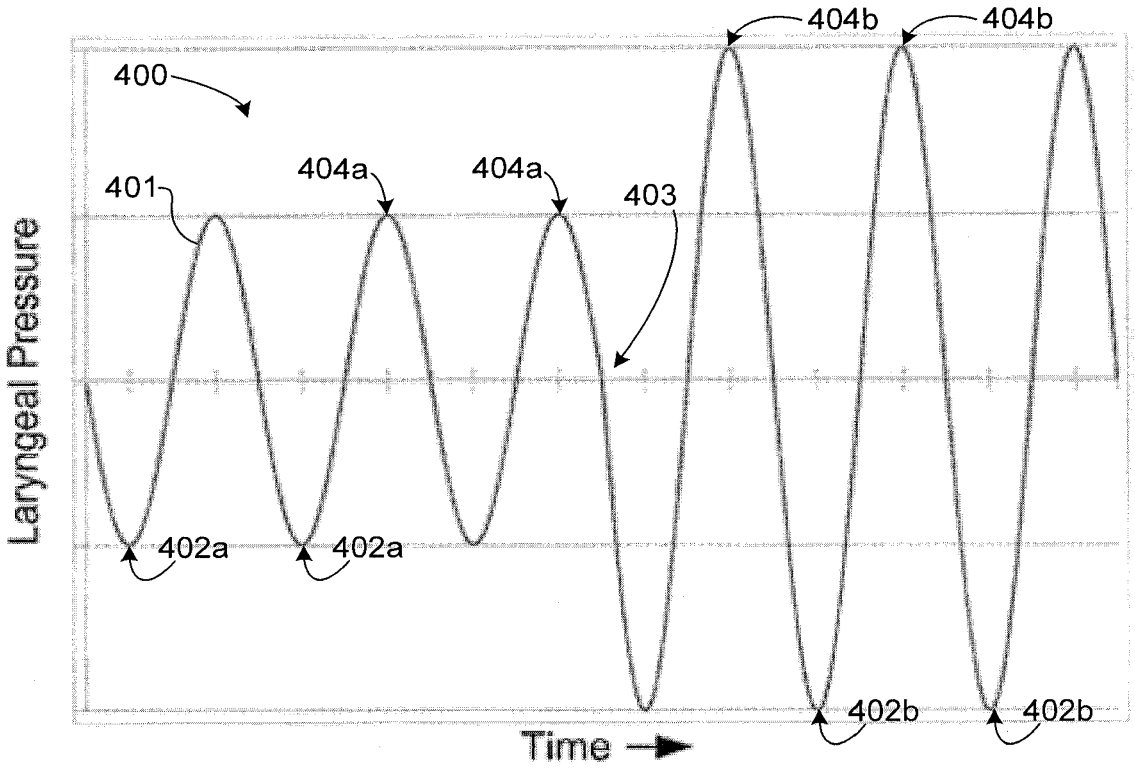


Figure 4

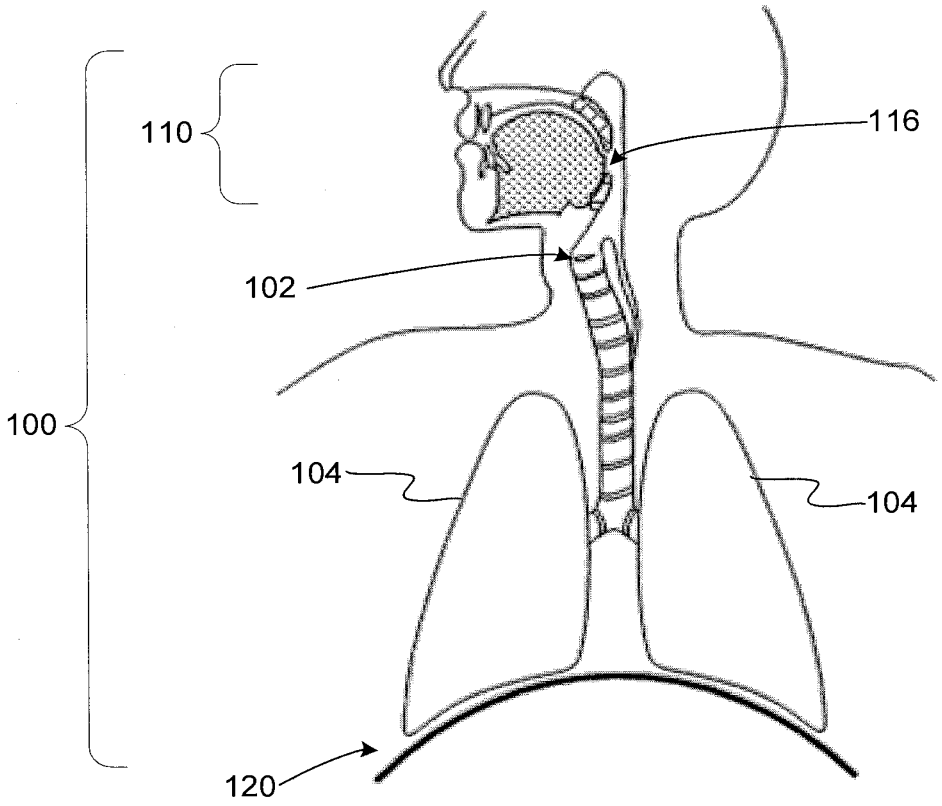


Figure 5

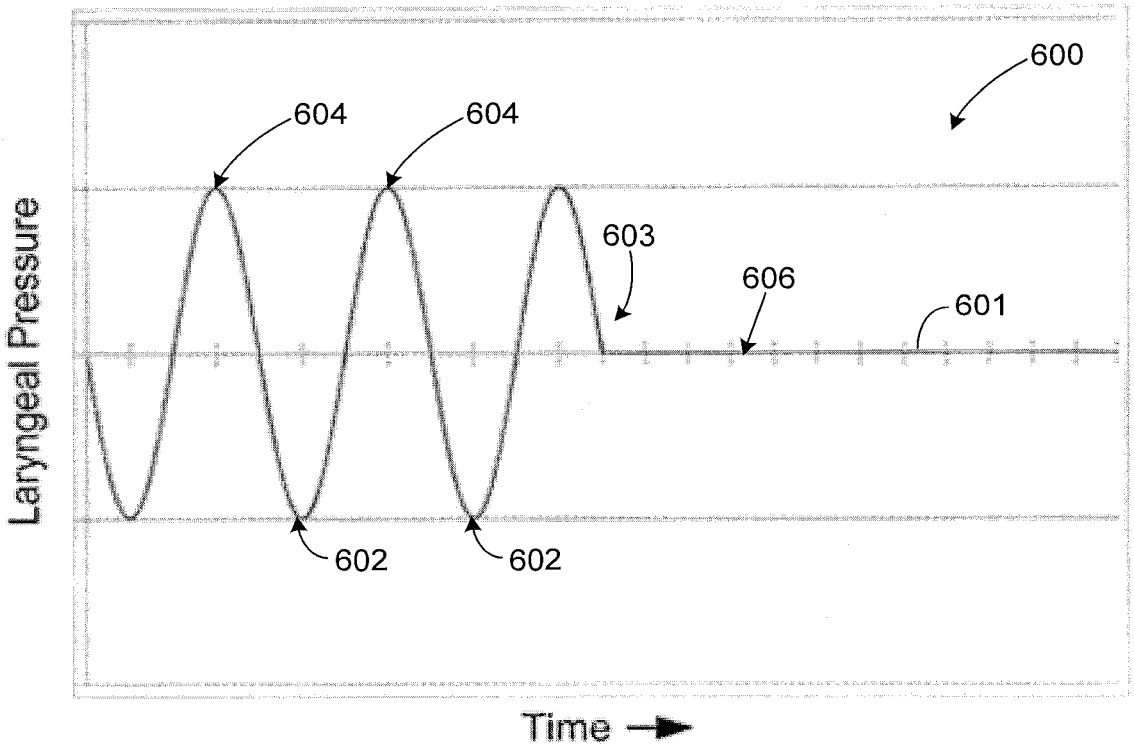


Figure 6

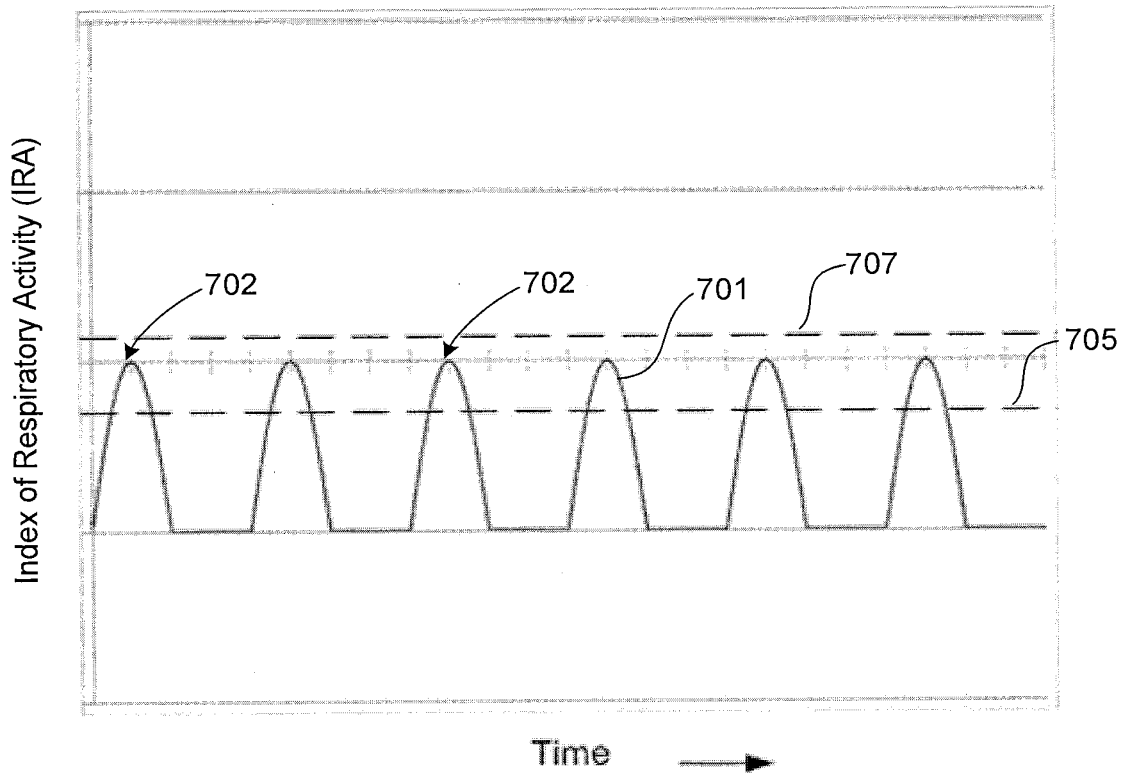


Figure 7

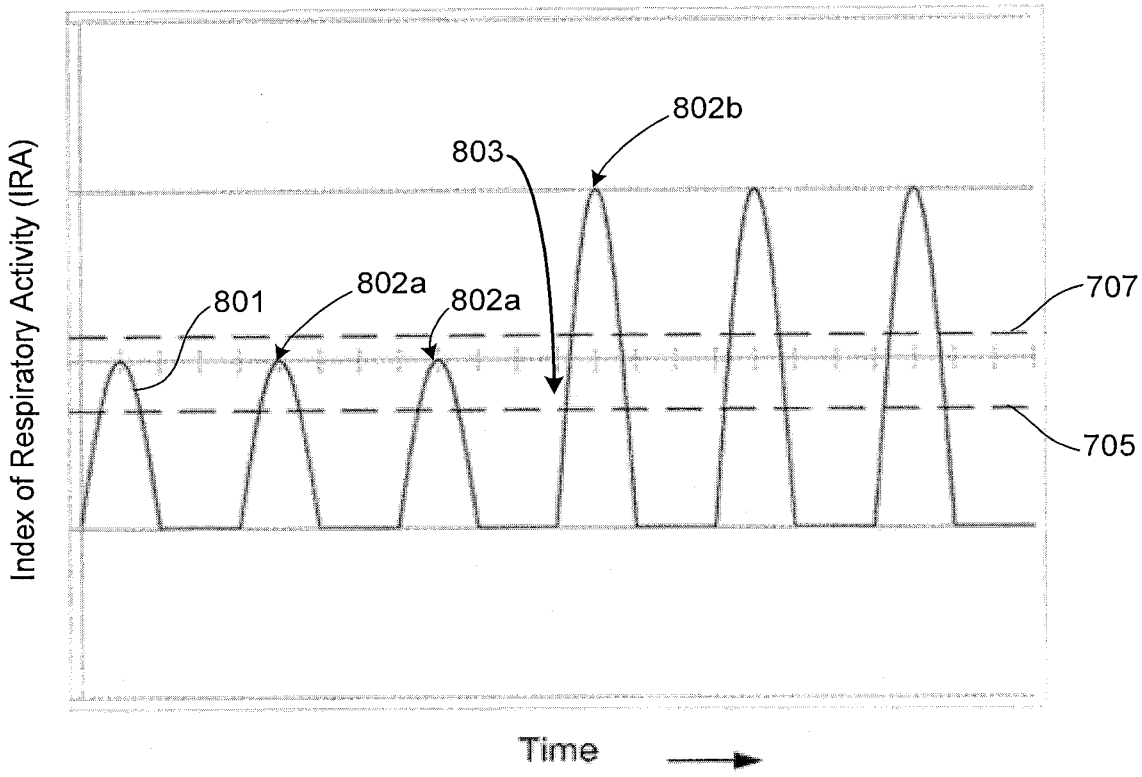


Figure 8

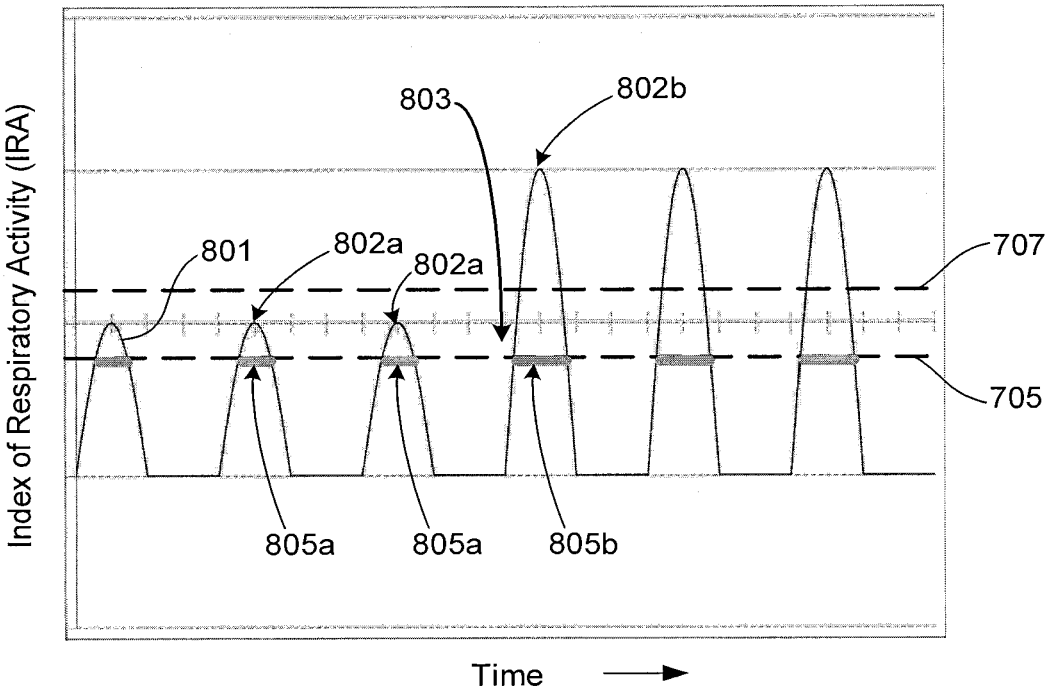


Figure 9

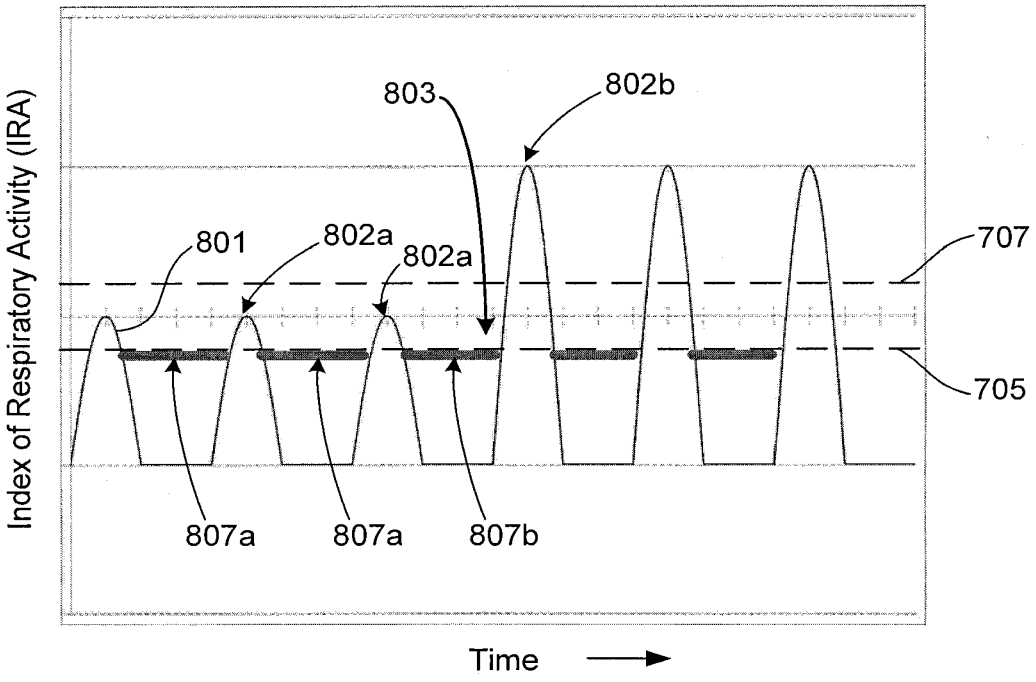


Figure 10

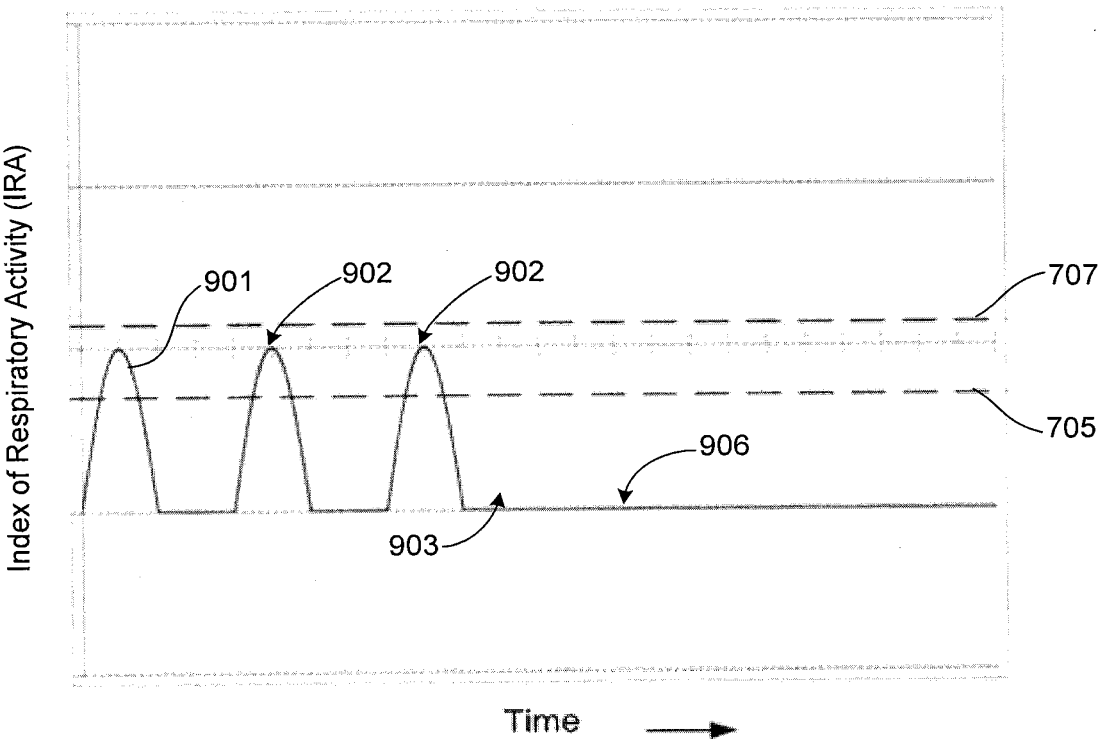


Figure 11

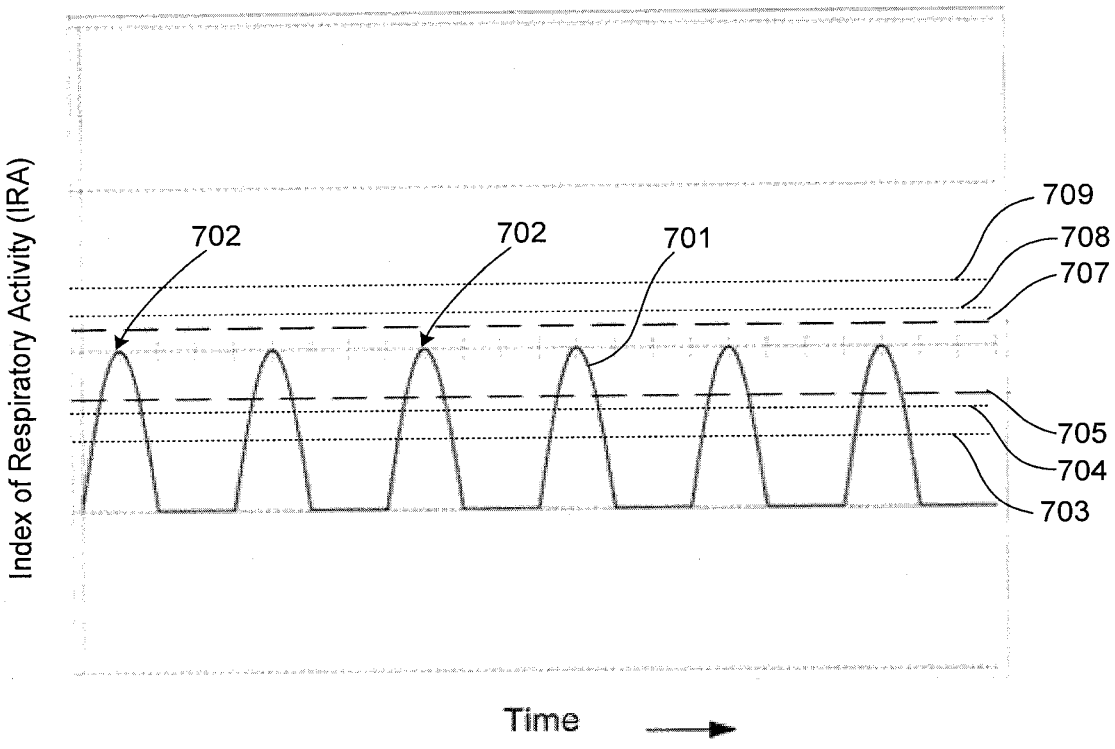


Figure 12

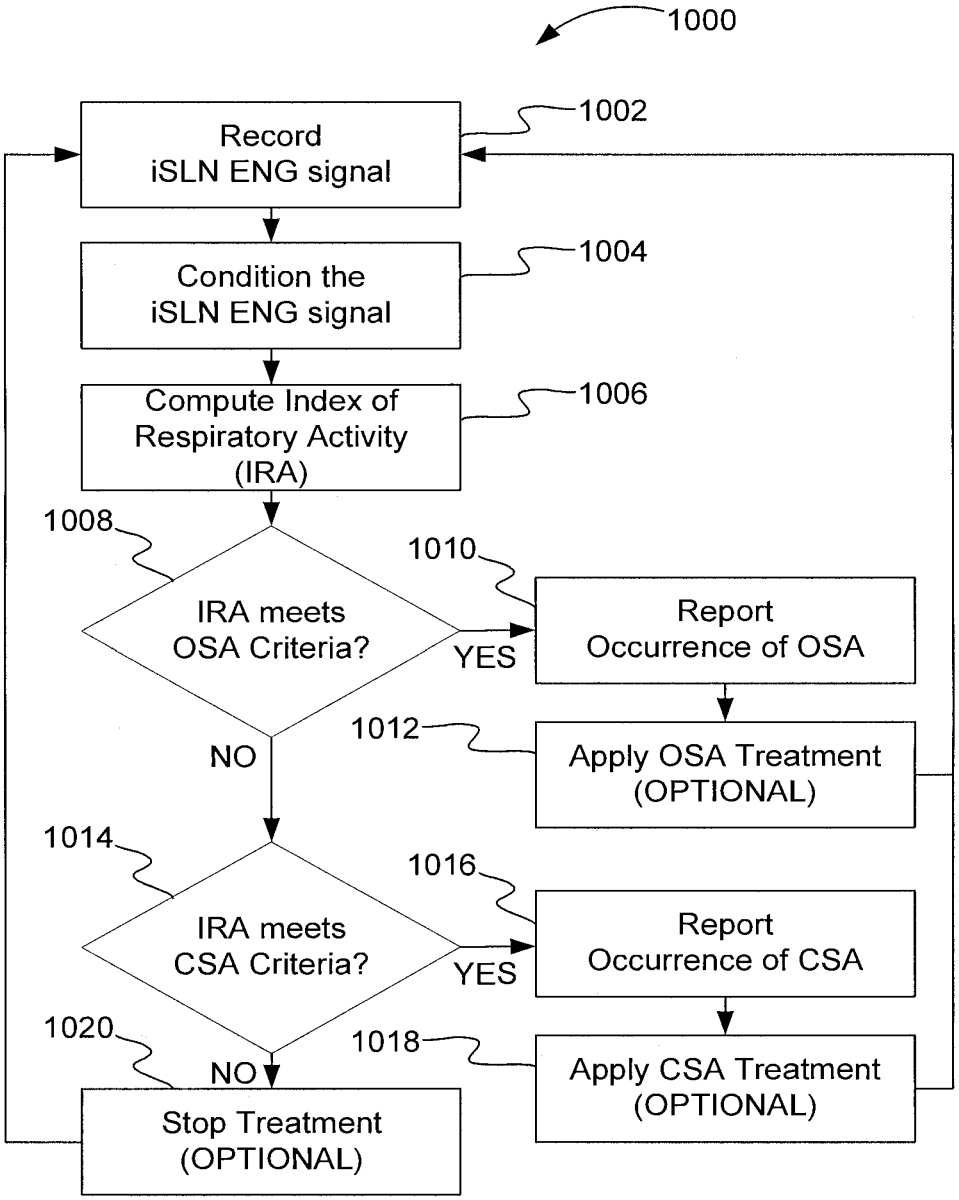

1000
Record iSLN ENG signal
1002
Condition the iSLN ENG signal
1004
Compute Index of Respiratory Activity (IRA)
1006
1008
IRA meets OSA Criteria?
YES
1010
Report Occurrence of OSA
NO
1012
Apply OSA Treatment (OPTIONAL)
1014
IRA meets CSA Criteria?
YES
1016
Report Occurrence of CSA
1018
Apply CSA Treatment (OPTIONAL)
1020
NO
Stop Treatment (OPTIONAL)

Figure 13

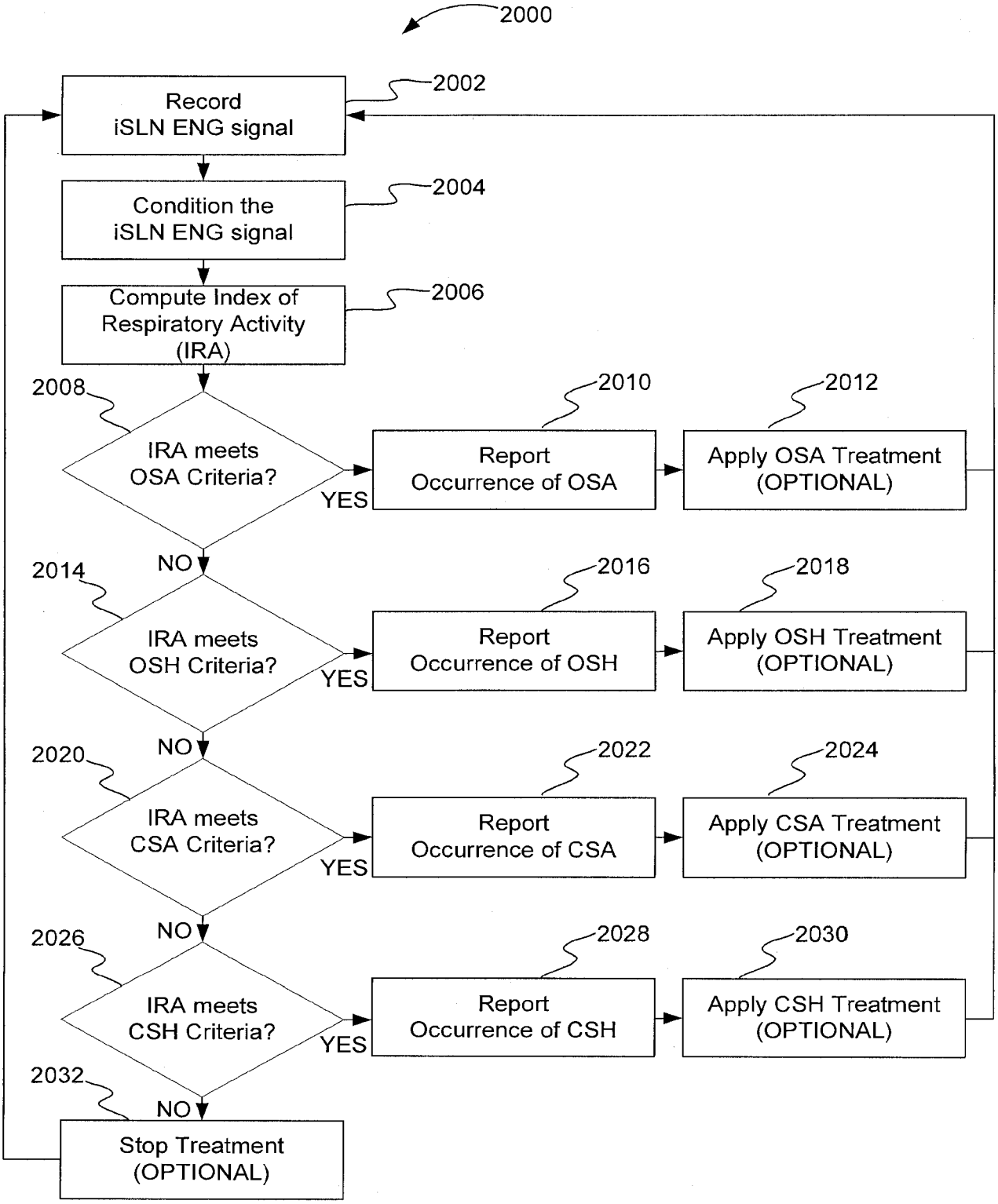

2000
Record iSLN ENG signal
2002
Condition the iSLN ENG signal
2004
Compute Index of Respiratory Activity (IRA)
2006
2008
IRA meets OSA Criteria?
YES
2010
Report Occurrence of OSA
2012
Apply OSA Treatment (OPTIONAL)
NO
2014
IRA meets OSH Criteria?
YES
2016
Report Occurrence of OSH
2018
Apply OSH Treatment (OPTIONAL)
NO
2020
IRA meets CSA Criteria?
YES
2022
Report Occurrence of CSA
2024
Apply CSA Treatment (OPTIONAL)
NO
2026
IRA meets CSH Criteria?
YES
2028
Report Occurrence of CSH
2030
Apply CSH Treatment (OPTIONAL)
2032
NO
Stop Treatment (OPTIONAL)

Figure 14

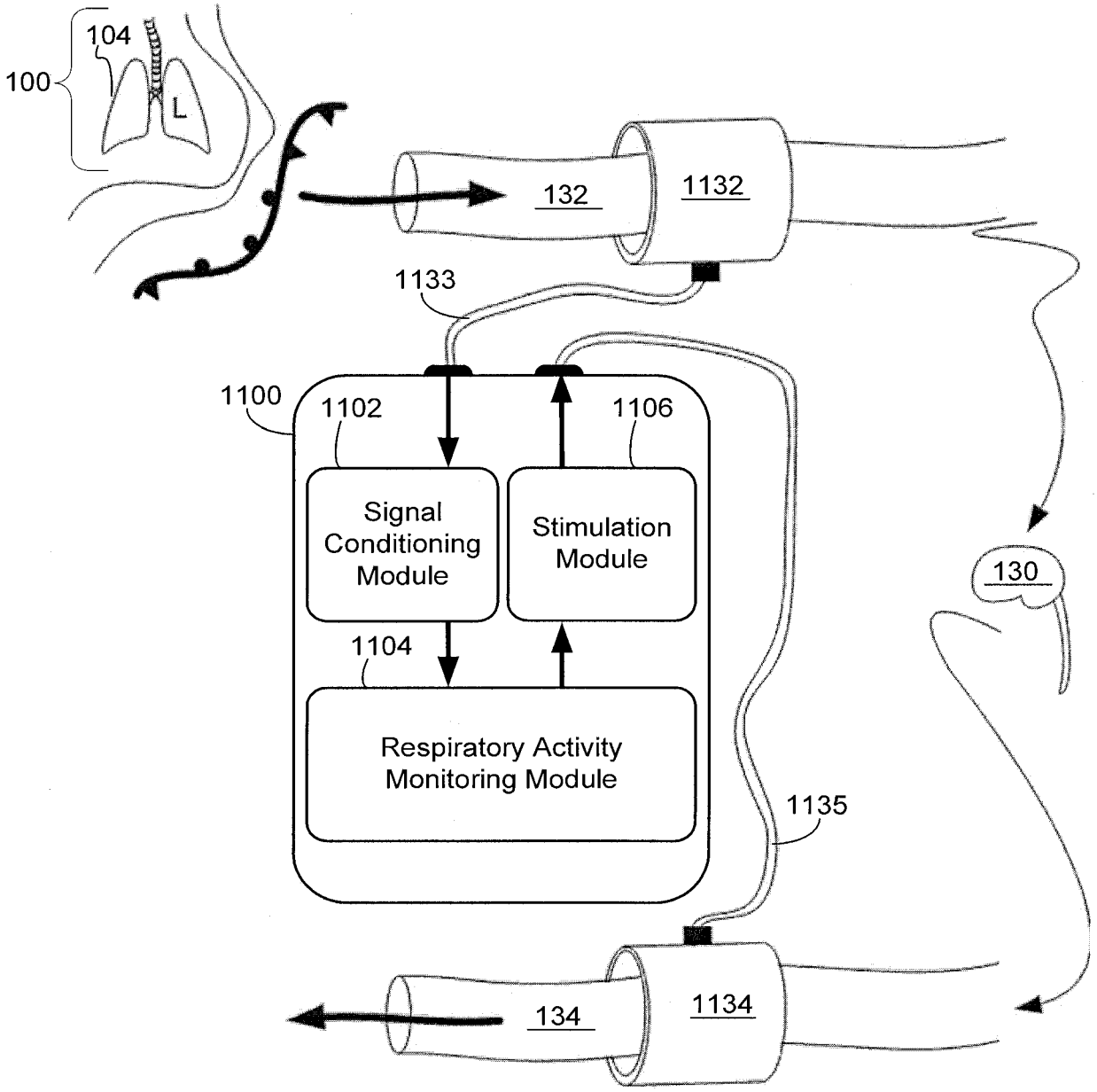

100
104
L
132
1132
1133
1100
1102
1106
Signal Conditioning Module
Stimulation Module
1104
Respiratory Activity Monitoring Module
130
1135
134
1134

Figure 15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/002036

A. CLASSIFICATION OF SUBJECT MATTER
IPC: ***A61B 5/04*** (2006.01) , ***A61F 5/56*** (2006.01) , ***A61N 1/36*** (2006.01) , ***A61N 1/372*** (2006.01)
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC: ***A61B*** (2006.1), ***A61F*** (2006.1), ***A61N*** (2006.1)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Canadian Patent Database (Intellect), United States Patent Database (WEST), Delphion and World Wide Web. Keywords: "superior laryngeal nerve", "glossopharyngeal nerve", "vagus nerve", sleep apnea, sleep disorder, apneic, obstructive, central, implant*.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2008/046190 (Astma et al.), 24 Apr. 2008 (24-04-2008) *See entire document	1, 8, 10, 12-18, 25, 26, 33, 34, 41, 42 and 55-100
A	US 2007/0150006 (Libbus et al.), 28 Jun. 2007 (28-06-2007) *See entire document	1, 8, 10, 12-18, 25, 26, 33, 34, 41, 42 and 55-100

[ ] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 April 2009 (21-04-2009)	28 July 2009 (28-07-2009)
Name and mailing address of the ISA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001-819-953-2476	Authorized officer Bryon Braymore 819- 934-6753

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2008/002036

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. [X] Claim Nos. : 2-7, 9, 11, 19-24, 27-32, 35-40, and 43-54
because they relate to subject matter not required to be searched by this Authority, namely :

These claims are directed to a method of medical treatment that treats a patient using a stimulation signal. This subject matter is excluded under Rule 67.1(iv) PCT.

2. [ ] Claim Nos. :
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

3. [ ] Claim Nos. :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

Group A: Claims 1-97 are directed to a method or system that monitors the interior branch of the superior laryngeal nerve to detect an apneic event.

Group B: Claims 98-100 are directed to a system that treats sleep apnea by stimulating the interior branch of the superior laryngeal nerve or the glossopharyngeal nerve of a subject in order to invoke a swallowing reflex in the subject.

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2008/002036

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO 2008046190A1	24-04-2008	None	
US 2007150006A1	28-06-2007	None	

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 May 2010 (27.05.2010)

PCT

(10) International Publication Number
WO 2010/059839 A2

(51) International Patent Classification:
A61N 1/36 (2006.01)

(21) International Application Number:
PCT/US2009/065165

(22) International Filing Date:
19 November 2009 (19.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/116,149 19 November 2008 (19.11.2008) US

(71) Applicant *(for all designated States except US)*: **INSPIRE MEDICAL SYSTEMS, INC.** [US/US]; 9700 63rd Avenue North, Suite 200, Maple Grove, Minnesota 55369 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CHRISTOPHERSON, Mark A.** [US/US]; 4100 Reiland Lane, Shoreview, Minnesota 55126 (US). **NI, Quan** [US/US]; 5812 Prairie Ridge Drive, Shoreview, Minnesota 55126 (US). **HERBERT, Timothy P.** [US/US]; 14707 62nd Avenue N., Maple Grove, Minnesota 55311 (US). **RONDONI, John** [US/US]; 2740 Fountain Lane, Plymouth, Minnesota 55447 (US).

(74) Agents: **GRUNZWEIG, Paul S.** et al.; Dicke, Billig & Czaja, PLLC, 100 S. Fifth Street, Suite 2250, Minneapolis, Minnesota 55402 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,

[Continued on next page]

(54) Title: METHOD OF TREATING SLEEP DISORDERED BREATHING

(57) Abstract: A system and method for automatically implementing a therapy for treating sleep disordered breathing.

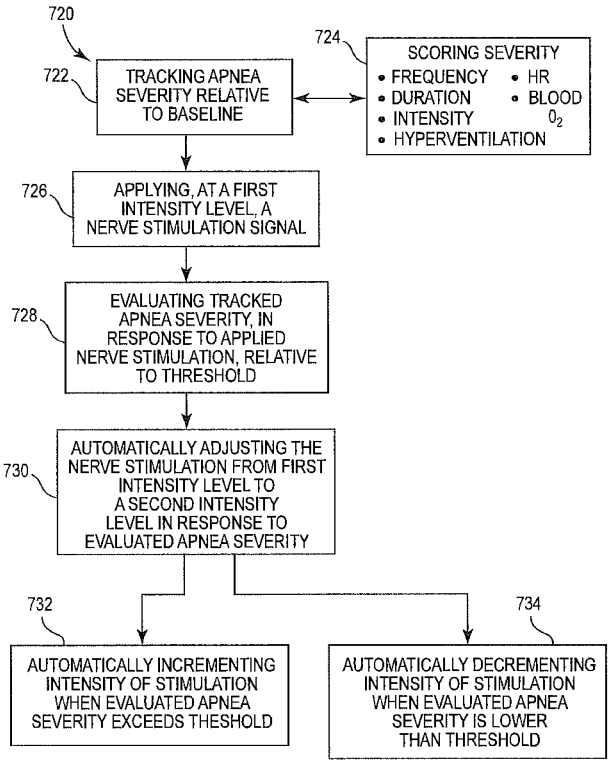


Fig. 8B

WO 2010/059839 A2

HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

METHOD OF TREATING SLEEP DISORDERED BREATHING

[001] This application is a Non-Provisional Application that claims priority to Provisional U.S. Patent Application Serial Number 61/116,149, entitled "METHOD OF TREATING SLEEP APNEA," having a filing date of November 19, 2008, and which is incorporated herein by reference.

BACKGROUND

[002] The present disclosure relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the present disclosure relates to a method of automatically initiating and adjusting therapeutic treatment of sleep apneas.

[003] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[004] One treatment for sleep disordered breathing behavior, such as obstructive sleep apneas and hypopneas, has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a nerve electrode cuff placed around the hypoglossal nerve.

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BRIEF DESCRIPTION OF THE DRAWINGS

[005] Aspects and features of the present disclosure will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments of the present disclosure when considered in connection with the accompanying drawings, wherein:

[006] FIG. 1 is a schematic illustration of an implantable stimulation system, according to an embodiment of the present disclosure;

[007] FIG. 2 is a schematic illustration of a method of placement for a respiratory pressure sensor, according to an embodiment of the present disclosure;

[008] FIG. 3A is a block diagram of an implantable pulse generator, according to an embodiment of the present disclosure;

[009] FIG. 3B is a block diagram of a therapy system including an implantable pulse generator, patient programmer, and a clinician programmer, according to an embodiment of the present disclosure;

[010] FIG. 4A is a block diagram of a multi-tier treatment system including different states of operation, according to an embodiment of the present disclosure;

[011] FIG. 4B is a graph schematically illustrating a probabilistic profile to determine a time interval between consecutive samples for detecting an apnea, according to an embodiment of the present disclosure;

[012] FIG. 4C is a graph schematically illustrating a probabilistic profile to determine a frequency at which stimulation will be suspended in order to detect apneas, according to an embodiment of the present disclosure;

[013] FIG. 4D is a block flow diagram schematically illustrating a method of suspending stimulation in order to detect apneas, according to an embodiment of the present disclosure;

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[014] FIG. 4E is a flow diagram schematically illustrating a method of correlating sleep study parameters and therapy parameters associated with an implantable pulse generator, according to an embodiment of the present disclosure;

[015] FIG. 4F is a block diagram schematically illustrating a correlation profile between sleep study parameters and therapy parameters associated with an implantable pulse generator, according to an embodiment of the present disclosure;

[016] FIG. 4G is a chart schematically illustrating an index for implantable pulse generators, according to an embodiment of the present disclosure;

[017] FIG. 4H is a flow diagram schematically illustrating a method of therapy based on an implantable pulse generator system calibrated relative to a sleep study, according to an embodiment of the present disclosure;

[018] FIG. 5 is a graph array schematically illustrating detection of an apnea via a bio-impedance signal, according to an embodiment of the present disclosure;

[019] FIG. 6 is a graph array schematically illustrating detection of an apnea via an respiratory pressure signal, according to an embodiment of the present disclosure;

[020] FIG. 7A is a graph array schematically illustrating detection of an apnea via mapping a bio-impedance signal and a respiratory pressure signal, according to an embodiment of the present disclosure;

[021] FIG. 7B is a graph schematically illustrating a grid of breathing states via mapping a bio-impedance signal relative to a respiratory pressure signal, according to an embodiment of the present disclosure;

[022] FIG. 7C is a flow diagram of a method of detecting sleep disordered breathing behavior, according to an embodiment of the present disclosure;

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[023] FIG. 8A is a flow diagram of a method of automatically adjusting the level of therapy, according to an embodiment of the present disclosure;

[024] FIG. 8B is a flow diagram of a method of automatically adjusting a level of therapy, according to an embodiment of the present disclosure;

[025] FIG. 9 is a block diagram of an auto-titrate module of a system for treating sleep disordered breathing behavior, according to an embodiment of the present disclosure; and

[026] FIG. 10 is a graph schematically illustrating a stimulation goodness function applied in a method of treating apneas, according to an embodiment of the present disclosure.

DESCRIPTION OF EMBODIMENTS

[027] The following detailed description is merely exemplary in nature and is not intended to limit the present disclosure or the application and uses of the present disclosure. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, or the following detailed description.

[028] FIG. 1 is a schematic diagram of an implantable stimulation system, according to an embodiment of the present disclosure. The system is adapted to treat sleep disordered breathing behavior, such as obstructive sleep apnea, hypopnea, and/or central sleep apnea. As illustrated in FIG.1, an example of an implantable stimulation system 10 according to one embodiment of the present disclosure includes an implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 20, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes a nerve cuff electrode or electrode system 65 and extends from the IPG 55 so that the electrode system 65 is positioned in proximity to a desired nerve, such as the hypoglossal nerve 53 of the patient

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20, to enable stimulation of the nerve 53, as described below in detail. It will be understood that in some embodiments, two leads 52 are provided with so that one lead 52 is implanted to be coupled relative to a nerve on a left side of the body and the other lead 52 is implanted to be coupled relative to a nerve on a second side of the body, as described in more detail below. An exemplary implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., which is incorporated herein by reference in its entirety. In this exemplary system, a sensor lead 57 electrically coupled to the IPG 55 and extends from the IPG 55 so that a sensor or transducer 60 can be positioned in the patient 20 for sensing of respiratory effort.

[029] In some embodiments, system 10 also comprises additional sensors to obtain further physiologic data associated with respiratory functions. For example, system 10 may include various sensors (e.g., sensors 67, 68, 69 in FIG. 1) distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals.

[030] In some embodiments, the sensing and stimulation system for treating sleep disordered breathing behavior is a totally implantable system which provides therapeutic solutions for patients diagnosed with sleep disordered breathing. In other embodiments, one or more components of the system are not implanted in a body of the patient. A few non-limiting examples of such non-implanted components include external sensors (respiration, impedance, etc.), an external processing unit, or an external power source. Of course, it is further understood that the implanted portion(s) of the system provides a communication pathway to enable transmission of data and/or controls signals both to and from the implanted portions of the system relative to the external portions of the system. The communication pathway includes a radiofrequency (RF) telemetry link or other wireless communication protocols.

[031] Whether partially implantable or totally implantable, the system is designed to stimulate the hypoglossal nerve (or other nerves related to

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affecting airway patency via tongue protrusion or other muscle contractions/relaxations) during inspiration to thereby prevent obstructions or occlusions in the upper airway during sleep. In one embodiment, the implantable system comprises an implantable pulse generator (IPG), a peripheral nerve cuff stimulation lead, and a pressure sensing lead.

[032] In one embodiment, the sensor 60 is a respiratory pressure sensor that is surgically implanted in a region that has pressure continuity with the pleura via an intrapleural placement or an extrapleural placement (including but not limited to an intercostal placement), as will be further described in association with Figure 2. The location for placement of the sensor 60 is, at least in part, chosen as a function of a delay, i.e. the propagation time associated with a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position. The chosen location is also a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. the amount of filtering that is necessary to remove waveforms other than the waveform associated with the desired sensed characteristic, such as the filtering required to remove cardiac waveform activity, for example. The positioning of the sensor 60 enables the IPG 55 to receive respiratory effort waveform information and to use this information to control delivery of the therapy.

[033] As schematically illustrated in Figure 2, in one embodiment of the present disclosure, an implantable stimulation system 10 comprises a sensing system 70 including a lead 75 configured to place a respiratory pressure sensor 71 within an intrapleural space 90 so that sensor 71 is positioned in close proximity to the lung 80. In this arrangement, the sensor 71 becomes directly coupled relative to the respiratory pressures at the pleura. In another aspect, the intrapleural space 90 includes the cavity between the parietal pleura 78 and a pulmonary pleura 79. Finally, it will be understood that FIG. 2 illustrates generous spacing between adjacent anatomical structures for illustrative purposes.

[034] In the one embodiment, lead 75 includes a lead body 72 that supports sensor 71 at its distal end and an anchor 74 (such as a wing-like

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fixation member) located at a more proximal portion of lead body 72. The anchor 74 ensures that sensor 71 remains positioned to orient the membrane portion of the sensor to face along the lung 80 subsequent to implantation of the sensor 71. The lead body 72 is positioned through an inter-costal space 91 into the pleural space 90 (with a position of sensor 71 and lead body 72 as indicated by reference numeral 88) so that the IPG 55 (Figure 1) receives sensor waveforms from the sensor 71, thereby enabling the IPG 55 (Figure 1) to deliver electrical stimulation synchronously with inspiration, according to a therapeutic treatment regimen in accordance with embodiments of the present disclosure.

[035] As further illustrated by Figure 2, the lead 75 will be inserted so that lead body 72 extends through the intercostal space (e.g. between two ribs 86) to position the sensor 71 for placement intrapleurally, as indicated generally via indicator 90. In one embodiment, the lead 75 incorporates a piezo-electric crystal mounted into a sealed housing and capable of monitoring intra-thoracic pressure associated with respiration. In other embodiments, monitoring the respiratory pressure comprises monitoring other physiological data indicative of respiratory pressure (in addition to or instead of monitoring intra-thoracic pressure). The sensor 71 is powered by the IPG 55 (FIG. 1) and the IPG 55 also contains internal circuitry to accept and process the respiration signal from the lead 75.

[036] In one embodiment, the system includes a lead anchor 74 located remotely (by a distance of several centimeters or so) from where the sensor 71 is placed intrapleurally. Tissue movements on the sensor and lead can induce unwanted signal components as well as lead migration/dislodgement; therefore anchoring of the lead body 72, close to where the lead 75 enters the thoracic cavity is warranted. With this in mind, the anchor 74 will be sutured to a subcutaneous connective tissue, such as an intra-costal muscle or fascia during implant, and the anchor 74 is fixed or secured to the lead body 72 and not allowed to slide.

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[037] In other embodiments, the respiratory sensor 71 is placed external to the intrapleural space. In yet other embodiments, the respiratory sensor can be any one of an airflow sensor, a pressure sensor, a volume sensor, an accelerometer, an acoustic sensor, a temperature sensor, a mechanical strain sensor, or an effort sensor.

[038] In one embodiment, sensing respiratory pressure is implemented in a manner substantially similar to the methods and systems of respiratory sensing disclosed in PCT Patent Application Number PCT/US2009/044207, entitled "Method and Apparatus for Sensing Respiratory Pressure in An Implantable Stimulation System," having a filing date of May 15, 2009, and which is incorporated herein by reference.

[039] Figure 3A is a block diagram schematically illustrating an implantable pulse generator (IPG) 100, according to one embodiment of the present disclosure. In one embodiment, IPG 100 comprises at least substantially the same features and attributes as IPG 55 of Figure 1. As illustrated in Figure 3A, IPG 100 includes a sensing module 102, a stimulation module 104, a therapy manager 106, a power management module 108, a controller 110 with a memory 111, and a communication module 112.

[040] Components and methods of the present disclosure, including but not limited to memory module 111, may be implemented in hardware via a microprocessor, programmable logic, or state machine, in firmware, or in software within a given device. Components and methods of the present disclosure, including but not limited to memory module 111, may reside in software on one or more computer-readable media. The term computer-readable media as used herein is defined to include any kind of memory, volatile or non-volatile, such as floppy disks, hard disks, CD-ROMs, flash memory, read-only memory (ROM), and random access memory (RAM).

[041] Via an array of parameters, the sensing module 102 of IPG 100 receives and tracks signals from various physiologic sensors in order to determine a respiratory state of a patient, such as whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. In one

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embodiment, at least some of the physiologic sensors are contained within or on a housing of the IPG and at least some of the physiologic sensors are external to the IPG. In any case, whether the physiologic sensors are external or internal to the IPG 100, the signals produced by those sensors are received and processed by the sensing module 102. In some embodiments, the sensing module 102 is contained within the IPG 100, although it will be understood that in other embodiments, at least a portion of the sensing module 102 can be external to a housing of the IPG 100 provided that communication is maintained between those external portions of sensing module 102 and the IPG 100.

[042] For example, in one embodiment, the sensing module 102 comprises a body parameter 130, which includes at least one of a position-sensing component 132 or a motion-sensing component 134. In one embodiment, the motion-sensing component 134 tracks sensing of "seismic" activity (via an accelerometer or a piezoelectric transducer) that is indicative of walking, body motion, talking, etc. In another embodiment, the position-sensing component 132 tracks sensing of a body position or posture via an accelerometer or other transducer. In one embodiment, the position-sensing component distinguishes whether a patient is lying down in a generally horizontal position or standing up (or sitting up) in generally vertical position. In some embodiments, when the patient is in a generally horizontal position, the position-sensing component distinguishes between a supine position (i.e., lying on their back) and a lateral decubitus position (i.e., lying on their side). In some embodiments, body parameter 130 utilizes signals from both the position-sensing component 132 and the motion-sensing component 134.

[043] Other parameters tracked via sensing module 102 include one or more of the following parameters: an ECG parameter 140; a time parameter 142; a bio-impedance parameter 144; a pressure parameter 150; a blood oxygen parameter 154 and/or a respiratory rate parameter 159. In one aspect, the ECG parameter 140 tracks electrocardiography information of the patient, and in some embodiments, a heart rate is tracked as a separate component via heart rate parameter 158. In one aspect, the pressure

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parameter 150 includes a respiratory pressure component 152, which includes a thoracic pressure component and/or other pressure component indicative of respiration of the patient. In one aspect, the time parameter 142 tracks elapsed time while in other aspects, the time parameter 142 tracks the time of day in addition to or instead of the elapsed time. In particular, in cooperation with a therapy manager 106, the time parameter 142 can be used to activate or deactivate a therapy regimen according to a time of day, as described later in association with at least Figures 4A and 8.

[044] In some embodiments, the bio-impedance parameter 144 tracks measurements of bio-impedance of the patient. In one embodiment, the bio-impedance parameter 144 includes a trans-thoracic bio-impedance parameter that tracks a trans-thoracic bio-impedance, such as that described in association with sensors 67, 68, and 69 of Figure 1, and as further described later in association at least Figures 5-7B. In another embodiment, the bio-impedance parameter 144 includes a bilateral nerve electrode (e.g. a cuff electrode) parameter that tracks a bio-impedance measured between a pair of nerve electrodes spaced apart from each other on opposite sides of the body, as described later in association with at least Figure 5.

[045] It is also understood that system 10 (Figure 1) would include, or be connected to, the analogous physiologic sensor (e.g., LED-type tissue perfusion oxygen saturation) implanted within or attached to the body of the patient to provide data to each one of their respective parameters (e.g., blood oxygenation parameter 154) of the sensing module 102.

[046] In some embodiments, sensing module 102 also includes a target nerve parameter 156 which represents physiologic data regarding the activity of a nerve to be stimulated, such as the hypoglossal nerve or other nerve related to influencing airway patency via muscle contraction.

[047] In some embodiments, sensing module 102 also includes an acoustic sensing parameter 157 which represents physiologic data from respiratory airflow or cardiac activity that is sensed acoustically and that is indicative of respiratory effort.

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[048] In some embodiments, when data from obtained one or more of physiologic sensing parameters 140-144, 150-154, 157-159 of sensing module 102 reveals an ongoing inconsistent respiratory pattern, this information is used to indicate a potential waking state in which therapy should not be applied. In one aspect, the indication of a potential waking state is corroborated with information obtained via body parameter 130 prior to reaching a decision to abort a therapy or to delay the initiation of therapy. In further reference to Figure 3A, therapy manager 106 of IPG 100 is configured to automatically control initiation of and/or adjustment of a sleep apnea therapy, in accordance with the principles of the present disclosure. In one embodiment, therapy manager 106 includes a multi-tier system 200 in which the IPG 100 will operate in one of three states of operation, including a first state 202, a second state 204, and a third state 206. This multi-tier system 200 will be later described in more detail in association with Figure 4A.

[049] In some embodiments, therapy manager 106 also includes an auto-titrate module 170 which may or may not operate in coordination with multi-tier system 200 (Figure 4A). The auto-titrate module 170 is configured to direct the IPG 100 to automatically increment or decrement the level of therapy as implemented by various treatment parameters 168 (including but not limited to an amplitude, frequency, and/or pulse width of stimulation as well as a stimulation duty cycle and/or application of bilateral or unilateral stimulation, etc.) to maximize efficacy while minimizing power consumption and/or patient annoyance. In one aspect, efficacy is measured according to the number of apnea/hypopnea events and/or an apnea severity score (e.g. severity score parameter 759 in Figure 9) that also incorporates a duration or an intensity (e.g., a decrease in blood oxygen) of each apnea/hypopnea event. Application of the auto-titrate module 170 is later described in more detail in association with at least Figures 8A, 8B, and 9.

[050] With this in mind, in some embodiments, auto-titrate module 170 comprises an evaluate function 172, an increment function 174, a decrement function 176, and a threshold function 178. The evaluate function 172 is configured to evaluate the severity of sleep disordered breathing behavior

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both before and after the application of therapeutic nerve stimulation. The threshold function 178 enables setting a threshold of the severity of sleep disordered breathing that requires treatment by therapeutic nerve stimulation. If the severity of the sleep disordered breathing behavior falls below the threshold by a substantial portion, then auto-titrate module automatically decrements (decreases in one or more measured steps) the intensity of the nerve stimulation via decrement function 176. However, if the severity of the sleep disordered breathing behavior meets or exceeds the threshold, then auto-titrate module automatically increments (increases in one or more measured steps) the intensity of the nerve stimulation via increment function 174. In this way, the auto-titrate module 170 persistently evaluates and adjusts an intensity of therapeutic nerve stimulation so that enough stimulation is provided to treat the sleep disordered breathing but also so that unnecessary stimulation is avoided. Further application of the auto-titrate module 170 is later described in more detail in association with at least Figures 8A, 8B, and 9.

[051] In some embodiments, therapy manager 106 also includes a detection monitor 180 which may or may cooperate with the multi-tier system 200 of Figure 4A. In general terms, the detection monitor 180 observes, via sensing module 102, physiologic conditions of the patient to detect whether sleep disordered breathing is occurring, and based on such observations, initiate, adjust, or terminate a therapeutic nerve stimulation according to the general principles of the present disclosure. In one embodiment, the detection monitor 180 includes a baseline function 182, an apnea function 184, a hyperventilation function 186, a duration function 188, and an intensity function 190. The baseline function 182 tracks and determines a baseline breathing pattern for the patient in the absence of sleep disordered breathing. The apnea function 184 detects sleep disordered breathing, such as obstructive sleep apneas, hypopneas, and/or central sleep apneas, relative to the baseline breathing patterns of the patient. The hyperventilation function 186 is configured to assist identifying a sleep disordered breathing behavior based on parameters associated with a hyperventilation period following the sleep disordered breathing behavior. The duration function 188 tracks a

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duration of sleep disordered breathing events and/or duration of the ensuing hyperventilation, while the intensity function 190 tracks an intensity or severity of sleep disordered breathing events and/or of an intensity of the ensuing hyperventilation. In some embodiments, the functions 182-189 of the detection monitor 180 are implemented via the systems and methods described in association with at least Figures 3A-7C.

[052] In one embodiment, controller 110 of IPG 100 comprises one or more processing units and associated memories 111 configured to generate control signals directing the operation of IPG 100, including the operation of at least sensing module 102, therapy manager 106, power module 108, stimulation module 104, and communication module 112. Accordingly, controller 110 is in communication with, and provides coordinated control over, each of the respective modules/managers 102-112 according to instructions in memory 111. In one aspect, in response to or based upon commands received via programming parameter 198 of communication module 112 and/or instructions contained in the memory 111 associated with controller 110 in response to physiologic data gathered via a sensing module 102, controller 110 generates control signals directing operation of stimulation module 104 to selectively control stimulation of a target nerve, such as the hypoglossal nerve, to restore airway patency and thereby reduce or eliminate apneic events. In one aspect, memory 111 stores a log of administered therapy and/or sensed physiologic data including data obtained during apnea/hypopnea events and data representing the efficacy of therapy during those events.

[053] It is also understood that at least some of the components and parameters of the various modules and managers 102-112 could be located in a different pattern among the modules and managers 102-112 than shown and described in association with Figure 3A.

[054] For purposes of this application, the term "processing unit" shall mean a presently developed or future developed processing unit that executes sequences of instructions contained in a memory. Execution of the sequences of instructions causes the processing unit to perform steps such

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as generating control signals. The instructions may be loaded in a random access memory (RAM) for execution by the processing unit from a read only memory (ROM), a mass storage device, or some other persistent storage, as represented by a memory 111 associated with controller 110. In other embodiments, hard wired circuitry may be used in place of or in combination with software instructions to implement the functions described. For example, controller 110 may be embodied as part of one or more application-specific integrated circuits (ASICs). Unless otherwise specifically noted, the controller is not limited to any specific combination of hardware circuitry and software, nor limited to any particular source for the instructions executed by the processing unit.

[055] In general terms, the stimulation module 104 of IPG 100 is configured to generate and apply a neuro-stimulation signal according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager 106. In one embodiment, stimulation module 104 includes a target nerve module 190 configured to track and apply the treatment parameters for a target nerve such as the hypoglossal nerve. In some embodiments, the target nerve module 190 comprises a multi-site parameter 194A, a bilateral parameter 194B, and/or a fascicle parameter 194C. The multi-site parameter 194A enables and tracks the stimulation of multiple sites (by using two or more different electrode cuffs) spaced apart along a single nerve (e.g., hypoglossal nerve) to selectively activate tongue-protruder muscles and/or tongue-retractor muscles. Accordingly the multi-site parameter 194A enables targeting multiple sites along the target nerve (including different trunks or branches) to stimulate multiple muscle groups associated with restoring airway patency.

[056] In some embodiments, the bilateral parameter 194B enables and tracks the stimulation of a single type of nerve on different sides of the body (e.g. left side and right side) via a pair of stimulation cuff electrodes spaced apart on opposite sides of the body. In one aspect, this arrangement enables alternating activation of a particular muscle (e.g. a tongue retractor or tongue protrusor) by alternating stimulation between the left and right side of the body

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to reduce the duty cycle to any one nerve by 50%, which in turn, reduces any potential for nerve fatigue. In another aspect, bilateral parameter 194B enables switching to simultaneous bilateral stimulation (i.e. stimulating both nerves synchronous with a certain phase of respiration) if the patient is in a period of sleep that requires more aggressive therapy to prevent apneas.

[057] In one embodiment, the fascicle parameter 194C enables selective stimulation and tracking of one or more different fascicles of a particular nerve being stimulated. This arrangement ensures stimulation occurs among a full range of different fascicles of a nerve, thereby potentially lessening overall fatigue of a nerve. Moreover, in some embodiments in which the nerve stimulation signal is configured to generate tone in the innervated muscle without causing a full contraction, stimulation of a fuller range of the fascicles can lead to more uniform tone throughout the muscle.

[058] In general terms, the communication module 112 of the IPG 100 is configured to facilitate wireless communication to and from the IPG 100 in a manner familiar to those skilled in the art. Accordingly, the communication module 112 includes a reporting module 196 configured to report activities of the IPG 100 (including sensed physiologic data, stimulation history, number of apneas and/or hypopneas detected, etc.) and a programming module 198 configured to receive initial or further programming of the IPG 100 from an external source, such as a patient programmer, clinician programmer, etc.

[059] Furthermore, in some embodiments, at periodic intervals (e.g., daily, weekly), a report is communicated to the patient. Accordingly, Figure 3B schematically illustrates a communication system 220 including IPG 100, clinician programmer 239, and patient programmer 230. First, at these periodic intervals, a history of the therapy is stored in records 228 (i.e. a portion of memory 111) of IPG 100. At the same periodic intervals or other periodic intervals, this history is communicated to the patient programmer in a reporting format that is easily discernible by the patient.

[060] Referring again to Figure 3B, in some embodiments, patient programmer 230 includes an on/off function 231, an increase/decrease

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function 250, an audio alert function 232, and/or a visual reporting function 234. The on/off function 231 provides the patient an option to control the power state of the IPG 100 to override the automatic functioning of the therapy applied via IPG 100. Likewise, the increase/decrease function 250 enables the patient to request a preference for a higher level of therapy in the event that the patient perceives that more therapy would be helpful or a preference for a lower level of therapy in the event that that the patient is experiencing discomfort. This increase/decrease function 250 of the patient programmer 230 activates an override function 459 of an auto-titrate module 750, described in association with Figure 9, that permits the patient to force a reduction or set an upper limit of stimulation in the otherwise automatically self-adjusting therapy. Of course, the physician is also able to limit how much control a patient is given to adjust or override their therapy.

[061] With further reference to Figure 3B, the audio alert function 232 provides an audio alert to the patient when attention to the patient programmer 230 or IPG 100 is warranted. Furthermore, the visual reporting function 234 is configured to communicate information about the history of therapy and/or about the state of the IPG 100 via one or more of a color light function 235, word function 236, symbol function 237, numeric function 238, and a time function 239. This information keeps the patient informed about the efficacy of the system and/or whether the system is functioning properly. For example, a green colored light in the color function 235 may indicate that the device is functioning properly while red light may indicate a malfunction. Via words and/or numerals, the patient programmer 230 also communicates details about the therapy in the last week or last day, such as the hours that stimulation was applied and how many apnea events were detected. Among other details, this information confirms to the patient that they are receiving efficacious therapy and/or can inform the patient to schedule a physician visit if the therapy is not working.

[062] In another aspect, the history of the therapy stored in records 228 of IPG 100 is sent to the physician via a telemetry internet link for the physician to review an entire daily or weekly therapy profile. Alternatively, the physician

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can also download or obtain this information directly from the patient while in their office using a clinician programmer 239. This information will include the circumstances of any instances in which a patient requested changes to the therapy, such as an attempted change via the increase/decrease function 250 of the patient programmer 230. Upon review, this information (e.g., AHI data) is used by the physician to further program the IPG to be more aggressive or less aggressive as necessary by directly programming the desired therapeutic regimen and/or defining at least some of the parameters guiding an automatic self-adjusting method of therapy.

[063] Moreover, in some embodiments, the patient programmer 230 includes an upper limit function 252 and a lower limit function 254. In one aspect, the upper limit function 252 enables a patient to set an upper limit of a therapy at which the patient is comfortable such that any increases made via the increase/decrease function 250 will be constrained by this upper limit. These limit functions 250, 252 are also controllable by a physician via communication between the clinician programmer 239 and the patient programmer 230 (or via communication directly between the clinician programmer 239 and the IPG 100). The lower limit function 254 constrains downward adjustments by the patient so that the therapy stays within a therapeutic range, and can be adjusted via the clinician programmer 239 in a manner previously described above.

[064] In one aspect, the history communicated from the patient to the physician via records parameter 228 includes, but is not limited to, a stimulation quantity 260 and a duration spent in each of the first, second, and third states 202-206 at 262 (including parameters of the applied stimulation signal). In addition, via an apneas module 264, records parameter 228 tracks a volume, frequency, and severity of sleep disordered breathing event. Via an activity parameter 270 and sleep parameter 266, patient programmer 230 tracks activity levels of the patient (both frequency and duration of activity or sleep), as illustrated in Figure 3B. In one aspect, this history and information is automatically formulated into graphical and numerical reports that provide the physician with a nightly synopsis of the patient's sleep apnea patterns and

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the effectiveness of the therapy. In addition, these reports may include a trend report within a night or for a period of multiple nights that enable detection of patterns or changes in the patient's health and/or enable evaluation of adjustments made to the therapy by the physician during the multiple night period. In some embodiments, some portion of this information available via records parameter 228 is reported to the patient.

[065] Moreover, as later described in more detail within this disclosure, in some embodiments, the IPG 100 and system 200 is operated in second state 204 for an extended period of time (or even all night) to provide the physician with an in-home pseudo sleep study. In one aspect, the information from this pseudo sleep study is sent via a patient internet appliance to the physician to enable the physician to adjust or tailor the patient's therapy regimen.

[066] It will be understood that the various components, functions, parameters, and modules of the systems and methods of the present disclosure can be configured, combined, and/or separated to form different groupings than those described and illustrated in Figures 1-10 while still achieving the general principles of the present disclosure described herein.

[067] Figure 4A is a schematic illustration of a system 200 for automatically treating sleep disordered breathing, according to one embodiment of the present disclosure. In one embodiment, system 200 comprises at least substantially the same features and attributes as the systems and components previously described in association with Figures 1-3B. As illustrated in Figure 4A, a multi-tiered system 200 automatically initiates, terminates, and/or applies a therapy with the system operating in one of three states. Among other features, this system provides on/off control of the therapy such that the patient does not have to manually turn the IPG on or off, which insures patient compliance with the therapy while also greatly improving the patient's satisfaction and quality of life.

[068] As illustrated in Figure 4A, in general terms, in a first state 202 of operation of system 200, system 200 determines whether sleep-indicative behavior is present and the sensed behavior is measured against a first

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threshold 290 (e.g. first criteria). In some embodiments, a degree of sleep-indicative behavior is measured via a body motion/activity sensor 310 that senses body posture and "seismic" activity that is indicative of walking, body motion, talking, etc. In one embodiment, this sensor 310 comprises an accelerometer configured to sense a body position or posture. In another embodiment, the body activity sensor 310 comprises an accelerometer or piezoelectric transducer, which is configured for sensing motion. In some embodiments, sensor 310 comprises both a position-sensing component and a motion-sensing component. In one aspect, this physiologic data is tracked via body motion parameter 130 of IPG 100. It is understood that in some embodiments, the awake or sleep state of the patient is alternatively indicated or further indicated via one of more of the physiologic parameters tracked in sensing module 102 (Figure 3A), including (but not limited to) the heart rate parameter 158 or respiratory rate parameter 159.

[069] In either case, the IPG 100 performs this sensing of sleep-indicative behavior for a short period of time (e.g., less than 1 minute) at periodic intervals (e.g. at least every 5 minutes). If the body activity sensor 310 detects inactivity for a significant period of time (e.g. greater than 10 minutes), the system would enter a second state of operation. It is understood that each of the specific times listed above (e.g. sensing for 1 minute between intervals of 5 minutes and providing 10 minutes for an inactivity threshold, respectively) are merely examples and that other times can be selected and/or can be programmed by a physician. In some instances, a brief occasion of activity and/or cyclic periods of activity may be indicative of sleep disordered breathing behavior. Accordingly, when operating in the first state 202, the system will monitor for consistent levels of sleep-indicative behavior, such as inactivity, as well as body posture, to ensure that the system is properly identifying whether the patient is awake or asleep to thereby determine whether the system should enter the second state 202.

[070] In some embodiments, the sensor polling times are performed on a probabilistic model in which sensing is performed according to a dynamic schedule based on the amount of body activity measured at a particular

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sensing time. For example, if a large amount of body activity is measured at time X, then the next polling time would take place much later at time Y. However, if a small amount of body activity is measured at time X, then the next polling time would take place at a time generally equal to (or less than) Y- X.

[071] In one non-limiting example, a probabilistic polling profile 336 (for sensing of potential apneas) is illustrated in Figure 4B in which a magnitude of a time interval between consecutive samples 332 (y-axis) is mapped relative to an amount of sensed body activity 334 (x-axis). As previously described, the general activity level of the patient is sensed according to body motion, body posture, heart rate, respiratory rate, and/or other parameters to determine whether or not the patient is asleep or awake, or somewhere in between a sleeping state and an awake state.

[072] As shown in Figure 4B, according to a probabilistic sampling function, when the amount of sensed body activity is relatively low (340), then a relatively short time interval between samples (338) is applied whereas when the amount of sensed body activity is relatively high (342), then a relatively larger time interval is provided between consecutive samples (339). In general, as the amount of body activity increases, the amount of time between samples (i.e., the size of the sampling interval 332) increases until a maximum sample interval (344) is reached, at which time the size of the sampling interval remains at the maximum until the body activity level drops below the point (346) at which the maximum sample interval is initiated. Stated in other terms, this probabilistic model expresses the probability of a change in sleep conditions such that as the amount of body activity increases to a high range of body activity, there is a much lower likelihood of a change in sleep conditions because the patient is fairly active, and therefore, a much greater time interval can occur between consecutive data samples regarding potential apneic events. In general terms, this probabilistic model conserves energy, thereby contributing the longevity of the IPG 100 in the patient, among other advantages.

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[073] Referring again to Figure 4A, in another aspect, because the body motion/activity sensor 310 (such as an accelerometer) is a low-power sensor, the first state 202 of operation minimizes current drain on the system. In other words, minimal energy is used to first determine a gross level of patient awake/activity (as compared to the activity in a sleep state) using a first level 300 of power before performing more power intensive sensing and signal processing, such as those actions that occur in the second state 202 or third state 206 of operation. In this regard, in accordance with principles of the present disclosure, in one embodiment controller 110 is configured to generate control signals to cause only the sensing module 102 (and not the stimulation module 104) to be supplied with power so that the IPG 100 conserves power until and unless sleep disordered breathing events are detected.

[074] Moreover, in one embodiment, controller 110 can be configured to further limit the power to just one or two select sensors of the system, such as the body motion sensor (e.g., accelerometer parameter 132), so the system is not unnecessarily using power to track numerous physiologic data during periods of normal patient activity (e.g., walking, eating, working, etc.). On the other hand, in some embodiments, controller 110 can also be configured to limit power consumption by deactivating certain sensors of the system when the patient goes to sleep.

[075] In another embodiment, controller 110 further limits power consumption by limiting the frequency at which one or more sensors capture data. For example, instead of continuously capturing data, controller 110 causes the one or more sensors to capture data once for a given time period, for example, once every 5 minutes or every 10 minutes. In yet another embodiment, to further reduce power consumption, the controller 110 causes the frequency of data capture for one set of sensors to be increased during therapy (in the third state 206) while the frequency of data capture for another set of sensors is decreased (or terminated) during therapy.

[076] In some embodiments, first state 202 comprises an on/off function 280 including a time parameter 142. In one aspect, when operating in an "off"

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mode, the on/off function 280 can prevent a false transition to second state 204 by deactivating the sensing functions in first state 202 during certain periods of time (in accordance with time parameter 142), such as a standard wakefulness time period (e.g. preset nominal awake hours between 6 am and 10 pm) or other programmable waking periods. This arrangement ensures that the treatment regimen will not be active during nominal awake hours. In addition, this limit provides power conservation by preventing a transition to a higher power consumption state. On the other hand, in this embodiment, when operating in an "on" mode, the on/off function 280 enables detection of an asleep state during nominal non-waking hours (e.g., between 10 p.m. and 6 a.m.) to confirm the sleep state of the patient prior to enabling any transition to second state 204. Accordingly, upon detecting that the patient is asleep, the "on" mode permits a transition to second state 204 to detect apneas and to potentially provide a therapy in the third state 206.

[077] In one embodiment, the on/off function 280 operates to provide an automatic nocturnal therapy function or sleep schedule parameter, in which the second state 204 of operation (and a potential implementation of the third state of operation) is automatically implemented during a standard sleeping time frame (e.g., preset nominal sleeping hours, such as but not limited to 10 p.m. to 6 a.m.).

[078] In another embodiment, instead of operating first state 202 to trigger a transition to second state 204 based upon sensing body position/posture and sensing body motion (to determine whether the patient is awake or asleep), first state 202 is operated solely as an on/off state such that during normal waking hours (i.e., a standard wakefulness period or awake schedule), the first state 202 will not permit a transition to second state 204, thereby preventing stimulation therapy during the "off" period (i.e., during waking hours). In this embodiment, during non-waking hours (e.g., a repeating nocturnal time period, such as 10 p.m. to 6 a.m.) first state 202 becomes effectively suspended and second state 204 is automatically implemented so that the system remains in at least the second state 204 throughout the non-waking hours to check for apneas and is authorized to provide therapy as

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needed without spending time or energy identifying whether the patient is awake or asleep.

[079] It will be further understood, that in some embodiments, the time function 142 is present in the second and third states 204, 206 of operation.

[080] In one aspect of the second state 204 of the system 200, the system operates at a second level 302 of power to conserve a significant amount of power by not enabling any electrical stimulation of the target nerve. Accordingly, power is not significantly increased from the second level 302 to the third level 304 of power until the system 200 reaches the third state 206, when the patient is detected to be in a sleep state and simultaneously in a state that requires therapy to treat the apneas/hypopneas. This power savings can significantly prolong the life of the system.

[081] In a second state 204 of operation of the system, the IPG continues to monitor the body motion/activity information, such that the system will return to the first state 202 if the sleep-indicative behavior (e.g., the patient's activity level and/or body position) fails to meet the first threshold 290, thereby indicating that the patient has entered awake or active state. In some embodiments, system 200 operates in an additive manner or progressive function such that operation in a successive state (e.g. second state 204) includes maintaining activation of or performance of the features of a previous state (e.g. first state 202) of operation.

[082] In addition to the use of a body activity/motion sensor, in a second state 204 the IPG 100 determines whether sleep disordered breathing, such as apneas/hypopneas, are occurring via monitoring additional physiologic data. For example, the other physiologic data gathered by the IPG can be obtained through the use of one or more of a respiratory sensor, a heart rate sensor, or blood oxygen sensor (e.g. for measuring oxygen saturation), or other sensors of the type previously described in association with Figure 3A. For example, while heart rate information can be used in a variety of ways, in some embodiments, an increased heart rate that substantially coincides with at least part of the sleep disordered breathing behavior is used to assist in

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confirming that the observed behavior is in fact sleep disordered breathing behavior. In particular, in one embodiment, sleep disordered breathing behavior is confirmed via detection of a decreasing heart rate generally coinciding with initiation of the sleep disordered breathing behavior and an increasing heart rate generally coinciding with the termination of the sleep disordered breathing behavior (e.g. an obstructive sleep apnea event). In another example, an identification of sleep disordered breathing behavior is corroborated by detecting a decrease in blood oxygen saturation that substantially coincides with at least part of the sleep disordered breathing behavior. In another example, confirmation of sleep disordered breathing behavior is provided via detection of hyperventilation that occurs (or is initiated) during part of the suspected sleep-disordered breathing behavior.

[083] In some embodiments, at 324 the second state 204 operates to sample physiologic conditions (in order to detect sleep disordered breathing) in a probabilistic manner or periodically at a frequency that is inversely related to the amount or type of body activity (and posture) sensed via sensor 310, in a manner consistent with that previously described in association with Figure 4B.

[084] In one embodiment, as illustrated in Figure 4A, the primary physiologic data used to determine whether or not an apnea is occurring includes a bio-impedance signal 312 (e.g., a trans-thoracic parameter or a non-thoracic parameter) and/or a respiratory pressure signal 314 (e.g., intrapleural or other respiratory parameter), as further described later in more detail in association with Figures 5-7. In the event that apneas or hypopneas suitable for treatment are detected, the system transitions from the second state 204 to the third state 206. In some embodiments, system 200 operates via a bypass function in which second state 204 is omitted thereby enabling the system 200 to operate in an acute mode. In this arrangement, as soon as a patient's patient sleep is detected in first state 202 (or the "on" function is activated), system 200 automatically proceeds to implementing therapy in the third state 206. In one non-limiting example, this arrangement is employed when a patient has an acute case of sleep disordered breathing (e.g.,

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obstructive sleep apnea, hypopneas, etc.) such that any time the patient enters a sleep state, it is practically assured that sleep disordered breathing will take place. Moreover, a physician can program system 200 to operate in an acute mode as patient circumstances warrant. In a third state 206 of operation of the system 200, the system 200 applies a therapy to treat sleep disordered breathing, such as the use of stimulation of the hypoglossal nerve (as represented by output 320 in Figure 4A) synchronous with inspiration to keep the upper airway from obstructing. In some embodiments, stimulation of the hypoglossal nerve is synchronized to be OFF during at least a portion of expiration. In some embodiments, the therapy is applied via an auto-titrate module 750 as will be further described in association with Figure 9.

[085] In this third state 206, the system 200 will periodically or temporarily suspend therapy at regular intervals (for example, every 5, 10, or 15 minutes) for a period of time (e.g., 30 seconds, 1, 2, 3, 4, 5 or more minutes) to determine whether or not apneas/hypopneas are occurring or whether an apnea severity score is above a predetermined threshold. In other words, system 200 is programmable to vary the amount of time that a stimulation protocol is suspended and to vary the frequency at which a stimulation protocol is suspended.

[086] In some embodiments, the frequency of suspending stimulation is based on a probabilistic profile 351 as schematically illustrated by graph 350 in Figure 4C. According to this profile 351, the greater the apnea severity score (based on at least a frequency and/or intensity of apneas), the less often that therapy will be suspended to check for apneas. On the other hand, when there is a lower apnea severity score, the more often that therapy will be suspended as fewer adjustments are expected to be made. In addition, in the latter scenario, the time of suspension can be longer as it is expected that less therapy is needed. Of course, in some embodiments, the system 200 is also programmable to have longer or shorter durations of suspended therapy independent of the frequency at which therapy is suspended.

[087] In some embodiments, additional parameters are considered in determining the duration or, or the frequency of, suspending therapy to check

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for apneas. For example, one parameter is how long sleep has been going on because too frequent or too long of a suspension of therapy early in the intended sleep period (e.g., the first hour) could inhibit the patient from getting to sleep. As another example, if other samples (in the early periods of the intended sleep period) have indicated a high apnea severity score requiring significant stimulation therapy, then another sample may not be needed for some time or even all night. On the other hand, if apnea severity scores early in the intended sleep period were low, then a longer suspension period may be needed to get a statistically significant respiration cycles. These determinations also can be linked to other sleep data. For example, if a body-motion sensor or body-position sensor indicates less restful sleep, then suspension should probably occur less frequently and for less time.

[088] A temporary suspension of the therapy reverts the system 200 to operation in the second state 204 in which the IPG 100 monitors physiologic data for detection of apneas and/or hypopneas without applying a therapy. If no apneas/hypopneas are detected during this temporary suspension of therapy (or if the apnea severity score is below the predetermined threshold), the IPG 100 will remain in the second state 202 of operation. On the other hand, if apneas or hypopneas are still detected (or the apnea severity score is above the predetermined threshold) during a temporary suspension of therapy, the system will once again resume operation in the third state 206 in order to deliver the needed stimulation therapy for treating the sleep disordered breathing behavior.

[089] While the automated decision by system 200 to suspend therapy can be based strictly on time parameters and/or a time-based probabilistic profile as previously described, in other embodiments the automated decision by system 200 to suspend therapy is made by additional factors independent of, or in combination with, time-based parameters. With this in mind, Figure 4D schematically illustrates a method of initiating and terminating suspension of therapy as performed as part of third state 206 (or as part of a state-less decision model). Figure 4D illustrates a loop 375 in which stimulation is applied (380) until or unless one or more triggers 382 are present, at which

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time a suspension function causes system 200 to move to a state of suspended therapy (at 384). One of these triggers 382 includes a preset time-based model, such as the probabilistic model previously described in association with Figure 4C or a fixed time interval. In some embodiments, a posture change function provides another trigger to temporarily suspend application of a stimulation signal based on a change in posture, such as a change in sleeping position when the patient rolls over between a supine and lateral position. In one example, such body position would be monitored by the position-sensing component 132 of body parameter 130 in sensing module 102 of implantable pulse generator 100, as illustrated in Figure 3A. These changes in position can interrupt an apneic state, and therefore such repositioning is an appropriate trigger to suspend therapy to enable detection of whether any apneas are occurring so that therapy is not unnecessarily applied when the changed sleeping position terminated the apnea(s).

[090] Moreover, even when a therapeutic nerve stimulation signal is not being applied when a patient in the supine position, in some embodiments, the sensed supine position is used to as a trigger to check for sleep-disordered breathing behavior more frequently (for example in the second state 204 in Figure 4A) because patients are generally more prone to exhibit sleep disordered breathing behavior in the supine position. Similarly, when other physiologic data such as respiratory waveforms, bio-impedance, heart rate, blood oxygen saturation etc. indicate that sleep disordered breathing behavior is occurring, knowing whether the patient is in the supine position or not helps to confirm whether or not the suspected sleep disordered breathing behavior is truly sleep disordered breathing behavior, as described herein in more detail in association with at least parameter 130 of Figure 3A, second state 204 in Figure 4A, and/or parameter 423 in Figure 4F.

[091] For example, if the monitored physiologic data in cooperation with the body position data reveals that a particular patient rarely exhibits sleep disordered breathing behavior when in a lateral decubitis (i.e., lying on their side), then this body sensing information helps to prevent false positives of sleep disordered breathing behavior when the patient in lying on their side.

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Alternatively, this same data would ensure the accuracy of indicating sleep disordered breathing behavior when the conclusion from primary physiologic data indicating sleep disordered breathing behavior is bolstered by sensing the patient is in a supine position, where most (if not all) of their sleep disordered breathing behavior takes place.

[092] In yet other embodiments, the body position data is used as part of method to determine the aggressiveness of a therapy regimen to apply to the patient. For example, in one embodiment, when the body position parameter 132 reveals that the patient is in a supine position they will receive (via a therapy manager 106 of IPG 100 in Figure 3A and auto-titrate module 750 in Figure 9) a first regimen of therapy and when in a lateral decubitis position (laying on their side), they will receive a second regimen of therapy that is less aggressive than the first regimen of therapy. However, for other patients, the body position data (via parameter 132) is used to apply a less aggressive therapy when the patient is in a supine position and a more aggressive therapy when the patient is in a lateral decubitis position.

[093] Another trigger also includes body activity, as a patient may get out of bed for a period of time, thereby terminating apneic events.

[094] In some embodiments, a severity score of the sleep disordered breathing behavior acts as a trigger (382) to suspend stimulation in order to detect or monitor for sleep disordered breathing behavior. For example, in one embodiment, a frequency of suspending stimulation (to monitor for sleep disordered breathing) is inversely proportional to the severity score of the sleep disordered breathing behavior. In other words, the more severe (e.g. frequency, duration, intensity) the sleep disordered breathing behavior, the less often that stimulation is suspended to check for such breathing behavior and the less severe the sleep disordered breathing behavior, the more often that stimulation is suspended to check for disordered breathing behaviors.

[095] In some embodiments, one or more different stages of sleep may act as triggers to warrant suspending therapy to check whether or not any sleep disordered breathings behavior is occurring. For example, if the sensed

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physiologic parameters reveal that the patient is likely in a deeper stage of sleep for a sufficient period of time, then these sleep stages would trigger the suspension of therapy to move the system 200 out of the stimulation mode and start detecting possible sleep disordered breathing. Accordingly, in some embodiments, as described later in more detail, system 200 is trained by operating simultaneously with a sleep study (e.g., polysomnography) in which different sleep stages (among other patterns) are recognized and in which a patient's different physiologic parameters are tracked relative to those sleep stages. By correlating these sleep study parameters with sensed physiologic parameters of the IPG 100 (Figure 3A), the IPG 100 becomes calibrated for a particular patient to recognize sleep stages and other sleep patterns which are useful in some embodiments for applying and/or suspending therapy via the IPG 100.

[096] With further reference to Figure 4D, a suspension of therapy is terminated and therapy is resumed via reversion to third state 206 according to one or more triggers 382 such as a preset (or probabilistic) time interval or when an apnea severity score detected during the suspended therapy rises above a threshold (e.g., an AHI of 10). It will be understood that in this context the term apnea is used to refer generally to obstructive sleep apnea, hypopneas, or central sleep apnea. Therapy is then applied until one of the triggers 382 forces suspension of therapy.

[097] In general terms, this arrangement insures that therapy is suspended when it is no longer necessary and resumed when necessary. This suspension mechanism aids in preventing overstimulation/fatigue of a nerve, conserves power, and reduces patient annoyance due to stimulation therapy that occurs when the patient is not sleeping.

[098] In some embodiments, this multi-tier system 200 illustrated in at least Figure 4A operates according to a progressive function that provides a dynamic or progressive activation of successive states of operation along with a reversion function in which the system 200 automatically reverts to one of the lower states of operation when operation in a higher state becomes unnecessary. In one aspect, the first and second state employ a sensing

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portion of the IPG 100 without activation of the stimulation portion of the IPG 100. This arrangement saves power in cooperation with power management module 108 (Figure 3A), which can increase the longevity of an implantable battery-operated device, such as the IPG 100. Moreover, because the first state of operation employs only a single sensing parameter (e.g. the body motion/activity sensing) in some embodiments, the IPG 100 can operate in a very low state of power most of the time. In addition to conserving power as part of the power management function of module 108, this arrangement minimizes patient annoyance by insuring that therapy is provided only when needed. Even when criteria to move from the first state 202 to the second state 204 of operation are met, a relatively low state of power is employed in a second state 204 of operation while sensing appropriate physiological sensors to detect sleep disordered breathing behavior. Moreover, this relatively low state of power in the second state 204 of operation is substantially less (for example, less by at least an order of magnitude) than the amount of power used in a third state 206 of operation to provide therapy via stimulating a target nerve.

[099] In another aspect, in addition to conserving power, limiting the first state 202 or second state 204 of operation to a low power state in which no stimulation takes place when not affirmatively providing a neuro-stimulation therapy (such as in the third state 206) also can avoid an unnecessary long term stimulation of the nerve.

[0100] Accordingly, a multi-tier system 200 in accordance with principles of the present disclosure ensures that the patient will automatically receive therapeutic treatment for their sleep disordered breathing behaviors at the appropriate time without undue interference with, or fatigue of, normal nerve function while the system 200 dynamically manages power consumption and operational states of the IPG 100.

[0101] It is also understood that the system 200 of providing therapy can also be provided via protocols other than the state-based protocol illustrated and described in association with Figure 3A. For example, in other embodiments, system 200 is implemented via rule based protocols and/or

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other protocols that do not strictly rely on the sequence and/or interaction of three states of operation.

[0102] It is also understood that the identification of a sleep apnea or hypopnea via an IPG 100 and the associated systems and methods described herein is performed in a manner that varies somewhat from how apneas/hypopneas are identified in a sleep study. For example, in a sleep study, an apnea or hypopneas is defined as a certain physiologic events, such as a decrease (e.g., 3%) in blood oxygen saturation for a period of at least ten seconds. Moreover, in a sleep lab, the physician scores events using predefined criteria, based on the sensor parameters obtained in a sleep lab, and this scoring results in the AHI count.

[0103] Accordingly, because the implantable systems described herein do not have sensors that correspond exactly with the types of sensors used in a sleep lab, the AHI count determined via the implantable systems in accordance with embodiments of the present disclosure will differ somewhat from the sleep lab- determined AHI count. Nevertheless, the implantable system/methods of embodiments of the present disclosure include a number of physiologically sensed data (e.g., internally measured blood oxygen saturation) that can act as surrogates for the types of information obtained in a sleep lab (e.g., externally measured blood oxygen saturation).

[0104] Figure 4E is a flow diagram that schematically illustrates a method 390 of correlating sleep study parameters with physiologic parameters of the implantable pulse generator system, in accordance with an embodiment of the present disclosure. As illustrated in Figure 4E, at 392 the method 390 includes operating, substantially simultaneously with a polysomnography (PSG) study, an implantable pulse generator (IPG) system in a monitoring mode. At 394, a first set of physiologic parameters is tracked, during the polysomnography study, via the IPG system in its monitoring mode. A second set of sleep study parameters is tracked, independent of the IPG system, via the polysomnography study (at 395). At 396, method 390 includes identifying sleep disordered breathing patterns (e.g. apneas and/or hypopneas) from the tracked second set of sleep study parameters and identifying which of these

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parameters are indicative of sleep disordered breathing for a particular patient. At 398, the implantable pulse generator is calibrated to recognize sleep disordered breathing for a particular patient via correlating the tracked physiologic IPG-based parameters/conditions relative to the tracked PSG-based sleep study parameters that are indicative of sleep disordered breathing behavior for that particular patient.

[0105] With this in mind, Figure 4F provides a chart 400 that schematically illustrates a comparison of some sleep study parameters 402 relative to some IPG therapy parameters 408. As previously noted, in some embodiments, the IPG therapy parameters 408 are calibrated relative to one or more related sleep study parameters 402. For example, an IPG 100 within a patient operates during a sleep study such that parameters for the IPG 100 and parameters for the polysomnograph (PSG) monitor are both tracked. By looking at profiles of sleep disordered breathing behavior, a correlation is made between the IPG parameters 418 and the PSG parameters 402 such that the IPG 100 is calibrated to sleep study data.

[0106] In one example, one sleep study parameter includes an airflow measured at the mouth-nostril airflow pathway (410), which is indicative of a sleep disordered breathing when this airflow is substantially reduced. In one aspect, the mouth-nostril airflow is measured at the nostrils and/or mouth. While this parameter may not be exactly reproduced in embodiments which are totally implantable, a combination of parameters to be described in more detail in association with Figures 5-7B provides a good indication of an sleep disordered breathing behavior that is commensurate with the extent to which the mouth-nostril-airflow parameter 410 of a sleep study indicates sleep disordered breathing. In particular, a dramatic change in the amplitude patterns 416 (and in opposite directions) of both a bio-impedance signal and a respiratory pressure signal provide an indication that a sleep disordered breathing behavior (e.g., an apneic event) 413 is occurring or has occurred. Accordingly, this combination of the amplitude patterns 416 of the bio-impedance and respiratory pressure signals (determined via IPG 100 and

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system 100) act as a surrogate to the mouth-nostril-airflow parameter 410 typically measured in a sleep study.

[0107] In another example, referring again to Figure 4F, the internally measured blood oxygen saturation parameter 417 (via IPG 100 and system 200) acts as a surrogate for the externally measured blood oxygen saturation parameter 411 available via a sleep study. While there are some differences between these two respective parameters 417 and 411, by training IPG 100 via a sleep study, the internally measured blood oxygen saturation parameter 417 (via IPG 100 and system 200) will be calibrated relative to the externally measured blood oxygen saturation parameter 411 to account for such differences. In this way, the internally measured blood oxygen saturation parameter 417 can function as an accurate trigger for occurrences of sleep disordered breathing in this patient.

[0108] In other respects, the one or more physiologic data points of the implantable systems/method of the present disclosure may provide information that is more helpful in determining an automatic self-adjusting therapy than information obtained via a sleep lab. For example, embodiments of the present disclosure measure intra-pleural pressures 418, which can be correlated to the degree of obstruction of the upper airway. As the obstruction increases in a progression from an open airway to hypopnea to a full obstruction, the magnitude of the intra-pleural pressure increases. Accordingly, embodiments of the present disclosure enable measurement and identification of increases in the intra-pleural pressures 418 which in turn, are indicative of sleep disordered breathing events 415. In one aspect, this feature enables the systems/methods of present disclosure to provide sleep disordered breathing scoring (e.g., apnea scoring) that is more sophisticated than conventional scoring methods associated with a sleep lab.

[0109] Moreover, in one embodiment, after initially calibrating the IPG 100 during a sleep study, the IPG 100 is permitted to operate during a second sleep study so that the IPG 100 is able to self-learn in direct association with the data provided via the PSG. Using this method, physiologic data sensed via the IPG 100 that is indicative of an sleep disordered breathing behavior is

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matched with indicative physiologic data/observations sensed via the PSG monitoring system that is indicative of sleep disordered breathing behavior. In one aspect, this direct calibration lessens the time that the IPG would spend self-learning an appropriate baseline therapy regimen for a patient because the PSG would allow direct real-time programming of the IPG as the sleep study occurs. In other words, the IPG would be automatically programmed with a pattern of the sleep disordered breathing patterns, sleep habits, etc. so that the IPG will know in advance for this patient which time of night, day of the week, body position, heart rate, etc. that will trigger apneic behavior or normal breathing. As a result, the automatic therapy regimen will be tailored to a specific patient's needs rather than having the patient receive a conventional one-size-fits-all stimulation therapy that would have a greater potential to consistently overstimulate or understimulate the patient.

[0110] In this regard, Figure 4F further illustrates such additional parameters which are correlated with the PSG-related primary parameters and the IPG-related primary parameters. In some instances, these additional parameters may or may not be tracked in a polysomnography study or via the IPG. As shown in Figure 4F, a night-of-week parameter 420 tracks which night or nights of the week that the sleep disordered breathing behavior occurs while time-of-day parameter 421 tracks one or more points in time within a 24 hour period that the sleep disordered breathing occurs. A sleep stage parameter 421 tracks which, and how many, stages of sleep within a sleeping period (such as 10pm to 6 am) that the sleep disordered breathing occurs. A body posture parameter 423 tracks which body posture coincides with occurrence of the sleep disordered breathing, and when (relative to a sleep stage, time of day, or night-of-the-week) the patient typically enters that body posture. Other parameters, such as patient demographic factors 424 are tracked as well, such as age, sex, smoker, weight, neck, hypertension, etc.

[0111] In some embodiments, this method of correlation includes correlating a sleep stage parameter 425 relative to sleep disordered breathing events and relative to an array of IPG-related parameters 426, such as a heart rate, a blood oxygen saturation, a bio-impedance, and/or a respiratory pressure.

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[0112] In another embodiment, as illustrated by chart 450 of Figure 4G, after a number of IPG-based systems 456 (e.g., IPG 1, IPG 2, etc.) are calibrated relative to sleep study parameters 454 (e.g. PSG 1, PSG 2, etc.) for a number of patients 452 (e.g. Joe, Fred, etc), embodiments of the present disclosure can use a correlation of the sleep study parameters relative to the IPG parameters to develop a predictive index 460 (e.g., responsive ratings) that would predict how beneficial an IPG might be for a particular patient prior to implantation of the IPG in the patient. In one aspect, the responsive rating expresses on a scale from 1 to 10 (with ten being the highest) how efficacious the implantable pulse generator would be to treat sleep disordered breathing for a patient having the type of polysomnography study and demographics like those provided in the chart.

[0113] In some embodiments, in addition to or instead of sensing physiologic parameters via IPG 100 during a formal sleep study, system 200 (Figure 4A) of an implanted IPG 100 is operated only in the second state 204 for an extended period of time (or even all night) to provide the physician with a pseudo sleep study performed in the home of the patient. In other words, the IPG 100 and system 200 act as an implanted polysomnography device. In one aspect, the data from the in-home pseudo sleep study is sent via a patient internet appliance (e.g., patient programmer 230 of Figure 3B) to the physician, thereby allowing the physician to better tailor the stimulation therapy to the sleeping habits/behavior of the patient. In some respects, the in-home pseudo sleep study can potentially provide better data than a formal sleep study regarding the actual sleeping behavior or habits of the patient because the patient would be sleeping in their normal sleeping environment, such as their own bed, under their own climate control, etc.

[0114] Accordingly, Figure 4H illustrates one embodiment of a method 475 of treating sleep disordered breathing, according to an embodiment of the present disclosure. As illustrated in Figure 4H, at 480 method 475 includes calibrating an IPG system via an in-home pseudo sleep study via sensing physiologic parameters, as surrogates for conventional sleep study parameters, with the IPG system. At 482, in initial therapeutic regimen of

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nerve stimulation therapy, based on the calibration, is programmed into the IPG system. At 484, method 475 includes performing an automatically adjustable stimulation therapy, via the programmed, calibrated IPG system, based on the initial therapeutic regimen.

[0115] In some embodiments, prior to performing the in-home pseudo sleep study, sensing parameters of the IPG 100 and system 200 are calibrated relative to conventional sensing parameters of a formal sleep study by operating the IPG 100 and system 200 in a sensing mode (e.g. second state 204 in Figure 4A) during the formal sleep study in a manner substantially the same as described above.

[0116] While any number of physiologic parameters can be used with varying success to detect sleep disordered breathing, such as an apnea and/or hypopnea, in one embodiment of the present disclosure, the sensing module 102 of the IPG 100 detects apneas/hypopneas via a trans-thoracic bio-impedance parameter. In particular, a measurement of trans-thoracic impedance is used to track the relative amplitude of the respiratory waveform. Physiologically speaking, the bio-impedance of the lungs varies as the lungs fill and empty with air. An air filled lung has a slightly higher impedance. In another aspect, a varying respiratory drive will also cause the amplitude of the bio-impedance to vary, with a larger respiratory drive increasing the signal amplitude of the bio-impedance.

[0117] Upon obtaining the trans-thoracic bio-impedance signal via the sensing module 102 of IPG 100, the bio-impedance signal is further processed to identify an average peak amplitude over time. A sleep disordered breathing event is detected by further identifying cyclic amplitude variations that occur for a duration substantially similar to the already known duration of a typical apneic event. In this regard, Figure 5 provides a graph 500 schematically illustrating a respiratory airflow signal 502 corresponding generally to respiratory drive/effort and a trans-thoracic, bio-impedance signal 504. As shown in Figure 5, a relative amplitude (represented by y-axis 508) of these signals is separately tracked over a time period (represented by x-axis 506).

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[0118] In the above-described embodiment, the bio-impedance signal 504 is obtained via a trans-thoracic sensing mechanism. However, in other embodiments, the bio-impedance signal 504 is obtained via other sensing mechanisms such as previously identified in association with bilateral nerve electrode parameter 148 of Figure 3A. For example, in one embodiment, when a stimulation cuff electrode is provided on each of the left and right sides of the body to enable potential bilateral stimulation (simultaneous or alternating), a bio-impedance can be measured between these respective nerve electrode cuffs, which are spaced apart on opposite sides of the body. In the event of a collapsed airway, a change in the pattern of this bio-impedance signal will be detected and can be used to indicate an apneic/hypopnea event. Of course, monitoring a bio-impedance signal in embodiments of the present disclosure is not strictly limited to either the trans-thoracic sensing mechanism or the sensing mechanism provided by the spaced apart stimulation cuffs.

[0119] In particular, in observing the amplitude signal (of the bio-impedance measurement) during a typical apneic event, the system would observe a 10 to 40 second time period of a low amplitude signal (which directly corresponds to the obstruction) followed by a very high amplitude signal (of the bio-impedance measurement) due to the arousal from sleep and the ensuing hyperventilation. In Figure 5, the bio-impedance signal 504 during normal respiration is represented by segment 540, while the relatively low amplitude bio-impedance signal 504 during the sleep disordered breathing event is represented by segment 542 which is then followed by the relatively high amplitude signal in high-effort segment 544. Moreover, the relatively low amplitude segment 542 of the bio-impedance signal 504 substantially corresponds to the relatively low amplitude segment 532 of the airflow signal 502 caused by the obstruction. Finally, the high amplitude segment 534 of airflow signal 502 represents an increase to respiratory drive as the patient is aroused and exerts a high effort (represented by portion 274) to recover from the sleep disordered breathing event(s).

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[0120] Accordingly, in one embodiment the IPG 100 uses this physiologic data illustrated in Figure 5 to identify a sleep disordered breathing behavior. In one aspect, this data would be detected via a sensing module 102 of IPG 100 with system 200 in a second state 204 of operation.

[0121] In another embodiment of the present disclosure, the sensing module 102 of IPG 100 detects an apnea or hypopnea via a respiratory pressure parameter. As previously described in association with Figures 1-2, a measurement of respiratory pressure can be made by placing a pressure sensor in the extrapleural space (represented by 89 in Figure 2) or the intrapleural space (represented by dashed lines 88 and identifier 90 in Figure 2). The respiratory pressure signal will provide a respiratory signal proportional to the negative pressures generated during inspiration. For example, the magnitude of the amplitude of the respiratory pressure will vary due to the level of respiratory drive or effort and also will vary based on any flow restriction in the upper airway.

[0122] In this regard, Figure 6 provides a graph 550 schematically illustrating the respiratory airflow signal 502 corresponding generally to respiratory drive/effort and a respiratory pressure signal 552. As shown in Figure 6, a relative amplitude (represented by y-axis 508) of these signals is separately tracked over a time period (represented by x-axis 506).

[0123] In particular, in observing the amplitude signal (of the respiratory pressure measurement) during a typical apneic event, the system would observe a 10 to 40 second time period of a high amplitude signal (which directly corresponds to the obstruction) continued by a very high amplitude signal (of the respiratory pressure measurement) due to the arousal from sleep and the ensuing hyperventilation. In Figure 6, the respiratory pressure signal 552 during normal respiration is represented by segment 560, while the relatively high amplitude respiratory pressure signal 552 during the sleep disordered breathing event is represented by segment 562 which is then followed by the relatively high amplitude signal in high-effort segment 564. Moreover, the relatively high amplitude segment 562 of the respiratory pressure signal 552 (representing an increased magnitude of inspiratory

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negative pressure) substantially corresponds to the relatively low amplitude segment 532 of the airflow signal 502 caused by the obstruction.

[0124] Thus, the sensing module 102 of the IPG 100 (when operating in second state 204 of multi-tier system 200) can detect apneas or hypopneas (using physiologic data such as that illustrated in Figure 6) by tracking the respiratory amplitude from a respiratory pressure sensor and identifying average peak pressures and detecting cyclic amplitude variations that have a time component similar to the period of apneic events.

[0125] In yet another embodiment, sensing module 102 of IPG 100 can detect an apnea or a hypopnea by using more than one primary physiologic signal as a determining factor. Accordingly, as illustrated in Figure 7A, both a bio-impedance signal 504 and a respiratory pressure signal 552 are used together to determine when an apnea or hypopnea is occurring. While the example shown in the Figure 7A illustrates a trans-thoracic bio-impedance signal, it is understood that other bio-impedance signals can be tracked and used in combination with a respiratory pressure signal 552 to determine whether an apnea or hypopnea is occurring.

[0126] While using either a bio-impedance sensing signal 504 (Figure 5) or a respiratory pressure sensing signal 552 (Figure 6) alone will provide some level of apnea detection, these respective sensing signals lack specificity as the signal amplitudes both vary with respiratory drive and with restricted/obstructed airflow (apnea/hypopnea). However, the combination of using physiologic data from both a bio-impedance sensor and a respiratory pressure sensor provides excellent apnea/hypopnea detection as both sensors have significant changes in amplitude due to increased respiratory drive. In some embodiments, these substantial changes comprise opposing amplitude changes during the occurrence of the apneas/hypopneas. In particular, as illustrated in Figure 7A, the respiratory pressure amplitude (signal 552) significantly increases (segment 562) due to the flow restriction and the bio-impedance signal (504) decreases (segment 542) to a negligible level in response to the flow restriction (segment 532) of airflow signal 502. As illustrated by the sleep disordered breathing 522 portion of graph 570 of

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Figure 7A, when the relative amplitudes of the two signals 504, 552 move in opposite directions (one increasing by large amounts and one decreasing by large amounts) as depicted in the sleep disordered breathing portion 522 of graph 570, then an obstructed air flow or apnea/hypopnea is detected. However, it will be understood that in some embodiments, because of variations from patient to patient, the respiratory pressure can decrease (instead of increasing) during at least part of the sleep disordered breathing behavior. To the extent that actual patient-to-patient behavior varies in the physiologic conditions exhibited during sleep disordered breathing, these variances are accounted for via calibration of an implantable pulse generator system (as described in association with at least Figures 4E-4H) such that the therapeutic stimulation regimen and detection model is tailored for each patient to ensure accuracy in identifying sleep disordered breathing for each particular patient. In some embodiments, when the sleep disordered breathing event is a central sleep apnea event, the substantial change in the amplitude of the sensed bio-impedance signal includes a substantial decrease in the amplitude of the sensed bio-impedance signal and the substantial change in the amplitude of the sensed respiratory pressure signal includes a substantial decrease in the amplitude of the sensed respiratory pressure signal. In other embodiments, the sleep disordered breathing event is a hypopnea event, and the substantial change in the amplitude of the sensed bio-impedance signal includes a substantial decrease in the amplitude of the sensed bio-impedance signal and the substantial change in the amplitude of the sensed respiratory pressure signal includes a substantial increase in the amplitude of the sensed respiratory pressure signal. However, in the case of the hypopnea event, the respective substantial decrease in the amplitude of the sensed bio-impedance signal and the respective substantial increase in the amplitude of the sensed respiratory pressure signal are of a lower magnitude change, respectively, than occur in an obstructive sleep apnea event.

[0127] In some embodiments, a method of detecting the presence of a sleep disordered breathing behavior includes mapping the bio-impedance signal relative to the respiratory pressure signal to identify whether a sleep

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disordered breathing behavior, and in particular, whether an obstructive sleep apnea has occurred. In one non-limiting example, Figure 7B is a graph 580 that schematically illustrates different breathing patterns as a grid 581 based upon the bio-impedance signal 582 (y-axis) relative to the respiratory pressure signal 584 (x-axis). As illustrated in Figure 7B, a combination of a normal amplitude 587 of respiratory pressures and a normal amplitude 591 of bio-impedance measurements indicate that normal breathing 596 is occurring.

[0128] However, as illustrated via graph 580 of Figure 7B, as an obstructive sleep apnea (or hypopnea) develops, the bio-impedance and respiratory pressure signals move in the opposite directions, resulting in a combination of a high amplitude 588 of respiratory pressures and a low amplitude 590 of bio-impedance signals to indicate an obstructive sleep apnea 597. As the body responds to the obstructive sleep apnea via hyperventilation, a combination of a high amplitude 588 of respiratory pressures and a high amplitude 592 of bio-impedance signals indicates a high effort or hyperventilation pattern 598. For example, in Figure 7A, hyperventilation is observable from the amplitude of respiration pressure (segment 564) being about twice the amplitude of respiration pressure during normal breathing (segment 560) and with the amplitude of bio-impedance during hyperventilation (segment 544) being substantially higher than the amplitude of bio-impedance during normal breathing (segment 540) or during the apneic event.

[0129] With these different breathing patterns in mind, graph 580 further illustrates a cycle 594 that moves from normal breathing (596) to apneic events (597) to hyperventilation (598) and then returning to normal breathing (596) as the obstruction lessens.

[0130] In some embodiments, in addition to monitoring the amplitude of hyperventilation following a sleep disordered breathing behavior, the system monitors a duration or length of a hyperventilation event. This duration also can be correlated to a level of oxygen desaturation caused by the preceding sleep disordered breathing event. In this manner, the duration of the hyperventilation event is used as at least one factor in determining a sleep disordered breathing severity score, with greater durations of hyperventilation

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being generally associated with, and representative of, more severe sleep disordered breathing and with lower durations of hyperventilation being representative of less severe sleep disordered breathing.

[0131] In some embodiments, a hyperventilation function (such as hyperventilation function 186 of therapy manager 106 in Figure 3A) identifies a hyperventilation period following a sleep disordered breathing event via identifying a substantial change in the amplitude of the sensed bio-impedance signal after the sleep disordered breathing event. Moreover, in some embodiments, the hyperventilation function is configured to identify the hyperventilation period via a substantial change in an amplitude of the sensed respiratory pressure signal after the sleep disordered breathing event that occurs substantially simultaneously with the substantial change in the amplitude of the sensed bio-impedance signal after the sleep disordered breathing event. In some embodiments, the hyperventilation function is configured to identify, a severity of a sleep disordered breathing event preceding the hyperventilation period based on at least one of a duration of the hyperventilation period, a duration of the sleep disordered breathing event, or a lowest blood oxygen saturation following the sleep disordered breathing event.

[0132] In some embodiments, a method of detecting the presence of a sleep disordered breathing behavior includes tracking a percentage change in both the bio-impedance signal and the respiratory pressure signal to determine whether an sleep disordered breathing has occurred. For example, one can track the bio-impedance signal and the respiratory pressure signal during normal respiration to establish a baseline and then identify a percentage decrease (or an absolute decrease) in the bio-impedance signal and a percentage increase (or an absolute increase) in the respiratory pressure signal during a potential sleep disordered breathing event. If one or both of the respective percentage decrease (bio-impedance) and percentage increase (respiratory pressure) exceed a predetermined threshold (e.g., 50%, 75%, 100 %, etc.), then the system concludes that an apnea/hypopnea event has taken place. As a further illustration, Figure 7A provides a non-limiting

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example and illustrates that bio-impedance signal 504 decreased generally by 100% (represented by amplitude 0) in segment 542 (as compared to amplitude A in normal respiratory segment 540) and that respiratory pressure signal 552 increased generally by 100% (as represented by amplitude 2A) in segment 562 (as compared to amplitude A in normal respiratory segment 560). Assuming that the measurement comprises an average (100%) of the two respective percentage changes (100, and 100), and the threshold is a 90% change, then the 100% average change in the respective signals exceed the threshold (e.g., 90 %) which indicates that an sleep disordered breathing event has occurred. The occurrence of this sleep disordered breathing event is modeled by the corresponding segment 532 of airflow signal 502.

[0133] In some embodiments, the threshold average percentage change is based on at least one of a minimum quantity of breaths, a minimum preset quantity of respiratory cycles, or a predetermined period of time including multiple respiratory cycles.

[0134] For these reasons, in accordance with the principles of the present disclosure, using a combination of the bio-impedance signal and the respiratory pressure signal enables a robust method of detecting apneas or hypopneas, which is less likely to produce a false positive identification of an apnea.

[0135] However, embodiments of the present disclosure are not limited to detecting an apnea (or hypopnea) solely through the use of the bio-impedance signal and/or the respiratory pressure signal. Other physiologic signals are known to provide an indication that apneas/hypopneas are occurring. These signals can be processed to further confirm that apneas/hypopneas are occurring to augment the approaches above. For example, a heart rate is known to decrease at the onset of an obstructive apnea, followed by a fast rise in heart rate toward the end of the apnea and immediately following the apnea. In another example, a blood oxygen level (measured optically via an implanted system) is known to drop during and following an apneic event. Accordingly, such physiologic data can be obtained via the sensing module 102 of the IPG 100 to further confirm the

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presence or absence of the apnea/ and hypopnea. Moreover, in addition to the primary physiologic data of the respiratory pressure and the bio-impedance illustrated in Figure 7A, the data from these physiologic signals (e.g., heart rate, blood oxygen) is additionally used to measure the duration and/or intensity of an apnea/hypopnea event, which provides an indication of the severity of the apnea/hypopnea event.

[0136] With these general principles in mind, Figure 7C schematically illustrates a method 600 of identifying sleep disordered breathing behavior (such as an apnea even or hypopnea event), in accordance with an embodiment of the present disclosure. As illustrated in Figure 7C, method 600 includes sensing a bio-impedance (at 602) and detecting whether a substantial change (such as substantial decrease) has occurred. At 610, method 600 includes sensing respiratory pressure and detecting whether a substantial change (e.g. increase) has occurred. If a substantial change in both the sensed bio-impedance and the sensed respiratory pressure is detected, then an apnea event (sleep disordered breathing) is identified at 608. However, additional thresholds can be used to further confirm the presence or absence of a sleep disordered breathing event. In some embodiments, as at 620, method 600 queries whether the percentage change in the sensed bio-impedance and/or the sensed respiratory pressure exceeds a threshold (e.g. a threshold percentage change). If not, the sensed behavior is determined not to be an apnea event (at 622). However, if the threshold is met or exceeded, then method confirms the presence of an apnea event at 624.

[0137] In some embodiments, further confirmation is provided in method 600 via observing, at 630, whether the sensed heart rate decreases during a portion of the potential apnea event and then increases after the potential apnea event. If not, then no apnea event occurred (at 632). However, if that heart rate behavior is confirmed, then further confirmation of an apnea event (i.e., sleep disordered breathing behavior) is provided. In some embodiments, further confirmation is provided in method 600, at 636, via observing a substantial decrease in blood oxygen saturation that substantially coincides

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with sleep disordered breathing behavior. If this observation is lacking, then method 600 could determine that no apnea event occurred 638. In some embodiments, further confirmation of sleep disordered breathing is made at 640 in method 600 via detecting hyperventilation after the potential apnea event. If the hyperventilation is not found, then no apnea event has occurred. However, if such hyperventilation is identified, then method confirms a presence of a sleep disordered breathing event or behavior. It will be understood that in some embodiments, the various confirmatory queries at 620, 630, 636, and 640 can be performed in any order or performed simultaneously, and that one or more of the particular queries can be omitted or other confirmatory queries based on physiologic conditions can be added.

[0138] Another embodiment of the present disclosure includes a system and method to automatically adjust the level of therapy to treat sleep disordered breathing behavior based on the measurement of AHI (Apnea Hypopnea Index) or another apnea severity index or scoring tool. With this system, the level of therapy will be automatically adjusted to match the needs of the patient, which are known to vary based on sleep state, body position, and other physiologic factors (e.g., alcohol use, sleepiness, etc.). Adjustments to the therapy include incrementing or decrementing the level of therapy, as described below in more detail. In addition, as will be apparent from the description below, this "auto-titration" system and method for automatically adjusting the level of therapy operates in a substantially different manner than conventional Continuous Positive Airway Pressure (CPAP) systems. Among other differences, an implantable neuro-stimulation system, in accordance with principles of the present disclosure, presents a substantially different type of approach to treating sleep disordered breathing behavior (such as, but not limited to obstructive sleep apneas). Consequently, the types of therapy parameters and control systems used in an implantable neuro-stimulation system are substantially different than the therapy parameters and control systems used in the CPAP systems.

[0139] Figure 8A is a flow diagram schematically illustrating a method 700 of automatically adjusting a level of therapy, in accordance with embodiments

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and principles of the present disclosure. In one embodiment, method 700 is performed using the systems, components and other methods previously described in association with Figures 1-7B. In other embodiments, method 700 is performed using other systems and components.

[0140] As shown in Figure 8A, at box 702 method 700 includes measuring the number of apneas (AHI) or an apnea severity score over a time period to track the frequency of apnea/hypopnea events based on physiologic signals 701 provided via sensing module 102 of IPG 100. The method includes establishing a predetermined setpoint corresponding to an acceptable number of apneas/hypopneas over a period of time (e.g. number of apneas per hour) or a setpoint corresponding to an acceptable apnea severity score. In some embodiments, the set point is fixed while in other embodiments, the setpoint is programmable (e.g., 0, 1, 3, 5, 10 events/hour etc.). In another embodiment, in addition to counting the number of apneas/hypopneas within a given time period, the method also looks at the intensity and/or duration of one or more apnea events to determine whether the measured patient behavior is above or below a setpoint. In this latter embodiment, the number of apneas, the duration of an apnea, and intensity of apneas (as well as other physiologic data) are combined into a severity score. In one embodiment, the intensity of an apnea event is at least partially determined by a percentage decrease (or absolute measurement) of blood oxygen level, a change in heart rate, and/or a duration of hyperventilation following an apnea.

[0141] As shown at box 704, the system/method periodically queries whether or not the measured AHI (or other index) is above the predetermined set point. If the query at box 704 is answered affirmatively (i.e. yes), then too many apnea/hypopneas are occurring, and method 700 proceeds to increment or increase the level of therapy, as represented by box 708. As the level of therapy is increased, method 700 continues the ongoing measurements of the number of apnea events (or an apnea severity score), as represented by box 702.

[0142] On the other hand, if the query at box 704 is answered negatively (i.e. no), then the current level of therapy is considered to be at least adequately

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treating the apnea/hypopnea condition of the patient. However, it is possible that a lower level of therapy could still adequately treat the apnea/hypopnea condition of the patient. Using a lower level of therapy would be desirable to avoid potential fatigue of the target nerve, while also reducing the amount of power consumed by the IPG 100. Once the level of therapy is decremented (as represented by box 706), method 700 maintains its measurements of the number of apnea events (or an apnea severity score) to determine if an adequate level of therapy is being maintained.

[0143] In this way, method 700 continually assesses the level of therapy administered to the patient and then automatically implements an increment or a decrement in the level of therapy, as warranted, to prevent the patient from receiving unnecessary stimulation (i.e., preventing overstimulation) to the target nerve while ensuring that at least a therapeutic level of therapy is maintained. In one aspect, this method 700 also terminates all stimulation when no therapy is warranted for an extended period of time. In some embodiments, an incremental increase in the level of therapy is executed in steps that are substantially larger (e.g. 50%, 100 %) than the steps in which the level of therapy is decremented. In other words, increases in the level of therapy are made more aggressively than decreases in therapy. With this arrangement, the method 700 moves more quickly to eliminate the apnea events but moves slower when attempting to find a lower beneficial level of therapy.

[0144] In one embodiment, the controller has either pre-determined or programmable maximum stimulation settings to prevent overstimulation to the target nerve or surrounding tissue, initiating a patient arousal, or inducing discomfort to the patient. These maximum levels may be programmed by a physician while conducting an office query of the functionality of the system. In this way, boundaries are established for the auto-titrate method such that the parameters of therapy generally remain within the limits of comfort of most patients. Moreover, in some embodiments, the method 700 includes a patient override function (represented as patient override function 459 in Figure 9) configured to enable the patient to override the method of automatic therapy

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to reduce the level (amplitude, duration, etc.) of therapy when the therapy is not comfortable for the patient. In some embodiments, this function is available by the increase/decrease function 250 of patient programmer 230, as previously described in association with Figure 2.

[0145] Figure 8B further illustrates a method 720 of automatically adjustable therapy to treat sleep disordered breathing, according to an embodiment of the present disclosure. As illustrated in Figure 8B, at 722 method 720 includes tracking a severity of sleep disordered breathing behavior relative to a baseline. This severity is based on one or more of a frequency of the sleep disordered breathing (SDB) events, a duration of the respective SDB events, an intensity of the respective SDB events, a presence of hyperventilation (as well as it duration or intensity), a change in heart rate, and/or a change in blood oxygen saturation.

[0146] At 726, method 720 includes applying, at a first intensity level, a nerve stimulation signal to an airway-patency related nerve. At 728, method 720 includes evaluating the tracked severity of the SDB behavior, in response to the applied nerve stimulation, relative to threshold. The nerve stimulation regimen is automatically adjusted, at 730, from the first intensity level to a second intensity level in response to the evaluated severity of the SBD behavior. This adjustment takes place either at 732 as an automatic incrementing of the intensity level of nerve stimulation when the evaluated SDB severity meets or exceeds a threshold or at 734 as an automatic decrementing of the intensity level of nerve stimulation when the evaluated SDB severity falls below that threshold.

[0147] In some embodiments, method 700 of automatically applying a therapy is at least partially governed by a stimulation goodness function. In particular, a setpoint is selected, monitored and adjusted dynamically according to a stimulation goodness function that balances at least the factors of patient comfort (based on feedback via the patient programmer or clinician programmer), therapeutic efficacy, and longevity. In one embodiment, the stimulation goodness function operates in a manner illustrated by Figure 10.

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[0148] Figure 10 schematically illustrates a method of automatically adjusting a setpoint in which increasing amounts of therapeutic stimulation 854 (y-axis) are mapped relative to a goodness parameter 852 of the therapy (x-axis). Increasing amounts of goodness correspond to increased levels of patient comfort, longevity of the device, and therapeutic efficacy in reducing the number or severity of apneic events. As shown in Figure 10, graph 850 depicts a stimulation goodness profile 860 and also identifies an upper limit 872 on the strength or power of stimulation (854) applied to the target nerve and a lower limit 570 on the strength or power of stimulation required to achieve a minimum level of efficacious treatment. In some embodiments, one or both of the lower limit and the upper limit corresponds to a physician defined setpoint while in other embodiments, one or both of the lower limit and the upper limit corresponds to a manufactured defined setpoint. Alternatively, the upper limit and/or the lower limit are determined algorithmically through monitoring apnea events and/or patient commands.

[0149] As can be seen from Figure 10, at lower amounts of strength/power, the measured goodness (852) is relatively low (shown at 873) and with increasing amounts of strength/power, the measured goodness gradually increases (shown by segments 874 and 882) providing a better therapeutic experience for the patient until an optimum point 880 is achieved. At this point, any further increases in strength/power will cause a gradual decrease in measured goodness (shown by segment 884) for the patient as further increases in strength/power is applied. In other words, the optimum point 880 represents the point above the minimum strength/power that provides the greatest overall benefit to the patient while any further increases in strength/power reduce the overall benefit to the patient, i.e., the point of diminishing returns. In other words, any increases in the intensity of stimulation beyond point 880 will result in a decrease in patient comfort, an increase in energy usage, and/or a decrease in efficacy. Accordingly, by implementing a stimulation goodness function, small dynamic increases in the level of stimulation above a minimum limit and/or physician-defined settings can lead to a large increase in the overall benefit to the patient. On the other hand, when the setpoint is too high, the stimulation goodness function can

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dynamically guide the setpoint to a lower value to increase the overall benefit to the patient.

[0150] In one embodiment, the level of therapy can be incremented or decremented via the auto-titrate module 170 (and the treatment parameters module 168) of the therapy manager 106 of IPG 100 shown in Figure 3A. In this regard, Figure 9 is a block diagram schematically illustrating additional features and attributes of the auto-titrate module 170 (and the treatment parameters module 168) that is employed in accordance with the method 700 of automatically adjusting a level of therapy to treat sleep disordered breathing behavior.

[0151] As illustrated in Figure 9, the auto-titrate module 750 is configured to maintain, increment, or decrement the level of therapy in accordance with method 700 illustrated by Figure 8A. In one embodiment, the auto-titrate module 750 includes one or more of the following functions and modules including: an on/off module 752; an intensity module 754; a duty cycle module 756; a reset module 758; a patient override function 459, and a sleep study parameter 797.

[0152] In one embodiment, the On/Off module 752 is configured to activate or deactivate stimulation to the target nerves/muscles of the upper airway (that restores airway patency). In one aspect, an "Off" state of module 752 corresponds to first state 202 or second state 204 of system 200 (see Figure 4A) in which the IPG 100 monitors the body motion or activity of the patient or is configured to detect apneas but a state in which no stimulation is applied. However, an "On" state of module 752 directly corresponds to third state 206 of system 200 in which a stimulation therapy is to be applied to the patient.

[0153] Moreover, when this On/Off module 752 is in an "On" state, stimulation to the target nerve may be applied continuously or synchronized (via stimulation module 104 of IPG 100 – Figure 3A) with respiration/inspiration in accordance with a continuous parameter 762 and a synchronous parameter 760, respectively. In another aspect, the intensity module 754 selects an amplitude (parameter 780), a rate (parameter 782),

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and/or a pulse width (parameter 784) of the stimulation signal to the target nerve to achieve a desired level of nerve recruitment. It is also understood that in some embodiments the intensity module 754 includes, or can operate in coordination with, a multisite parameter 194A, bilateral parameter 194B, and fascicle parameter 194C, as previously described in association with IPG 100 of Figure 3A. Moreover, intensity module 754 is configured to further modulate the stimulation intensity by applying a sub-threshold intensity that provides minor tone to the innervated muscle (as represented by tone parameter 786), a twitch intensity (represented by twitch parameter 788), and/or varying levels of nerve/muscle recruitment all the way up to full nerve/ muscle recruitment (as represented by full parameter 790).

[0154] In one embodiment, the auto-titrate module 750 is self-learning. In other words, by using a predetermined order of parameter adjustments to adjust the amplitude, rate, and/or pulse width of stimulation (i.e., stimulation parameter settings), a desired level of nerve recruitment is achieved. In some embodiments, this predetermined order is automatically used prior to obtaining data in response to a therapy on a given patient and may be based on statistical analysis of a population of patients. In use, the auto-titrate module 750 will monitor the available sensing and stimulation parameters, evaluate the response to therapy (using the predetermined order/level of settings) for a given patient, and then identify (and implement) the optimal settings for stimulation therapy. In another aspect, the auto-titrate module 750 iteratively repeats the process of applying the most recently determined optimal parameter settings, evaluates the therapy response, and adjusts the parameter settings. In this way, the auto-titrate module 750 self learns the best therapy setting as the therapy is applied over a period of time.

[0155] In one embodiment, as previously described, the auto-titrate module 750 includes a sleep study parameter 797 configured to direct that the IPG 100 (as part of system 200 and/or method 700) implanted within the patient learn therapy parameters for that particular patient in coordination with a polysomnograph or other sleep study system. In this arrangement, the sensing module 102 of IPG 100 (Figure 2) is active during the sleep study so

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that parameters sensed via IPG 100 are correlated with, and calibrated, relative to known sleep study parameters that are indicative of various apnea-related physiologic events, patterns, and behaviors. A few examples of such correlation was previously described in association with Figure 4E, Accordingly, via the sleep study the IPG 100 learns a patient's physiologic patterns surrounding an apnea event, which helps to establish a baseline or initial set of stimulation therapy settings for auto-titrate module 750 (as part of system 200 and method 700). After this baseline is established, the system 200 and/or method 700 operates in substantially the same manner previously described in association with at least Figures 1-8.

[0156] In some embodiments, the auto-titrate module 750 also includes a stimulation duty cycle module 756 that manages the duration of the stimulation time, including the amount of time the stimulation starts before inspiration onset or after inspiration onset, as the timing of this onset (as represented by onset parameter 794) is known to affect the aggressiveness and effectiveness of the therapy. For example, starting stimulation after the onset of inspiration may be ineffective due to the airway obstructing prior to stimulation (and once obstructed stimulation may not be capable of overcoming the obstruction.). However, starting stimulation well in advance of inspiration onset may be beneficial in preventing flow restriction or full obstruction by providing stimulation before the airway closes. Accordingly, one method of treatment includes triggering stimulation of the target nerve prior to inspiration onset. One patent describing the time period surrounding inspiration onset (in relation to triggering stimulation of a nerve to treat apnea) is Christopherson U.S. Patent 5,944,680, titled RESPIRATORY EFFORT DETECTION METHOD AND APPARATUSES, and which is hereby incorporated by reference in its entirety. In another aspect, an incomplete emptying of the lungs will reduce the volume of fresh air that can be inspired in the next breath. Accordingly, in some embodiments, the duty cycle module 756 includes a termination parameter 796 that controls the timing of stimulation turn-off (i.e., termination) before or after the end of inspiration.

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[0157] Referring again to Figure 9, in some embodiments of the present disclosure, auto-titrate module 750 includes a reset module 758. In general terms, the reset module 758 is configured to facilitate synchronizing stimulation of the upper airway with respiration. Signal processing of the respiration waveform can become challenging during cycles of apneas or hypopneas, primarily due to the widely varied morphologies of the respiratory signals. Yet, once stable synchronization of the stimulation with the respiratory waveform is achieved, apneas/hypopneas are readily prevented.

[0158] Accordingly, in light of the difficulty in performing such signal processing during the cycles of apneas/hypopneas, in this one embodiment, the reset module 758 applies (during the cycles of apneas/hypopneas) a substantially continuous or continuous burst of stimulation (or other predetermined time period) that effectively "resets" the patient to stable respiration. In some embodiments, this burst of stimulation can last about twenty seconds. In one embodiment, the substantially continuous burst of stimulation lasts a first time period greater than a duration of two nominal respiration cycles. During this reset, the system can better synchronize the stimulation with respiration because the patient is in a non-apneic period of respiration. This "reset" stimulation allows several unobstructed breaths to occur and allows the signal processing to track a stable respiratory signal. After the reset, each separate application of stimulation is limited to a duration corresponding to a portion (or fraction) of a single respiratory cycle (according to the methods of treatment and embodiments of the present disclosure previously described herein) to ensure that nerve/muscle fatigue does not occur. In one embodiment, the reset module 758 also tracks the respiratory pressure signal during the reset mode to observe the efficacy of the substantially continuous burst of stimulation.

[0159] In another embodiment, when consistent respiratory information cannot be obtained because of a noisy environment (or for other reasons), stimulation is completely suspended until suitable respiratory information is obtainable or stimulation is converted to an alternate stimulation having a fixed, intermittent duty cycle. In one non-limiting example, the alternate

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stimulation has a duty cycle of 2 seconds stimulation separated by 3 second periods of no stimulation.

[0160] In another embodiment, a bilateral function 791 of auto-titrate module 750 (such as auto-titrate module 170 of therapy manager 106 in Figure 3A) cooperates with the bilateral parameter 194B of stimulation module 104 (Figure 3A) to determine whether to alternately (via function 792) or simultaneously (via function 793) stimulate the left side and right side of the body. Moreover, when used in conjunction with the multi-site parameter 194A of stimulation module 104 (Figure 3A), the auto-titrate module 750 also determines whether to simultaneously or alternately stimulate different sites along one or more nerves, whether on the left side or the right side of the body.

[0161] While at least one exemplary embodiment has been presented in the foregoing detailed description, it should be appreciated that variations exist. It should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope, applicability, or configuration of the present disclosure in any way. Rather, the foregoing detailed description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the present disclosure as set forth in the appended claims and the legal equivalents thereof.

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1. A method of identifying a sleep disordered breathing event, comprising:

sensing a bio-impedance signal of a patient;

sensing a respiratory pressure signal of the patient; and

identifying a sleep disordered breathing event via identifying a substantial change in an amplitude of the sensed bio-impedance signal that occurs at substantially the same time as a substantial change in an amplitude of the sensed respiratory pressure signal.

2. The method of claim 1, wherein the sleep disordered breathing event is an obstructive sleep apnea event, and the substantial change in the amplitude of the sensed bio-impedance signal includes a substantial decrease in the amplitude of the sensed bio-impedance signal and wherein the substantial change in the amplitude of the sensed respiratory pressure signal includes a substantial increase in the amplitude of the sensed respiratory pressure signal.

3. The method of claim 1, wherein the sleep disordered breathing event is a central sleep apnea event, and the substantial change in the amplitude of the sensed bio-impedance signal includes a substantial decrease in the amplitude of the sensed bio-impedance signal and wherein the substantial change in the amplitude of the sensed respiratory pressure signal includes a substantial decrease in the amplitude of the sensed respiratory pressure signal.

4. The method of claim 1, wherein the sleep disordered breathing event is a hypopnea event, and the substantial change in the amplitude of the sensed bio-impedance signal includes a substantial decrease in the amplitude of the sensed bio-impedance signal and wherein the substantial change in the amplitude of the sensed respiratory pressure signal includes a substantial increase in the amplitude of the sensed respiratory pressure signal, wherein the respective substantial decrease and the respective substantial increase are of a lower magnitude change than in an obstructive sleep apnea.

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5. The method of claim 1, comprising:

implanting a first nerve electrode about a first respiratory-related nerve on a first side of the body and implanting a second nerve electrode about a second respiratory-related nerve on a second side of the body; and

performing sensing of the bio-impedance signal via sensing the bio-impedance signal between the first nerve electrode on the first side of the body and the second nerve electrode on the second side of the body.

6. The method of claim 1, comprising:

performing sensing of the bio-impedance signal as sensing a trans-thoracic bio-impedance signal.

7. The method of claim 3, comprising:

identifying the substantial change in the amplitude of the sensed bio-impedance signal relative to a baseline cyclic amplitude of the sensed bio-impedance signal during non-disordered breathing; and

identifying the substantial change in the amplitude of the sensed respiratory pressure signal relative to determining a baseline cyclic amplitude of the sensed respiratory pressure signal during non-disordered breathing.

8. The method of claim 7, comprising:

identifying the substantial change when a percentage change in the amplitude of the sensed bio-impedance signal, relative to the baseline cyclic amplitude of the sensed bio-impedance signal, has a greater magnitude than a threshold percentage change.

9. The method of claim 8, wherein the threshold percentage change is at least 50%.

10. The method of claim 8, comprising:

identifying the substantial change when a percentage change in the amplitude of the sensed respiratory pressure signal, relative to the baseline cyclic amplitude of the sensed respiratory pressure signal, has a greater magnitude than a threshold percentage change.

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11. The method of claim 10, comprising:

computing an average of the percentage change in the amplitude of the sensed respiratory pressure signal and of the percentage change in the amplitude of the sensed trans-thoracic bio-impedance signal; and

identifying the sleep disordered breathing event based on the average exceeding a threshold average percentage change.

12. The method of claim 1, comprising:

confirming the sleep disordered breathing event via detecting a decreasing heart rate that generally coincides with initiation of the sleep disordered breathing event and an increasing heart rate that generally coincides with termination of the sleep disordered breathing event and with a post-sleep disordered breathing period.

13. The method of claim 1, comprising:

confirming the sleep disordered breathing event via detecting a substantial decrease in a blood oxygen saturation of the patient that generally coincides with the sleep disordered breathing event and a post-sleep disordered breathing period.

14. The method of claim 1, comprising:

determining at least one of a duration or a severity of the sleep disordered breathing event based on at least one of:

detecting a decreasing heart rate that generally coincides with initiation of the sleep disordered breathing event and an increasing heart rate that generally coincides with termination of the sleep disordered breathing event and with a post-sleep disordered breathing period; and

detecting a substantial decrease in a blood oxygen saturation of the patient that generally coincides with the sleep disordered breathing event and a post-sleep disordered breathing period.

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15. The method of claim 1, comprising:

identifying a hyperventilation period following the sleep disordered breathing event via identifying a substantial increase in the amplitude of the sensed bio-impedance signal after the sleep disordered breathing event that occurs at substantially the same time as a substantial increase in an amplitude of the sensed respiratory pressure signal after the sleep disordered breathing event.

16. The method of claim 15, comprising:

identifying, based on a duration of the hyperventilation period, a severity of the sleep disordered breathing event preceding the hyperventilation period.

17. A system for identifying a sleep disordered breathing event in a patient, comprising:

a bio-impedance sensor configured to detect a bio-impedance signal in the patient;

a respiratory pressure sensor configured to detect a respiratory pressure signal in the patient; and

a monitor configured to detect a sleep disordered breathing event via identifying a substantial change in an amplitude of the sensed bio-impedance signal that occurs at substantially the same time as a substantial change in an amplitude of the sensed respiratory pressure signal.

18. The system of claim 17, wherein the sleep disordered breathing event comprises at least one of an obstructive sleep apnea event, a hypopnea event, or a central sleep apnea event.

19. The system of claim 17, wherein the bio-impedance sensor, the respiratory pressure sensor, and the signal monitor are all implantable in the patient.

20. The system of claim 17, wherein the bio-impedance sensor comprises a combination of:

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a first nerve electrode configured to be coupled to a first airway patency-related nerve on a first side of the body; and

a second nerve electrode configured to be coupled to a second airway patency-related nerve on a second side of the body opposite the first side,

wherein the monitor and the sensor are configured, in cooperation with each other, to measure the bio-impedance between the first nerve electrode and the second nerve electrode.

21. The system of claim 17, wherein the bio-impedance sensor comprises an implantable trans-thoracic bio-impedance sensor.

22. The system of claim 21, wherein the trans-thoracic bio-impedance sensor includes an array of impedance sensors configured to be arranged in a spaced apart configuration on a thorax region of a patient.

23. The system of claim 17, wherein the monitor includes:

a bio-impedance parameter configured to identify the substantial change in the amplitude of the sensed bio-impedance signal relative to a baseline cyclic amplitude of the sensed bio-impedance signal during non-disordered breathing; and

a respiratory pressure parameter configured to identify the substantial change in the amplitude of the sensed respiratory pressure signal relative to determining a baseline cyclic amplitude of the sensed respiratory pressure signal during non-disordered breathing.

24. The system of claim 23, wherein the bio-impedance parameter of the monitor is configured to identify the substantial change when a percentage change in the amplitude of the sensed bio-impedance signal, relative to the baseline cyclic amplitude of the sensed bio-impedance signal, has a greater magnitude than a threshold percentage change.

25. The system of claim 24, wherein the threshold percentage change is at least 50%.

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26. The system of claim 24, wherein the respiratory pressure parameter is configured to identify the substantial change when a percentage change in the amplitude of the sensed respiratory pressure signal, relative to the baseline cyclic amplitude of the sensed respiratory pressure signal, has a greater magnitude than a threshold percentage change.

27. The system of claim 26, wherein the monitor is configured, via the bio-impedance parameter and the respiratory pressure parameter, to:

compute an average of the percentage change in the amplitude of the sensed respiratory pressure signal and of the percentage change in the amplitude of the sensed trans-thoracic bio-impedance signal; and

identify the sleep disordered breathing event based on the average exceeding a threshold average percentage change, wherein the threshold average percentage change is based on at least one of a minimum quantity of breaths, a minimum preset quantity of respiratory cycles, or a predetermined period of time including multiple respiratory cycles.

28. The system of claim 27, comprising:

a heart rate sensor; and

a heart rate parameter of the monitor that is configured to confirm the sleep disordered breathing event by detecting, via the heart rate sensor, a decreasing heart rate that generally coincides with initiation of the sleep disordered breathing event and an increasing heart rate that generally coincides with termination of the apnea event and with a post-disordered breathing period.

29. The system of claim 27, comprising:

a blood oxygen saturation sensor; and

a blood oxygen saturation parameter of the monitor that is configured to confirm the sleep disordered breathing event by detecting, via a blood oxygen saturation sensor, a substantial decrease in a blood oxygen saturation of the patient that generally coincides with the sleep disordered breathing event and a post-disordered breathing period.

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30. The system of claim 17, wherein the monitor includes a hyperventilation module configured to identify a hyperventilation period following the sleep disordered breathing event via identifying a substantial change in the amplitude of the sensed bio-impedance signal after the sleep disordered breathing event.

31. The system of claim 30, wherein the hyperventilation module is configured to identify the hyperventilation period via a substantial change in an amplitude of the sensed respiratory pressure signal after the sleep disordered breathing event that occurs substantially simultaneously with the substantial change in the amplitude of the sensed bio-impedance signal after the sleep disordered breathing event.

32. The system of claim 30, wherein the hyperventilation module is configured to identify, a severity of the sleep disordered breathing event preceding the hyperventilation period based on at least one of a duration of the hyperventilation period, a duration of the sleep disordered breathing event, or a lowest blood oxygen saturation following the sleep disordered breathing event.

33. A method for automatically adjusting a therapy to treat sleep disordered breathing, comprising:

automatically tracking a severity of sleep disordered breathing behavior relative to a baseline severity of sleep disordered breathing behavior;

applying, at a first intensity level, a nerve stimulation signal to a nerve innervating an airway patency-related muscle;

evaluating the tracked severity of sleep disordered breathing behavior relative to a threshold in response to the applying the nerve stimulation signal at the first intensity level; and

automatically adjusting the nerve stimulation signal from the first intensity level to a second intensity level in response to the evaluated, tracked severity of the sleep disordered breathing behavior.

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34. The method of claim 33, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

35. The method of claim 33, wherein the first intensity level or second intensity level is based on a frequency, an amplitude, a pulse width, or a polarity of the nerve stimulation signal.

36. The method of claim 33, wherein the first intensity level or the second intensity level is based on applying the nerve stimulation signal bilaterally to both sides of the body or unilaterally to one side of the body.

37. The method of claim 33, wherein applying the nerve stimulation signal includes alternating application of the nerve stimulation signal between two different sides of the body.

38. The method of claim 33, wherein automatically modifying the nerve stimulation level comprises at least one of:

upon the tracked severity exceeding the threshold, automatically incrementing an intensity of the nerve stimulation signal so that the second intensity level is higher than the first intensity level; or

upon the tracked severity being less than the threshold, automatically decrementing the intensity of the nerve stimulation signal so that the second intensity level is lower than the first intensity level.

39. The method of claim 38, comprising:

performing the automatically incrementing at increments that are substantially greater in magnitude than decrements by which the automatically decrementing is performed.

40. The method of claim 39, wherein the increments in intensity level are 50 percent larger than the decrements in intensity level.

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41. The method of claim 39, wherein the increments in intensity level are 100 percent larger than the decrements in intensity level.

42. The method of claim 33, comprising:

determining the severity of the sleep disordered breathing behavior based on at least one of a quantity of sleep disordered breathing events within a time period, a duration of the respective sleep disordered breathing events, and an intensity of the respective sleep disordered breathing events.

43. The method of claim 42, comprising:

determining the respective intensity of the sleep disordered breathing events based on at least one of:

a change in heart rate during the sleep disordered breathing event;

a change in heart rate after the sleep disordered breathing event;

a change in blood oxygen saturation during or after the sleep disordered breathing event;

an amplitude of hyperventilation following the sleep disordered breathing event; or

a duration of a hyperventilation following the sleep disordered breathing event

44. A system for automatically adjusting a therapy to treat sleep disordered breathing, comprising:

a sensing module configured to sense physiologic conditions indicative of sleep disordered breathing behavior;

an implantable pulse generator configured to apply, at a first intensity level, a nerve stimulation signal to a first nerve innervating an airway patency-related muscle, the implantable pulse generator including a therapy manager including:

an untreated sleep disordered breathing monitor configured, via the sensed physiologic conditions, to automatically track a severity of sleep disordered breathing behavior relative to a baseline severity of sleep disordered breathing behavior;

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a therapy evaluation monitor configured, in response to the applying the nerve stimulation signal at the first intensity level, to evaluate the severity of sleep disordered breathing behavior relative to a threshold; and

an automatic adjustment module configured, in response to the evaluated, tracked severity of sleep disordered breathing behavior performed by the therapy evaluation monitor, to modify the nerve stimulation signal from the first intensity level to a second intensity level.

45. The system of claim 44, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

46. The system of claim 44, wherein the therapy manager is configured to determine the first intensity level or the second intensity level based on at least one of a frequency, an amplitude, a pulse width, and a polarity of the nerve stimulation signal.

47. The system of claim 46, comprising:

a first nerve electrode adapted to apply the nerve stimulation signal to the first nerve on a first side of the body;

a second nerve electrode adapted to apply the nerve stimulation signal to a second nerve on a second side of the body opposite the first side of the body.

wherein the therapy manager is configured to determine the first intensity level or the second intensity level of the nerve stimulation signal based on applying the nerve stimulation signal bilaterally to both the first and second nerve electrodes.

48. The system of claim 46, comprising:

a first nerve electrode adapted to apply the nerve stimulation signal to the first nerve on a first side of the body;

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a second nerve electrode adapted to apply the nerve stimulation signal to a second nerve on a second side of the body opposite the first side of the body.

wherein the therapy manager is configured to determine the first intensity level or the second intensity level of the nerve stimulation signal based on applying the nerve stimulation signal in an alternating manner between the first nerve electrode and the second nerve electrode.

49. The system of claim 44, wherein the auto adjustment module of the therapy manager comprises at least one of:

an automatic increment function configured, upon the tracked severity score exceeding the threshold, automatically incrementing an intensity of the nerve stimulation signal so that the second intensity level is higher than the first intensity level; or

an automatic decrement function configured, upon the tracked severity score being less than the threshold, automatically decrementing the intensity of the nerve stimulation signal so that the second intensity level is lower than the first intensity level.

50. The system of claim 49, wherein the automatic increment function of the auto adjustment module is configured to perform the automatic incrementing at increments that are substantially greater in magnitude than decrements by which the automatically decrementing is performed by the automatic decrement function.

51. The system of claim 50, wherein the increments in intensity level are 50 percent larger than the decrements in intensity level.

52. The system of claim 50, wherein the increments in intensity level are 100 percent larger than the decrements in intensity level.

53. The system of claim 44, wherein the sleep disordered breathing monitor and the therapy evaluation monitor are configured to determine the severity of the sleep disordered breathing behavior based on at least one of a

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quantity of sleep disordered breathing events within a time period, a duration of the respective sleep disordered breathing events, and an intensity of the respective sleep disordered breathing events.

54. The system of claim 53, wherein the sleep disordered breathing monitor and the therapy evaluation monitor are configured to determine the intensity of the respective sleep disordered breathing events based on at least one of:

a change in heart rate during the sleep disordered breathing event;

a change in heart rate after the sleep disordered breathing event;

a change in blood oxygen saturation during or after the sleep disordered breathing event;

an amplitude of hyperventilation following the sleep disordered breathing event; or

a duration of a hyperventilation following the sleep disordered breathing event.

55. A method of applying a therapy to treat sleep disordered breathing, comprising:

detecting sleep-indicative behavior via monitoring, in a first mode of operation of an implantable pulse generator system, physiologic conditions of the patient;

entering a second mode of operation of the implantable pulse generator system, including monitoring physiologic conditions of the patient to detect sleep disordered breathing behavior, when the detected sleep-indicative behavior meets a first criteria; and

upon detecting sleep disordered breathing behavior above a threshold in the second mode of operation, converting operation into a third mode of operation of the implantable pulse generator system including applying a nerve stimulation signal, synchronous with inspiration, to an airway patency-related nerve.

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56. The system of claim 55, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

57. The method of claim 55, wherein detecting sleep-indicative behavior via monitoring physiologic conditions comprises monitoring at least one of a body activity, a posture, a heart rate, or a time of day.

58. The method of claim 55, wherein entering the second mode of operation includes maintaining the first mode of operation substantially simultaneously with the second mode of operation.

59. The method of claim 58, wherein entering the third mode of operation includes maintaining the respective first and second modes of operation substantially simultaneously with the third mode of operation.

60. The method of claim 58, wherein entering the third mode of operation includes maintaining the first mode of operation substantially simultaneously with the third mode of operation while suspending the second mode of operation.

61. The method of claim 58, comprising:

upon detecting sleep-indicative behavior that fails to meet the first criteria, terminating the respective second and third mode of operation while maintaining the first mode of operation.

62. The method of claim 55, comprising:

entering the second mode of operation upon detecting that the sleep-indicative behavior meets the first criteria.

63. The method of claim 55, comprising:

performing sampling of physiologic conditions in the second mode at intervals according to an inverse relationship between an amount of body activity of the sleep-indicative behavior and the frequency of sampling, such

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that upon sensing a higher degree of body activity, performing a lower frequency of sampling physiologic conditions and upon sensing a lower degree of body activity of the sleep-indicative behavior, performing to a higher frequency of sampling physiologic conditions.

64. The method of claim 55, comprising:

suspending the first mode of operation during a repeating nocturnal time period; and

entering the second mode of operation during the repeating nocturnal time period and exiting the second mode of operation upon expiration of the repeating nocturnal time period.

65. The method of claim 55, comprising:

automatically suspending the first mode of operation during a first daily time period to prevent initiation into the respective second and third modes of operation; and

automatically implementing the second mode of operation, and authorizing potential implementation of the third mode of operation, during a second time period not coinciding with the first daily time period.

66. The method of claim 65, wherein the first daily time period is a standard wakefulness time frame and the second daily time period is a standard sleeping time frame.

67. The method of claim 55, comprising:

activating in response to a user request, substantially at initiation of a sleeping period, the implantable pulse generator system to operate in at least one of the respective first mode, second mode, and third mode of operation; and

deactivating in response to a user request, substantially at termination of the sleeping period, the implantable pulse generator system to terminate operation in the respective first mode, second mode, and third mode of operation.

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68. The method of claim 55, comprising:

upon detecting the sleep disordered breathing behavior falling below the first threshold, suspending the third mode of operation and maintaining the respective first and second modes of operation.

69. The method of claim 55, comprising:

upon detecting a sleep state in the first mode of operation, bypassing the second mode of operation and immediately implementing the third mode of operation.

70. The method of claim 55, comprising:

periodically suspending the third mode of operation while maintaining the respective first and second modes of operation during the periodic suspensions;

detecting whether the monitored sleep disordered breathing behavior is above the second threshold, and implementing at least one of:

maintaining suspension of the third mode of operation if the monitored sleep disordered breathing behavior is below the first threshold; or

resuming the third mode of operation if the monitored sleep disordered breathing behavior exceeds the second threshold.

71. The method of claim 70, wherein periodically suspending the third mode of operation comprises suspending the third mode of operation at a frequency and for a predetermined suspension time period.

72. The method of claim 71, wherein the frequency of suspending includes at least one of five, ten, or fifteen minutes, and the repeating suspension time period includes at least one of thirty seconds, one minute, two minutes, three minutes, four minutes, or five minutes.

73. The method of claim 71, wherein the frequency of suspending is inversely proportional to the severity score of the sleep disordered breathing behavior.

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74. The method of claim 70, wherein periodically suspending the third mode of operation comprises automatically foregoing suspension of the third mode of operation during a first time period of a daily sleep period.

75. The method of claim 70, wherein periodically suspending the third mode of operation comprises automatically foregoing suspension of the third mode of operation for a daily sleep period upon detecting that the monitored sleep disordered breathing behavior is substantially greater than the second threshold.

76. The method of claim 55, comprising:

upon detecting in the first mode of operation, a change in substantial change in posture between a supine position, a substantially vertical position, and a lateral decubitis position, suspending the third mode of operation in order to monitor for sleep disordered breathing behavior.

77. The method of claim 76, comprising:

upon the change in posture being a change from a supine to lateral decubitis, suspending the third mode of operation while maintaining the second mode of operation to identify whether sleep disordered breathing behavior is occurring above the second threshold.

78. The method of claim 55, comprising:

upon the patient being in a supine position, providing a first program of therapy via the stimulation signal in the third mode of operation; and

upon the patient being in a lateral decubitis position, providing a second program of therapy via the stimulation signal in the third mode of operation, wherein the second program of therapy is less aggressive than the first program of therapy.

79. The method of claim 55, comprising:

implementing the first mode of operation using a first quantity of power;

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implementing the second mode of operation using a second quantity of power greater than the first quantity of power;

implementing the third mode of operation using a third quantity of power that is substantially greater than either the first quantity of power or the second quantity of power.

80. The method of claim 79, comprising:

automatically moving from the third quantity of power to the respective first or second quantities of power, upon detecting that operation in the treatment mode is not needed.

81. The method of claim 79, comprising:

when operating in the first mode and detecting bodily activity/motion above the first threshold, preventing operation in the second mode with the second quantity of power or the third mode with the third quantity of power.

82. The method of claim 55, wherein detecting sleep disordered breathing behavior above the second threshold via monitoring the physiologic conditions in the second mode of operation comprises:

identifying that the sleep disordered breathing behavior exceeds the second threshold upon detecting a substantial decrease in an amplitude of a trans-thoracic bio-impedance signal that substantially coincides with a substantial decrease in an amplitude of a respiratory pressure signal.

83. The method of claim 82, comprising:

identifying that the sleep disordered breathing behavior exceeds the second threshold via additional parameters including at least one of:

an increased heart rate substantially coinciding with at least part of the sleep disordered breathing behavior;

a decrease in blood oxygen saturation that substantially coincides with the at least part of the sleep disordered breathing behavior; or

occurrence of hyperventilation initiated at least during part of the sleep disordered breathing behavior.

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84. The method of claim 55, comprising:

applying, substantially synchronous with inspiration, the nerve stimulation signal to a first airway patency-related nerve via a first nerve electrode on a first side of the body simultaneously with applying, substantially synchronous with inspiration, the nerve stimulation signal to a second airway patency-related nerve via a second nerve electrode on a second side of the body.

85. The method of claim 84, wherein at least one of the first airway patency-related nerve and the second airway patency-related nerve is a hypoglossal nerve.

86. The method of claim 55, comprising:

applying, on a first respiration cycle, the nerve stimulation signal to an airway patency-related nerve via a first nerve electrode on a first side of the body;

applying, on a second respiration cycle following the first respiration cycle, the nerve stimulation signal to an airway patency-related nerve via a second nerve electrode on a second side of the body; and

iteratively repeating application of the nerve stimulation signal through successive respiration cycles in an alternating manner between the first side of the body and the second side of the body.

87. The method of claim 55, comprising:

overriding, via the patient programmer, the automatically-determined intensity level of nerve stimulation signal.

88. The method of claim 87, wherein overriding the intensity level comprises at least one of:

requesting, via the patient programmer, an increase in the intensity level of the nerve stimulation signal via the patient programmer; or

requesting, via the patient programmer, a decrease in the automatically determined intensity level of the nerve stimulation signal.

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89. The method of claim 88, wherein the requesting a decrease comprises:

setting, via the patient programmer, an upper limit on the intensity level of the nerve stimulation signal.

90. The method of claim 88, wherein requesting the decrease or requesting the increase comprises:

constraining the respective patient-requested increase by a maximum intensity level set by a physician; and

constraining the respective patient-requested decrease by a minimum intensity level set by the physician.

91. The method of claim 55, comprising:

communicating to at least one of a physician or a patient, via a patient programmer, a history of at least one of:

a quantity of nerve stimulation over a time period;

a duration of operation in each of the three different first, second, and third modes;

a volume of sleep disordered breathing behavior;

a severity of sleep disordered breathing behavior; or

a sleep-and-activity pattern.

92. A system of applying a treatment therapy for sleep disordered breathing, comprising:

a sensing module including an array of sensors configured to sense physiologic conditions, the array including at least one of a body activity sensor, a body posture sensor, and a respiration sensor;

an implantable pulse generator in communication with the sensing module and including an automatic therapy manager configured to operate in:

a first state to detect sleep indicative behavior by sensing physiologic conditions via at least the respective body activity sensor and body posture sensor;

a second state to monitor the sensed physiologic conditions to detect sleep disordered breathing behavior, wherein the therapy

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manager transitions into the second state when the detected sleep-indicative behavior meets a first criteria; and

a third state to apply a nerve stimulation signal, synchronous with inspiration, to an airway patency-related nerve, wherein the therapy manager transitions into the third state upon detecting, in the second state, sleep disordered breathing behavior exceeding a second criteria.

93. The system of claim 92, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

94. The system of claim 92, wherein the automatic therapy manager includes a progressive function configured to cause, upon entry into the second state of operation, maintaining the first mode of operation substantially simultaneously with the second mode of operation.

95. The system of claim 94, wherein the progressive function of the automatic therapy manager is configured to cause, upon entry into the third state of operation, maintaining the respective first and second states of operation substantially simultaneously with the third state of operation.

96. The system of claim 92, wherein the automatic therapy manager includes a power management function configured to cause, upon entry into the third state of operation, maintaining the first mode of operation substantially simultaneously with the third state of operation while suspending the second state of operation.

97. The system of claim 92, wherein the automatic therapy manager includes a reversion function configured to cause, upon the detected sleep-indicative behavior failing to meet the first criteria, termination of the respective second and third states of operation while maintaining the first state of operation.

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98. The system of claim 92, the automatic therapy manager is configured to cause automatic entry into the second state of operation upon the detected sleep-indicative behavior meeting the first criteria.

99. The system of claim 92, wherein the detected sleep-indicative behavior includes a body posture measured via the body position sensor and a body activity measured via the body activity sensor.

100. The system of claim 99, wherein a substantially vertical body posture measured via the body position sensor fails to meet the first criteria and a body activity exceeding ten seconds measured via the body activity sensor fails to meet the first criteria.

101. The system of claim 92, the automatic therapy manger includes a probabilistic sampling function configured, in cooperation with the sensing module, to perform sampling of physiologic conditions in the second state at intervals according to an inverse relationship between the amount of patient body activity and the frequency of sampling, such that upon sensing a higher degree of patient body activity, performing a lower frequency of sampling physiologic conditions and upon sensing a lower degree of patient body activity, performing a higher frequency of sampling physiologic conditions.

102. The system of claim 92, wherein the automatic therapy manager includes an automatic nocturnal therapy function configured to:

suspend the first state of operation during a repeating nocturnal time period; and

initiate entry into the second state of operation during the repeating nocturnal time period and cause exit out of the second state of operation upon expiration of the repeating nocturnal time period.

103. The system of claim 92, wherein the automatic therapy manager includes:

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an awake schedule parameter configured to automatically suspend the first state of operation during a first daily time period to prevent initiation into the respective second and third state of operation; and

a sleep schedule parameter configured to automatically implement the second state of operation, and authorizing potential implementation of the third state of operation, during a second time period not coinciding with the first daily time period.

104. The system of claim 103, wherein the first daily time period is a standard wakefulness time frame and the second daily time period is a standard sleeping time frame.

105. The system of claim 92, wherein the automatic therapy manager includes a suspension function configured, upon detecting the sleep disordered breathing behavior falling below the second threshold, to suspend the third state of operation and maintaining the respective first and second state of operation.

106. The system of claim 92, wherein the automatic therapy manager includes a bypass function configured, upon detecting a sleep state in the first state of operation, to bypass the second state of operation and immediately implement the third state of operation.

107. The system of claim 92, wherein the automatic therapy manager includes a periodic suspension function configured to:

periodically suspend the third state of operation while maintaining the respective first and second state of operation during the periodic suspensions;

detect whether the monitored sleep disordered breathing behavior exceeds the second criteria; and

implement at least one of maintaining suspension of the third state of operation if the monitored sleep disordered breathing behavior fails to meet the second criteria or resuming the third state of operation if the monitored sleep disordered breathing behavior meets or exceeds the second criteria.

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108. The system of claim 107, wherein the periodic suspension function is configured to periodically suspend the third state of operation at a frequency and for a predetermined suspension time period.

109. The system of claim 108, wherein the frequency of suspending includes at least one of five, ten, or fifteen minutes, and the predetermined suspension time period includes at least one of thirty seconds, one minute, two minutes, three minutes, four minutes, or five minutes.

110. The system of claim 108, wherein the frequency of suspending is inversely proportional to the severity score of the sleep disordered breathing behavior.

111. The system of claim 108, wherein the periodic suspension function is configured to automatically forego suspension of the third state of operation during an initial sleep stage of a daily sleep period.

112. The system of claim 108, wherein the periodic suspension function is configured to automatically forego suspension of the third state of operation for a daily sleep period upon detecting that the monitored sleep disordered breathing behavior is substantially exceeds the second criteria.

113. The system of claim 92, wherein the automatic therapy manager includes a posture change function configured, during the first and third states of operation, to:

detect a substantial change in posture between a supine position, a substantially vertical position, and a lateral decubitis position; and

suspend, upon the detected substantial change, the third mode of operation in order to monitor for sleep disordered breathing behavior.

114. The system of claim 113, wherein the posture change function is configured, upon the change in posture being a change from a supine to lateral decubitis, to suspend the third state of operation while maintaining the

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second state of operation to identify whether sleep disordered breathing behavior exceeds the second criteria.

115. The system of claim 92, wherein the automatic therapy manager includes a posture change function configured to provide, upon the patient being in a supine position, a first therapeutic regimen via the stimulation signal in the third state of operation and to provide, upon the patient being in a lateral decubitis position, a second therapeutic regimen via the stimulation signal in the third state of operation, wherein the second therapeutic regimen is substantially less aggressive than the first therapeutic regimen.

116. The system of claim 92, wherein the automatic therapy manager includes a posture change function configured to provide, upon the patient being in one of a left lateral decubitis position or a right lateral decubitis position, a first therapeutic regimen via the stimulation signal in the third state of operation and to provide, upon the patient being in the other one of the respective left and right lateral decubitis positions, a second therapeutic regimen via the stimulation signal in the third state of operation, wherein the second therapeutic regimen is substantially less aggressive than the first therapeutic regimen.

117. The system of claim 92, wherein the automatic therapy manager includes a power management function configured to:

implement the first state of operation using a first quantity of power;

implement the second state of operation using a second quantity of power greater than the first quantity of power;

implement the third state of operation using a third quantity of power that is substantially greater than either the first quantity of power or the second quantity of power.

118. The system of claim 117, wherein the power management function is configured, when operation occurs in the first state and patient body activity is above the first threshold, to prevent operation in the second state with the

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second quantity of power or prevent operation in the third mode with the third quantity of power.

119. The system of claim 92, wherein the automatic therapy manager, when operating in the second state, detects sleep disordered breathing behavior via identifying that the sleep disordered breathing behavior exceeds the second criteria upon detecting a substantial change in an amplitude of a trans-thoracic bio-impedance signal that substantially coincides with a substantial change in an amplitude of a respiratory pressure signal.

120. The system of claim 119, wherein the substantial change in the amplitude of the respiratory pressure signal includes at least one of a substantial increase or a substantial decrease.

121. The system of claim 119, wherein the automatic therapy manager is configured to identify that the sleep disordered breathing behavior exceeds the second threshold via additional parameters including at least one of:

a heart rate parameter configured to identify an increased heart rate substantially coinciding with at least part of the sleep disordered breathing behavior;

a blood oxygen parameter configured to identify a decrease in blood oxygen saturation that substantially coincides with the at least part of the sleep disordered breathing behavior; or

a hyperventilation parameter configured to identify an occurrence of hyperventilation initiated at least during part of the sleep disordered breathing behavior; or

an arousal parameter configured to identify, via at least one of the body activity sensor and the body posture sensor, an awakening arousal substantially coinciding with at least part of the sleep disordered breathing behavior.

122. The system of claim 92, wherein the automatic therapy manager comprises a bilateral stimulation parameter configured to cause application, substantially synchronous with inspiration, of the nerve stimulation signal to a

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first airway patency-related nerve via a first nerve electrode on a first side of the body simultaneously with applying, substantially synchronous with inspiration, the nerve stimulation signal to a second airway patency-related nerve via a second nerve electrode on a second side of the body.

123. The system of claim 92, wherein the automatic therapy manager comprises a bilateral stimulation parameter configured to:

apply, on a first respiration cycle, the nerve stimulation signal to an airway patency-related nerve via a first nerve electrode on a first side of the body;

apply, on a second respiration cycle following the first respiration cycle, the nerve stimulation signal to an airway patency-related nerve via a second nerve electrode on a second side of the body; and

iteratively repeat application of the nerve stimulation signal through successive respiration cycles in an alternating manner between the first side of the body and the second side of the body.

124. The system of claim 92, wherein the automatic therapy manager comprises an override function configured to override, via a patient programmer, an automatically-determined intensity level of the nerve stimulation signal.

125. The system of claim 124, wherein the override function includes:

an increase request function configured to request, via the patient programmer, an increase in the automatically determined intensity level of the nerve stimulation signal via the patient programmer; or

a decrease request function configured to request, via the patient programmer, a decrease in the automatically determined intensity level of the nerve stimulation signal.

126. The system of claim 125, wherein the decrease request function is configured to set, via the patient programmer, an upper limit on the intensity level of the nerve stimulation signal.

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127. The system of claim 126, wherein the increase request function is configured to constrain the respective patient-requested increase by a maximum intensity level set by a physician, and wherein the decrease request function is configured to constrain the respective patient-requested decrease by a minimum intensity level set by the physician.

128. The system of claim 92, comprising:

communicating to at least one of a patient and a physician, via a patient programmer, a history of at least one of:

a quantity of nerve stimulation over a time period;

a duration of operation in each of the three different first, second, and third modes;

a volume of sleep disordered breathing behavior;

an intensity of sleep disordered breathing behavior; or

a sleep-and-activity pattern.

129. A method of sleep disordered breathing therapy comprising:

operating, substantially simultaneously with a polysomnography study, an implantable pulse generating system in a monitoring mode of operation;

tracking, during the polysomnography study, a first set of physiologic parameters via the implantable pulse generating system in the monitoring mode;

tracking, independent of the implantable pulse generator, a second set of sleep study parameters via the polysomnography study;

identifying a pattern of sleep disordered breathing behavior from the tracked second set of sleep study parameters and identifying which respective parameters of the second set of sleep study parameters are indicative of sleep disordered breathing behavior; and

calibrating the implantable pulse generating system to recognize sleep disordered breathing behavior via correlating the tracked respective physiologic parameters of the first set of physiologic parameters relative to the tracked respective sleep study parameters that are indicative of sleep disordered breathing behavior.

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130. The method of claim 129, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

131. The method of claim 129, comprising:

recognizing sleep disordered breathing behavior in the monitoring mode of the calibrated implantable pulse generating system; and

applying, via a therapy mode of the calibrated implantable pulse generating system, a therapeutic nerve stimulation signal to prevent sleep disordered breathing behavior.

132. The method of claim 129, wherein the identified pattern of sleep disordered breathing behavior is based on at least one of:

a time-of-day pattern of sleep disordered breathing behavior;

a night-of-week pattern of sleep disordered breathing behavior;

a sleep stage pattern of sleep disordered breathing behavior; and

a body posture pattern of sleep disordered breathing behavior.

133. The method of claim 129, comprising:

performing the calibration for a plurality of implantable pulse generating systems with each implantable pulse generating system associated with a different patient of a plurality of patients; and

developing, via the plurality of calibrated pulse generating systems, a predictive index of whether the implantable pulse generating system will provide efficacious patient therapy based on a correlation of the respective sleep study parameters relative to the tracked sleep disordered breathing behavior and the respective physiologic parameters.

134. The method of claim 129, comprising:

performing the polysomnography study in a sleep lab;

after calibrating the implantable pulse generating system, further calibrating the implantable pulse generating system via performing an in-home sleep study via sensing of the physiologic parameters, as surrogates for the sleep study parameters, with the implantable pulse generating system;

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programming an initial therapeutic regimen of nerve stimulation based on the further calibrated implantable pulse generating system; and

performing an automatically adjustable therapy based on the initial therapeutic regimen.

135. The method of claim 129, comprising:

defining the tracked respective sleep study parameters to include at least an externally measured blood oxygen saturation parameter;

defining the tracked respective physiologic parameters to include at least an internally measured blood oxygen saturation parameter;

using recognized periods of sleep disordered breathing behavior, correlating the tracked internally measured blood oxygen saturation parameter of the implantable pulse generator relative to the tracked externally measured blood oxygen saturation parameter of the polysomnography;

recognizing sleep disordered breathing behavior using the internally measured blood oxygen saturation parameter as a surrogate for externally measured blood oxygen saturation parameter.

136. The method of claim 129, comprising:

defining the tracked respective sleep study parameters to include at least a mouth-nostril-airflow respiratory parameter;

defining the tracked respective physiologic parameters to include at least an internally measured respiratory parameter;

using recognized periods of sleep disordered breathing behavior, correlating the tracked internally measured respiratory parameter of the implantable pulse generator relative to the tracked mouth-nostril-airflow respiratory parameter;

recognizing sleep disordered breathing behavior using the internally measured respiratory parameter as a surrogate for the mouth-nostril-airflow parameter.

137. The method of claim 136, comprising:

providing the internally measured respiratory parameter as an internally measured respiratory pressure signal.

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138. The method of claim 137 comprising:

measuring the internally measured respiratory pressure signal via coupling the respiratory pressure sensor to a pleural space.

139. The method of claim 136, comprising:

providing the internally measured respiratory parameter as a trans-thoracic bio-impedance parameter.

140. The method of claim 136, comprising:

providing the internally measured respiratory parameter via a combination parameter of a trans-thoracic bio-impedance parameter and internally measured respiratory pressure parameter.

141. The method of claim 140, comprising:

identifying patterns of mouth-nostril-airflow indicative of sleep disordered breathing behavior;

identifying a pattern of the combination respiration parameter indicative of sleep disordered breathing behavior;

calibrating the indicative pattern of the combination parameter relative to the indicative pattern of the mouth-nostril-airflow parameter;

using the calibrated combination parameter to detect sleep disordered breathing behavior in the monitoring mode of the implantable pulse generating system.

142. The method of claim 141, wherein the indicative pattern of the combination parameter includes a pattern of a substantial change in an amplitude of an internally measured respiratory pressure that substantially coincides with a substantial change in an amplitude of a trans-thoracic bio-impedance parameter.

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01299

143. The method of claim 129, comprising:

identifying, via the implantable pulse generator system, a pattern of an internally sensed body posture parameter indicative of sleep disordered breathing behavior;

identifying, via the polysomnography study, an externally observed pattern of body posture indicative of sleep disordered breathing behavior;

calibrating the indicative pattern of the internally sensed body posture parameter relative to the indicative pattern of the externally observed pattern of body posture;

using the calibrated internally sensed body posture parameter to detect sleep disordered breathing behavior in the monitoring mode of the implantable pulse generating system.

144. An implantable device for treating sleep disordered breathing behavior, the device comprising:

a conditions monitor configured to internally sense physiologic conditions and automatically track a severity of sleep disordered breathing behavior relative to a baseline severity of sleep disordered breathing behaviors;

at least one stimulation electrode configured to be coupled to an airway patency-related nerve; and

an implantable pulse generator coupled to the conditions monitor and coupled to the at least one stimulation electrode to apply a nerve stimulation signal to the airway patency-related nerve, wherein the implantable pulse generator includes:

an automatic therapy module configured to automatically identify sleep disordered breathing behavior, based on the sensed physiologic conditions, and to automatically apply the nerve stimulation signal to the airway patency-related nerve.

145. The device of claim 144, wherein the sleep disordered breathing behavior comprises at least one of an obstructive sleep apnea behavior, a hypopnea behavior, or a central sleep apnea behavior.

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01300

146. The device of claim 144, wherein the device is fully implantable.

147. The device of claim 144, wherein the automatic therapy module is configured to automatically select, based on the sensed physiologic conditions, a first intensity level of the applied nerve stimulation signal, and wherein the conditions monitor is configured to track the severity of the sleep disordered breathing behavior in response to the first intensity level of the applied nerve stimulation signal.

148. The device of claim 147, wherein the automatic therapy module is configured to automatically adjust, based on the tracked severity of the sleep disordered breathing behavior, the nerve stimulation signal from the first intensity level to a second intensity level.

149. The device of claim 144, comprising:

a respiration reset module configured to apply a substantially continuous burst of stimulation to the airway patency-related nerve for a predetermined time period longer than two nominal respiration cycles.

150. The device of claim 149, wherein the predetermined time period is 20 seconds.

151. A method of therapy to treat sleep disordered breathing, comprising:

applying substantially continuous stimulation, via an implantable pulse generator, to an airway patency-related nerve for a first time period longer than a duration of two nominal respiration cycles;

monitoring, via a respiration sensor, a respiration waveform during the substantially continuous stimulation; and

after the first period, applying stimulation synchronous with inspiration based on the monitored respiration waveform and for a second time period less than a duration of a single respiration cycle.

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01301

152. The method of claim 151, comprising:

implementing the applying substantially continuous stimulation in a presence of a sleep disordered breathing behavior.

153. The method of claim 151, comprising:

omitting the applying substantially continuous stimulation in an absence of a sleep disordered breathing behavior.

154. A computer readable medium storing computer executable instructions for performing a method of therapy, the method comprising:

applying substantially continuous stimulation, via an implantable pulse generator, to an airway patency-related nerve for a first time period longer than a duration of two nominal respiration cycles;

monitoring, via a respiration sensor, a respiration waveform during the substantially continuous stimulation; and

after the first period, applying stimulation synchronous with inspiration based on the monitored respiration waveform and for a second time period less than a duration of a single respiration cycle.

155. The medium of claim 154, comprising:

implementing the applying substantially continuous stimulation in a presence of sleep disordered breathing behavior.

156. The medium of claim 154, comprising:

omitting the applying substantially continuous stimulation in an absence of sleep disordered breathing behavior.

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01302

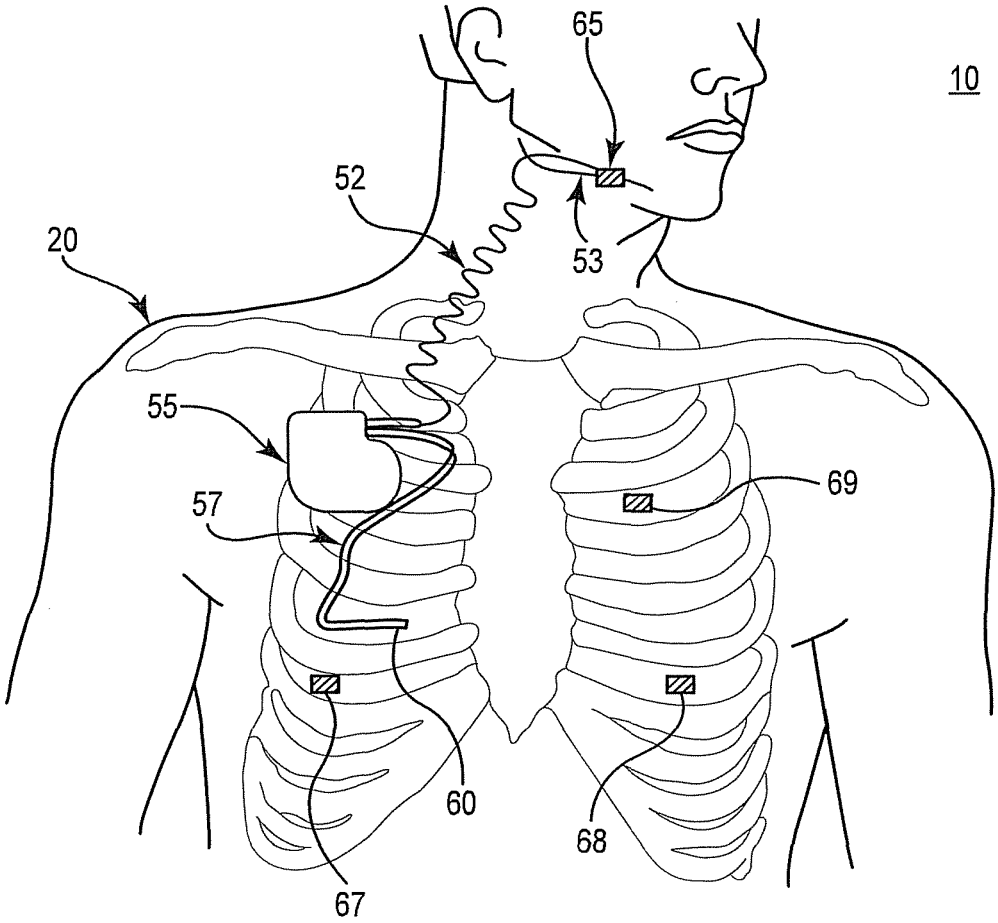


Fig. 1

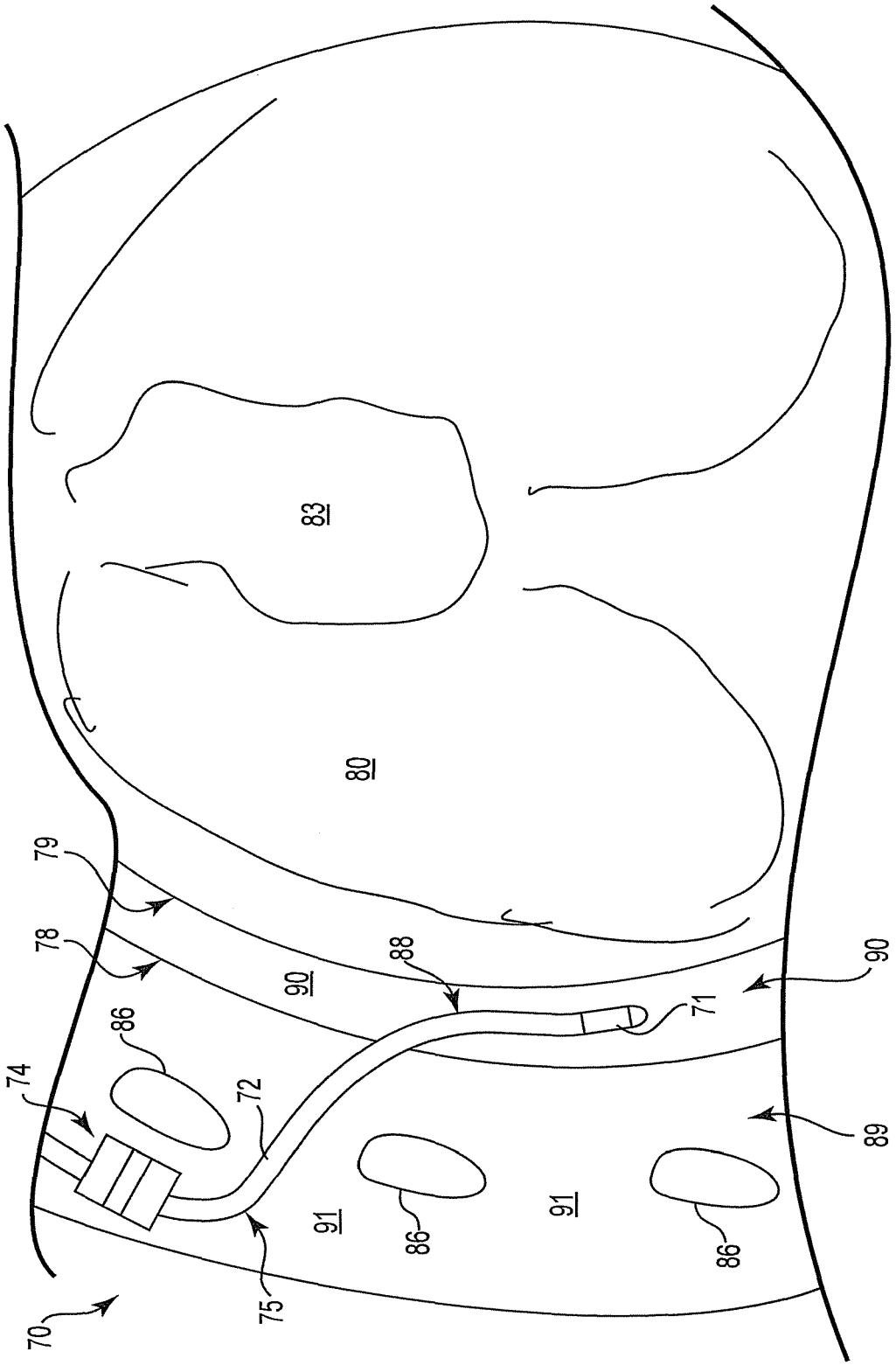


Fig. 2

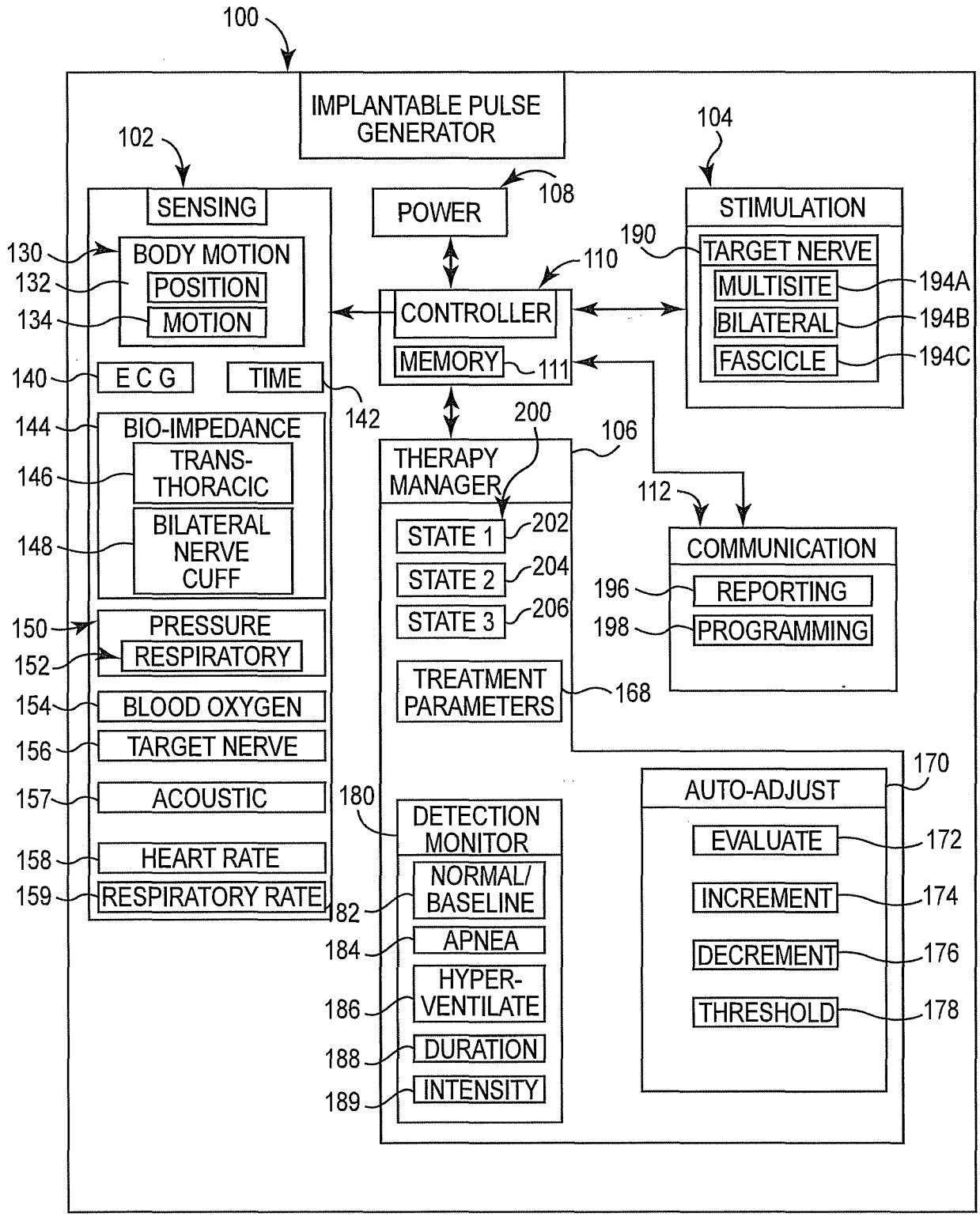

100
IMPLANTABLE PULSE GENERATOR
102
SENSING
130
BODY MOTION
132
POSITION
134
MOTION
140
E C G
TIME
142
144
BIO-IMPEDANCE
146
TRANS-THORACIC
148
BILATERAL NERVE CUFF
150
PRESSURE
152
RESPIRATORY
154
BLOOD OXYGEN
156
TARGET NERVE
157
ACOUSTIC
158
HEART RATE
159
RESPIRATORY RATE
POWER
108
110
CONTROLLER
MEMORY
111
200
THERAPY MANAGER
106
STATE 1
202
STATE 2
204
STATE 3
206
TREATMENT PARAMETERS
168
180
DETECTION MONITOR
182
NORMAL/ BASELINE
184
APNEA
186
HYPER-VENTILATE
188
DURATION
189
INTENSITY
104
STIMULATION
190
TARGET NERVE
MULTISITE
194A
BILATERAL
194B
FASCICLE
194C
112
COMMUNICATION
196
REPORTING
198
PROGRAMMING
170
AUTO-ADJUST
EVALUATE
172
INCREMENT
174
DECREMENT
176
THRESHOLD
178

Fig. 3A

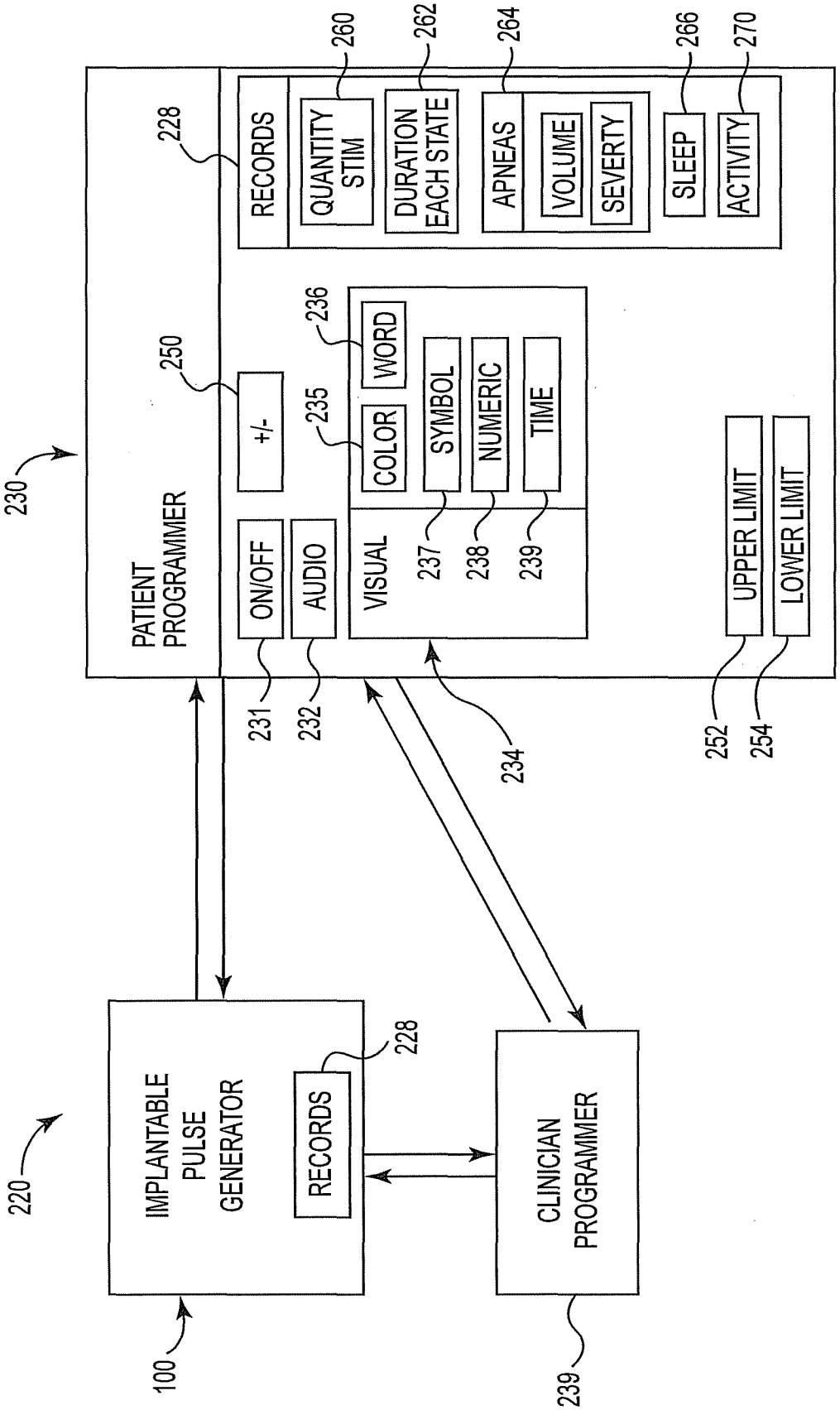

220
IMPLANTABLE PULSE GENERATOR
RECORDS
228
100
CLINICIAN PROGRAMMER
239
230
PATIENT PROGRAMMER
228
RECORDS
QUANTITY STIM
260
DURATION EACH STATE
262
APNEAS
264
VOLUME
SEVERTY
SLEEP
266
ACTIVITY
270
250
+/-
ON/OFF
AUDIO
231
232
VISUAL
235
COLOR
236
WORD
SYMBOL
NUMERIC
TIME
237
238
239
234
UPPER LIMIT
LOWER LIMIT
252
254

Fig. 3B

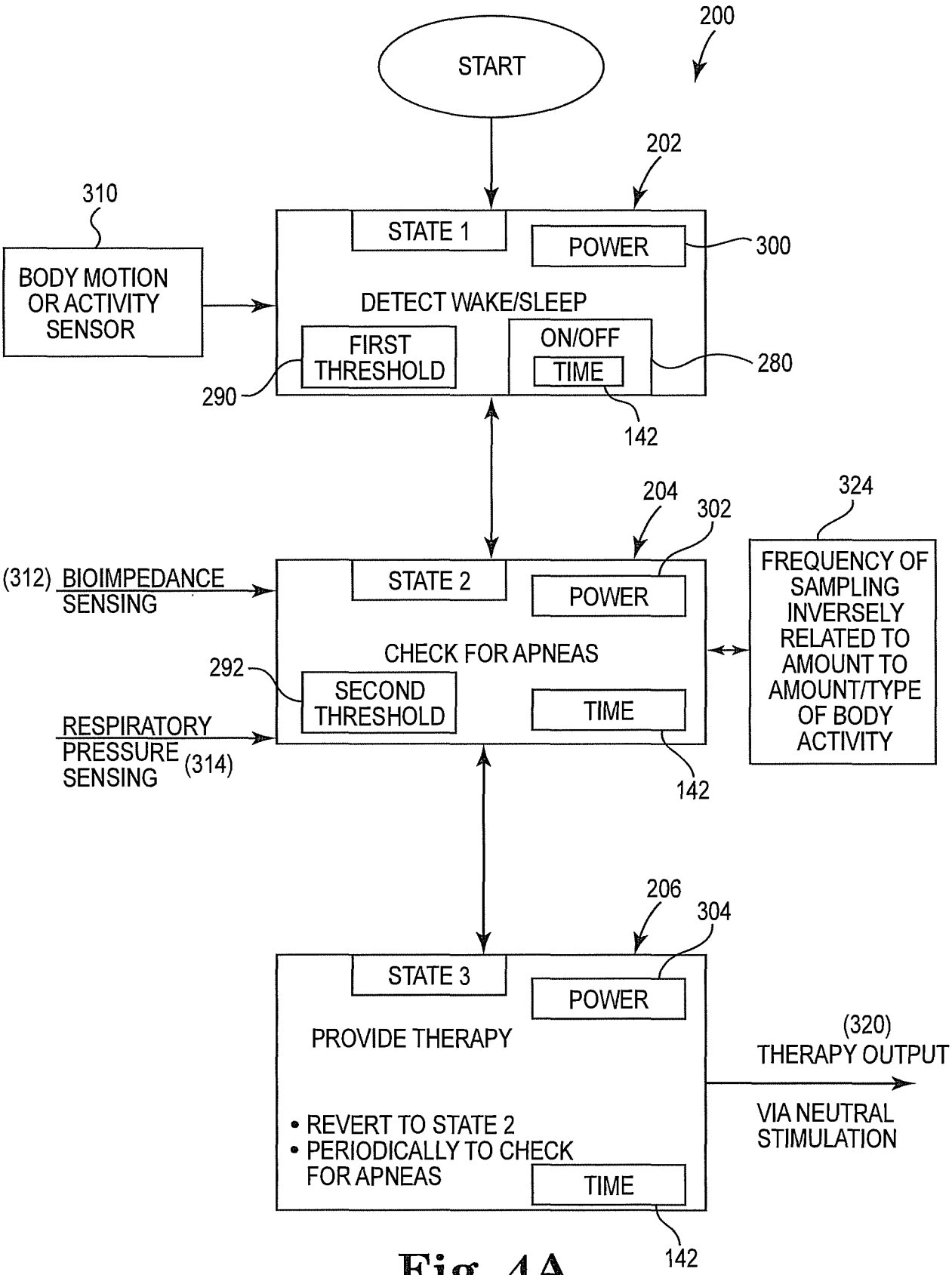

200
START
202
310
BODY MOTION OR ACTIVITY SENSOR
STATE 1
POWER
300
DETECT WAKE/SLEEP
FIRST THRESHOLD
290
ON/OFF
TIME
280
142
204
302
324
(312) BIOIMPEDANCE SENSING
STATE 2
POWER
FREQUENCY OF SAMPLING INVERSELY RELATED TO AMOUNT TO AMOUNT/TYPE OF BODY ACTIVITY
CHECK FOR APNEAS
292
SECOND THRESHOLD
TIME
RESPIRATORY PRESSURE SENSING (314)
142
206
304
STATE 3
POWER
PROVIDE THERAPY
(320) THERAPY OUTPUT
VIA NEUTRAL STIMULATION
• REVERT TO STATE 2
• PERIODICALLY TO CHECK FOR APNEAS
TIME
142

Fig. 4A

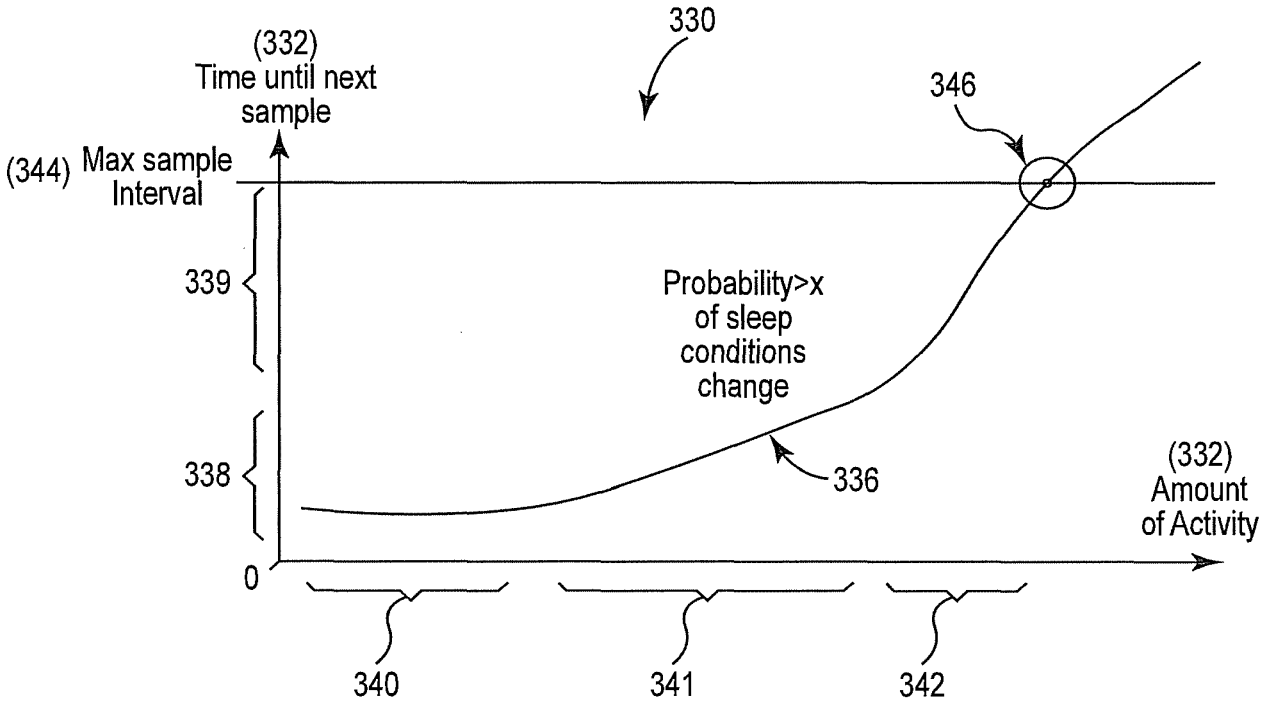

330
(332)
Time until next
sample
346
(344) Max sample
Interval
339
Probability>x
of sleep
conditions
change
338
336
(332)
Amount
of Activity
0
340
341
342

Fig. 4B

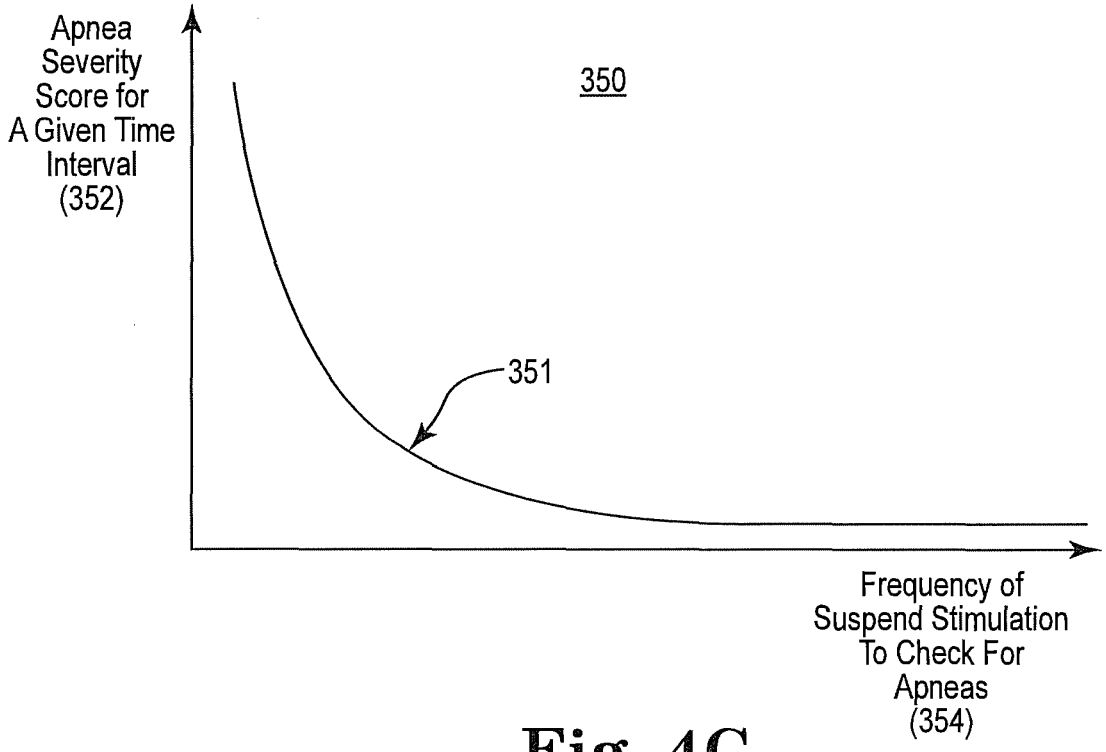

Apnea
Severity
Score for
A Given Time
Interval
(352)
350
351
Frequency of
Suspend Stimulation
To Check For
Apneas
(354)

Fig. 4C

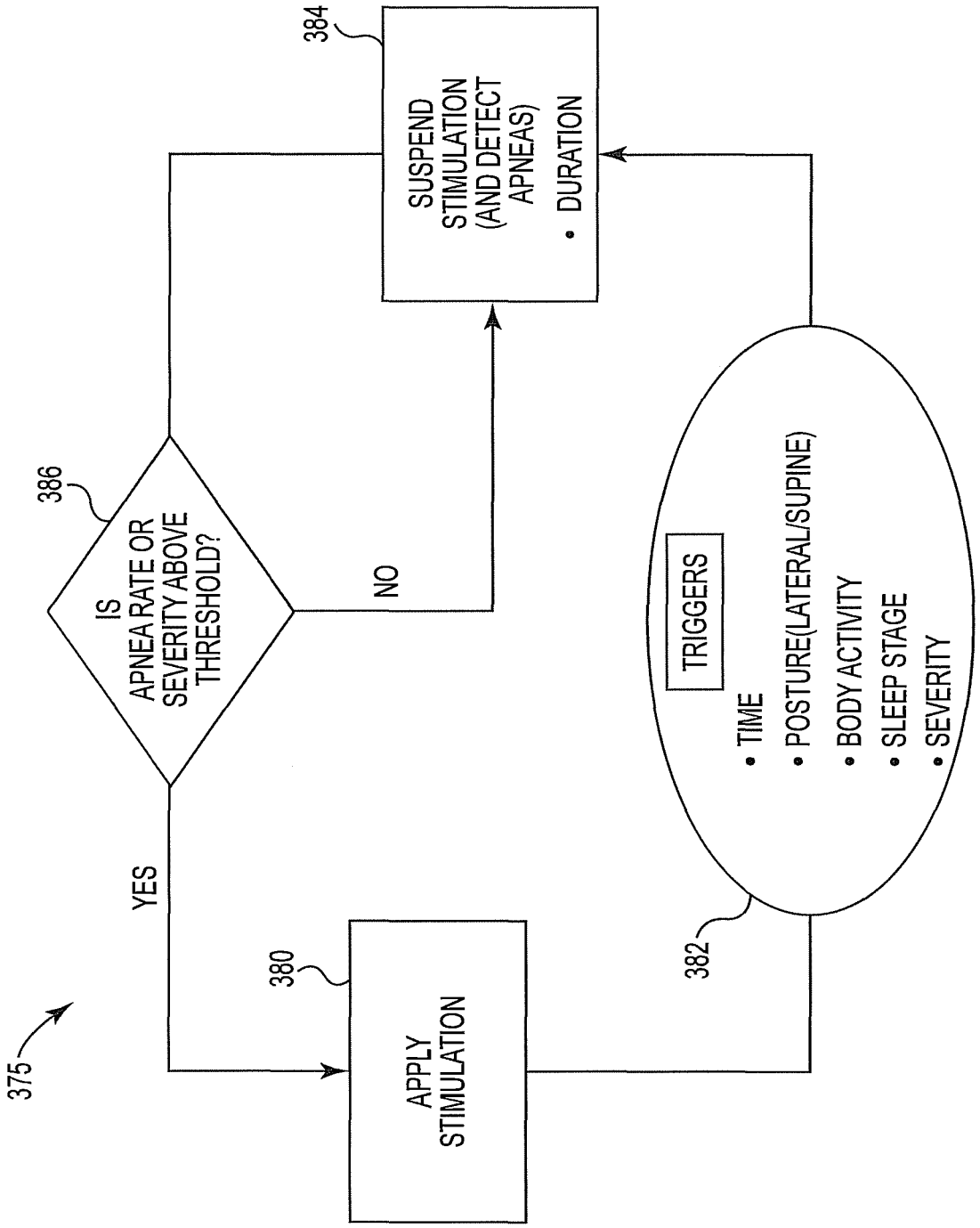

375
380
APPLY STIMULATION
382
TRIGGERS
• TIME
• POSTURE(LATERAL/SUPINE)
• BODY ACTIVITY
• SLEEP STAGE
• SEVERITY
386
IS APNEA RATE OR SEVERITY ABOVE THRESHOLD?
YES
NO
384
SUSPEND STIMULATION (AND DETECT APNEAS)
• DURATION

Fig. 4D

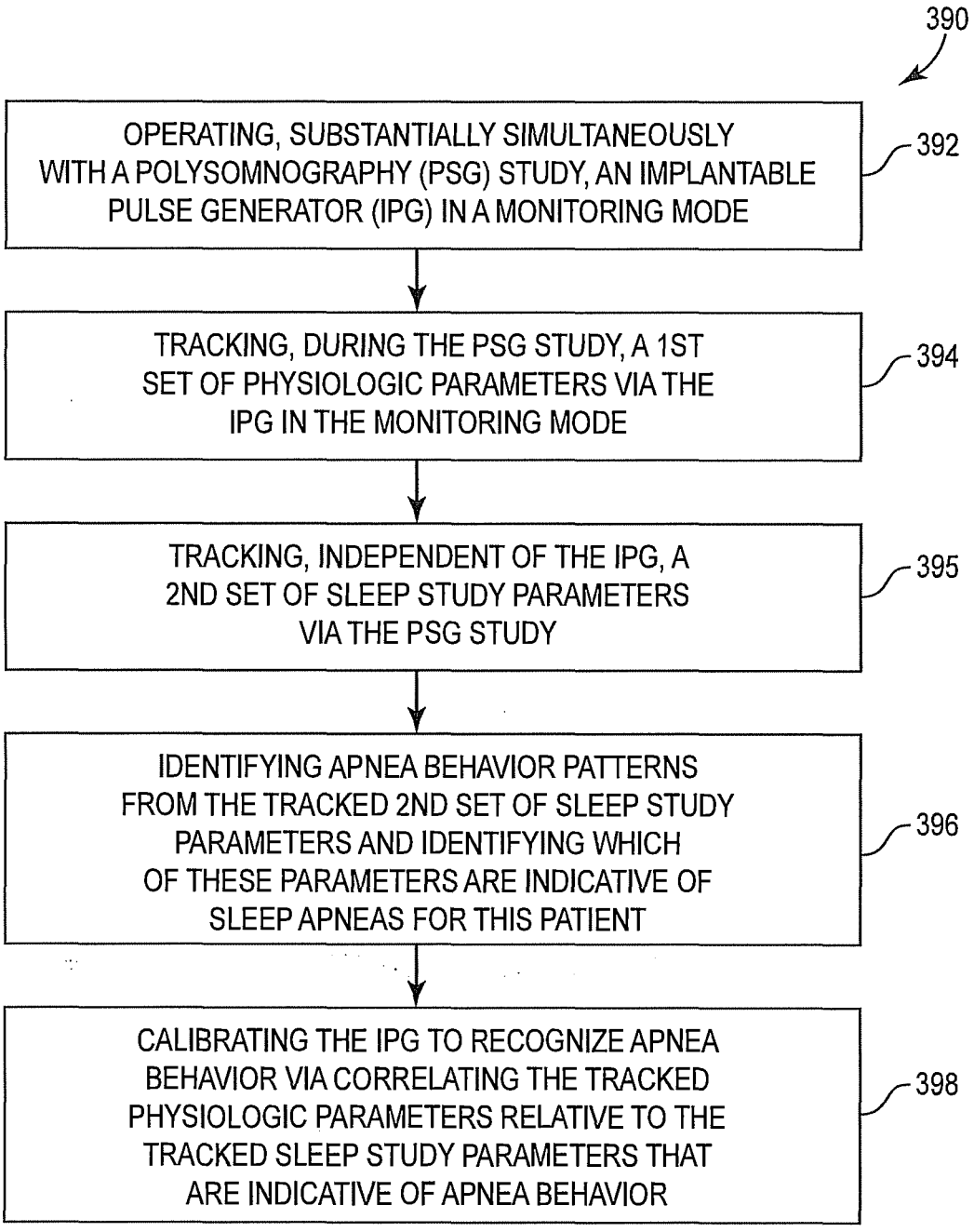

390
OPERATING, SUBSTANTIALLY SIMULTANEOUSLY WITH A POLYSOMNOGRAPHY (PSG) STUDY, AN IMPLANTABLE PULSE GENERATOR (IPG) IN A MONITORING MODE
392
TRACKING, DURING THE PSG STUDY, A 1ST SET OF PHYSIOLOGIC PARAMETERS VIA THE IPG IN THE MONITORING MODE
394
TRACKING, INDEPENDENT OF THE IPG, A 2ND SET OF SLEEP STUDY PARAMETERS VIA THE PSG STUDY
395
IDENTIFYING APNEA BEHAVIOR PATTERNS FROM THE TRACKED 2ND SET OF SLEEP STUDY PARAMETERS AND IDENTIFYING WHICH OF THESE PARAMETERS ARE INDICATIVE OF SLEEP APNEAS FOR THIS PATIENT
396
CALIBRATING THE IPG TO RECOGNIZE APNEA BEHAVIOR VIA CORRELATING THE TRACKED PHYSIOLOGIC PARAMETERS RELATIVE TO THE TRACKED SLEEP STUDY PARAMETERS THAT ARE INDICATIVE OF APNEA BEHAVIOR
398

Fig. 4E

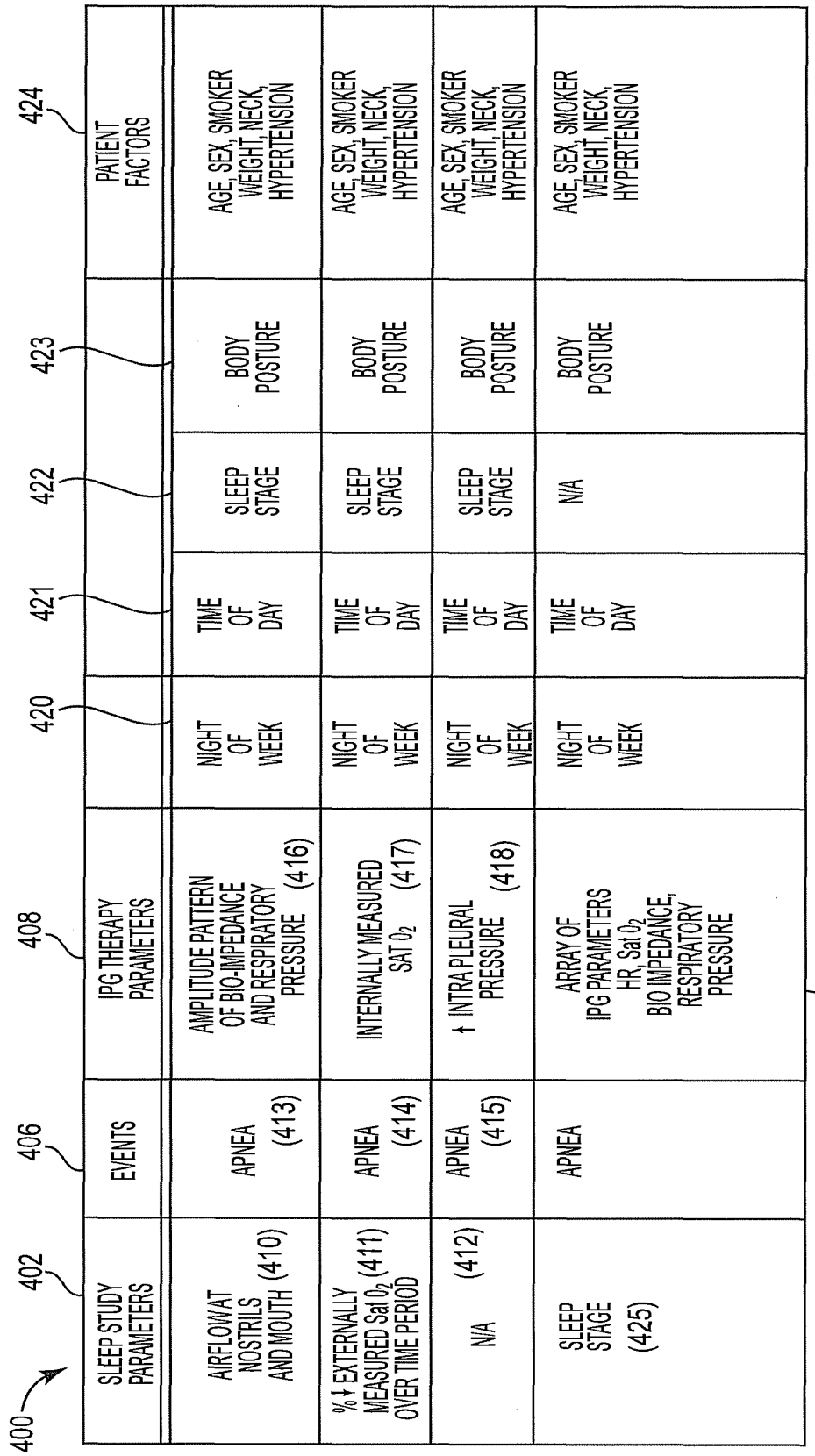

400
402
406
408
420
421
422
423
424
426
SLEEP STUDY PARAMETERS
EVENTS
IPG THERAPY PARAMETERS
PATIENT FACTORS
AIRFLOW AT NOSTRILS AND MOUTH (410)
APNEA (413)
AMPLITUDE PATTERN OF BIO-IMPEDANCE AND RESPIRATORY PRESSURE (416)
NIGHT OF WEEK
TIME OF DAY
SLEEP STAGE
BODY POSTURE
AGE, SEX, SMOKER WEIGHT, NECK, HYPERTENSION
% ↓ EXTERNALLY MEASURED Sat 0_2 (411) OVER TIME PERIOD
APNEA (414)
INTERNALLY MEASURED SAT 0_2 (417)
NIGHT OF WEEK
TIME OF DAY
SLEEP STAGE
BODY POSTURE
AGE, SEX, SMOKER WEIGHT, NECK, HYPERTENSION
N/A (412)
APNEA (415)
↑ INTRA PLEURAL PRESSURE (418)
NIGHT OF WEEK
TIME OF DAY
SLEEP STAGE
BODY POSTURE
AGE, SEX, SMOKER WEIGHT, NECK, HYPERTENSION
SLEEP STAGE (425)
APNEA
ARRAY OF IPG PARAMETERS HR, Sat 0_2 BIO IMPEDANCE, RESPIRATORY PRESSURE
N/A
BODY POSTURE
AGE, SEX, SMOKER WEIGHT, NECK, HYPERTENSION

Fig. 4F

450

452 PATIENT	454 PSG	456 IPG	458 DEMO	460 RESPONSIVE RATING
JOE	PSG 1	IPG 1	AGE, ETC	8
FRED	PSG 2	IPG 2	AGE, ETC	2
SUE	PSG 3	IPG 3	AGE, ETC	4
RON	PSG 4	IPG 4	AGE, ETC	9

Fig. 4G

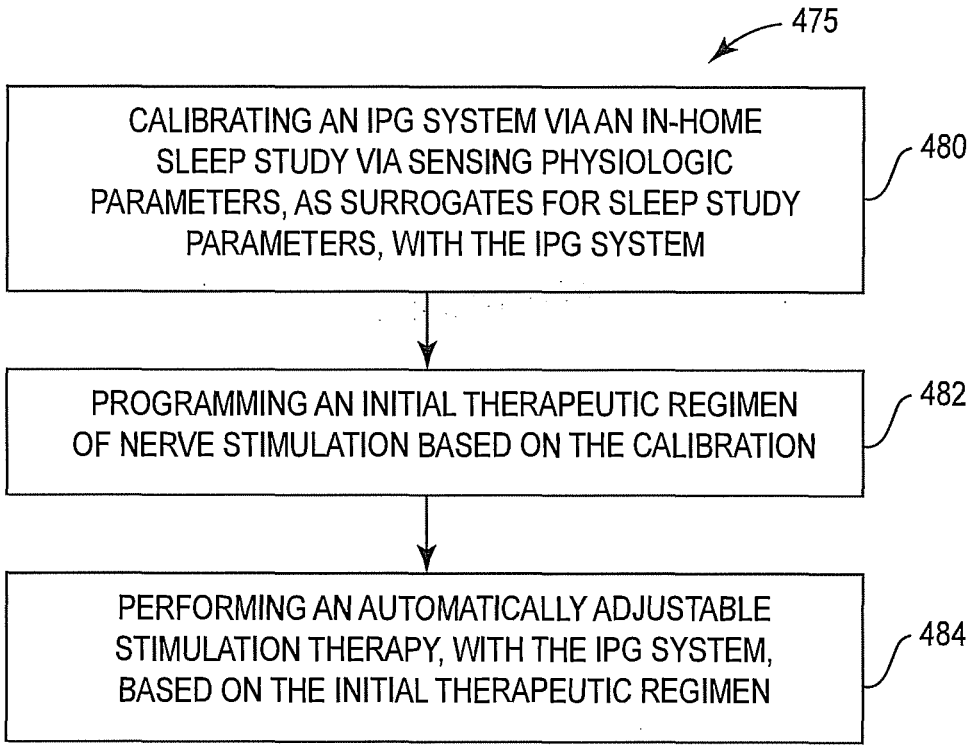


Fig. 4H

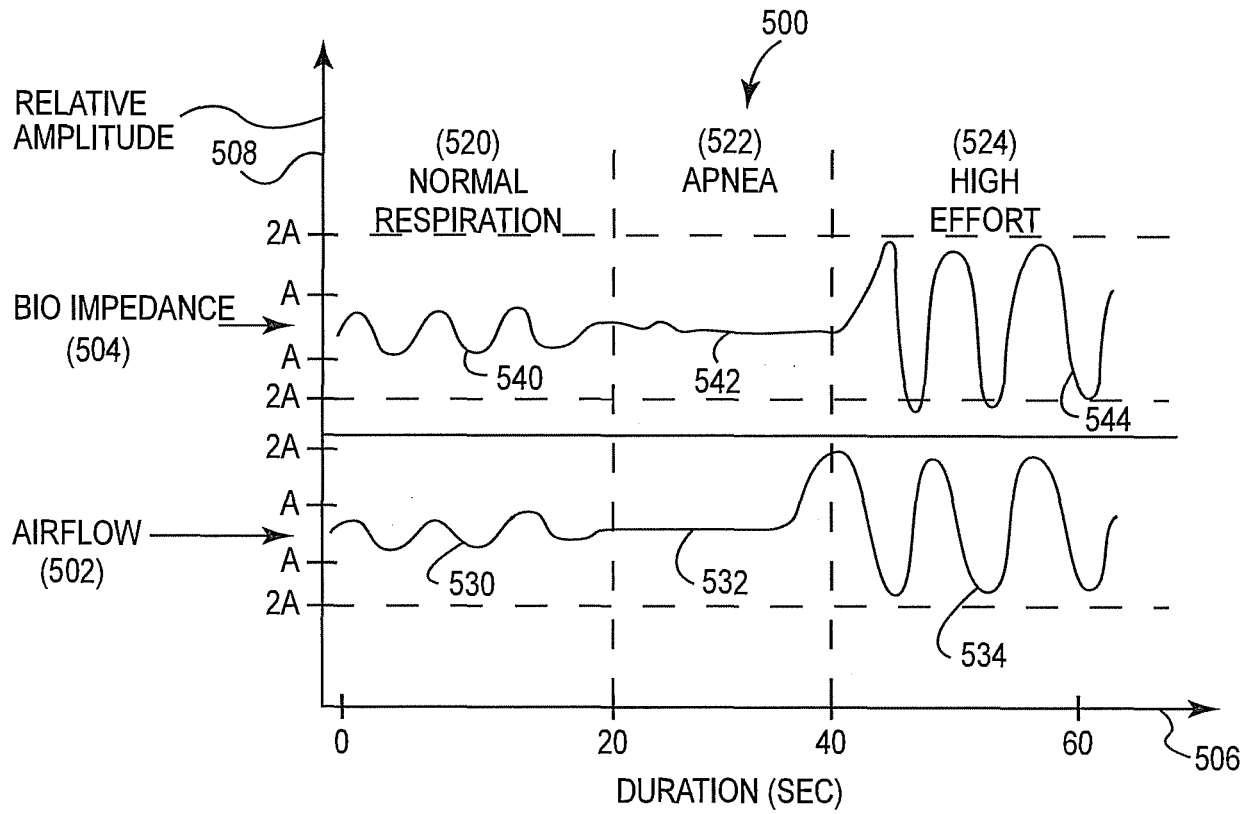

500
RELATIVE AMPLITUDE
508
(520) NORMAL RESPIRATION
(522) APNEA
(524) HIGH EFFORT
2A
A
BIO IMPEDANCE (504)
540
542
544
AIRFLOW (502)
530
532
534
0
20
40
60
506
DURATION (SEC)

Fig. 5

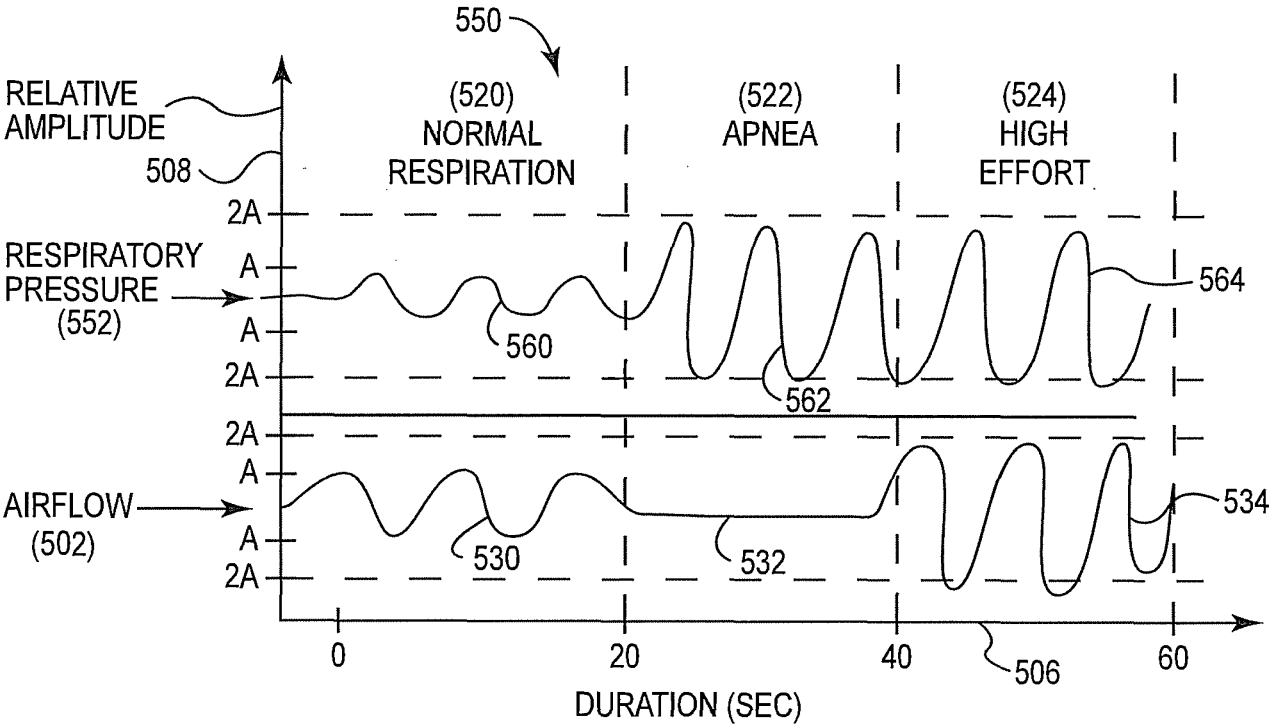

550
RELATIVE AMPLITUDE
508
(520) NORMAL RESPIRATION
(522) APNEA
(524) HIGH EFFORT
2A
A
RESPIRATORY PRESSURE (552)
560
562
564
AIRFLOW (502)
530
532
534
0
20
40
60
506
DURATION (SEC)

Fig. 6

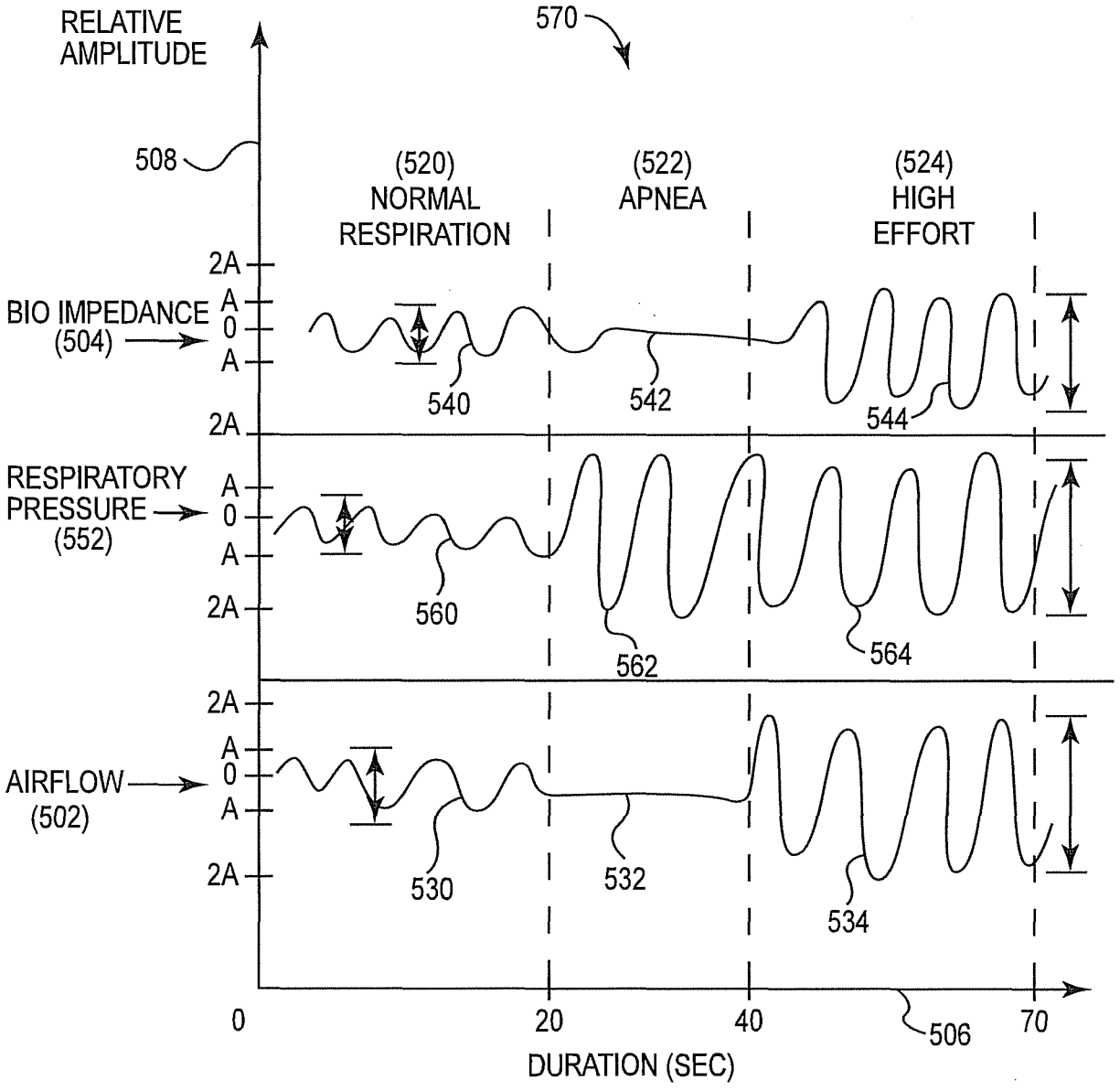

RELATIVE AMPLITUDE
570
508
(520) NORMAL RESPIRATION
(522) APNEA
(524) HIGH EFFORT
2A
A
0
A
2A
BIO IMPEDANCE (504)
540
542
544
RESPIRATORY PRESSURE (552)
560
562
564
AIRFLOW (502)
530
532
534
0
20
40
70
506
DURATION (SEC)

Fig. 7A

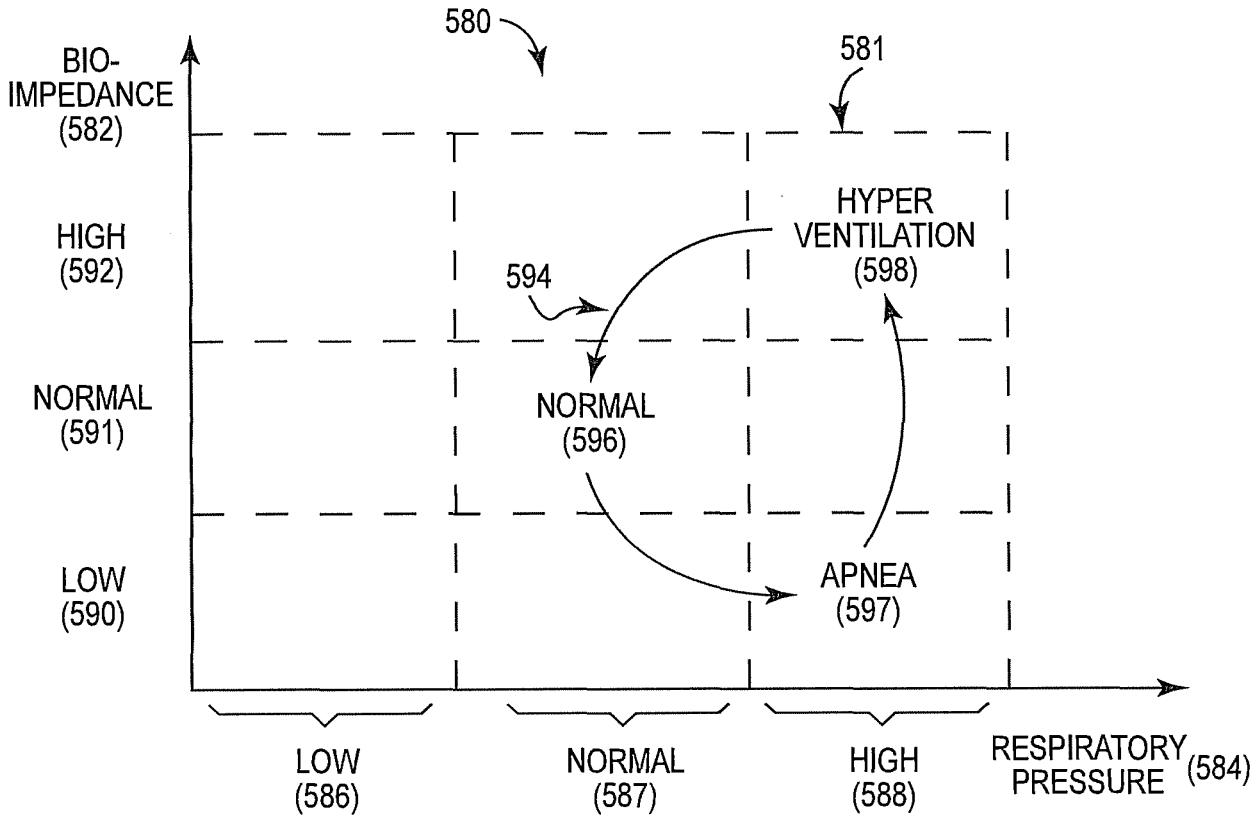

580
581
BIO-
IMPEDANCE
(582)
HIGH
(592)
NORMAL
(591)
LOW
(590)
HYPER
VENTILATION
(598)
594
NORMAL
(596)
APNEA
(597)
LOW
(586)
NORMAL
(587)
HIGH
(588)
RESPIRATORY
PRESSURE
(584)

Fig. 7B

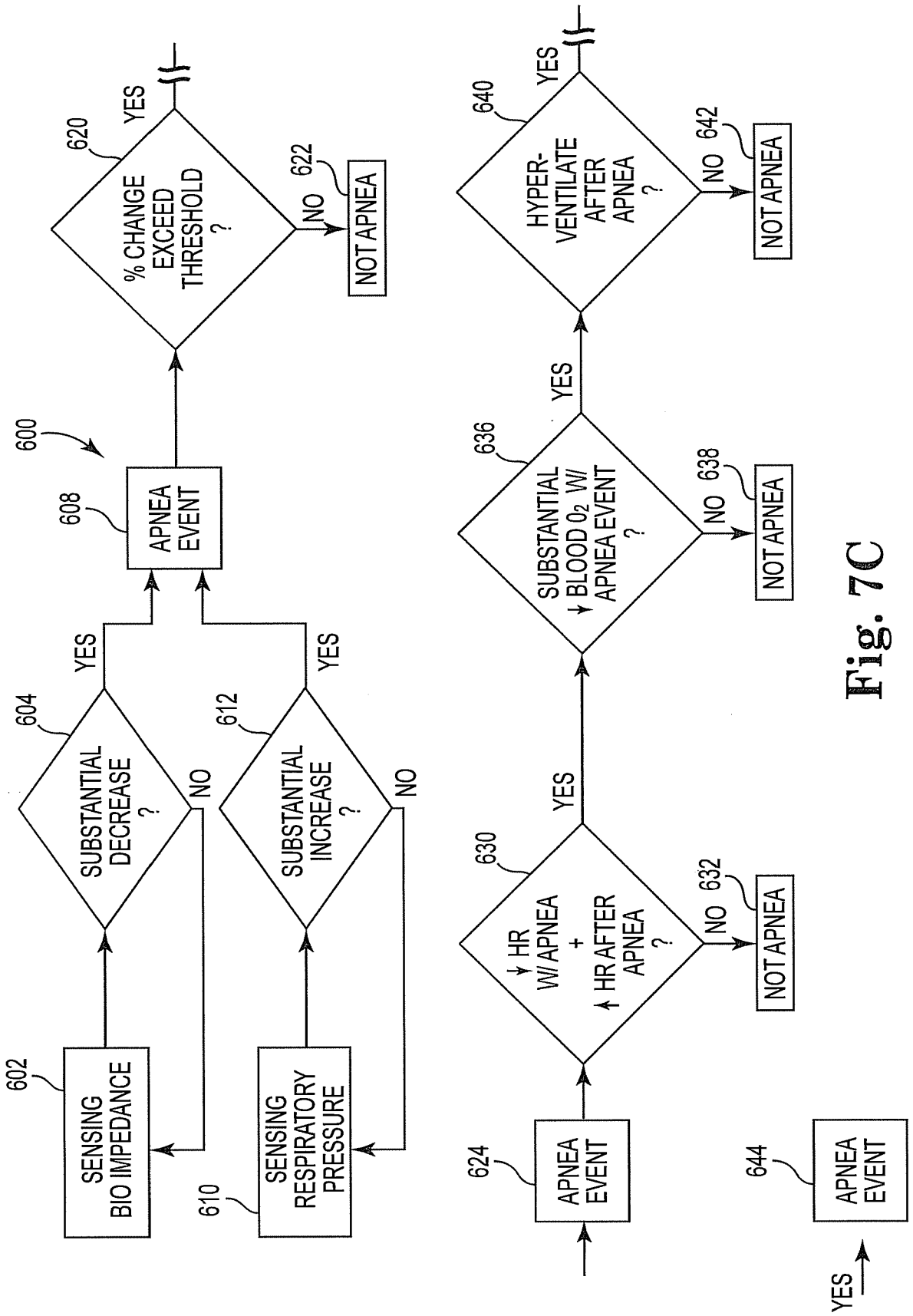

600
602
SENSING BIO IMPEDANCE
604
SUBSTANTIAL DECREASE ?
YES
NO
608
APNEA EVENT
610
SENSING RESPIRATORY PRESSURE
612
SUBSTANTIAL INCREASE ?
YES
NO
620
% CHANGE EXCEED THRESHOLD ?
YES
NO
622
NOT APNEA
624
APNEA EVENT
630
↓ HR W/ APNEA + ↑ HR AFTER APNEA ?
YES
NO
632
NOT APNEA
636
SUBSTANTIAL ↓ BLOOD O_2 W/ APNEA EVENT ?
YES
NO
638
NOT APNEA
640
HYPER-VENTILATE AFTER APNEA ?
YES
NO
642
NOT APNEA
644
APNEA EVENT
YES

Fig. 7C

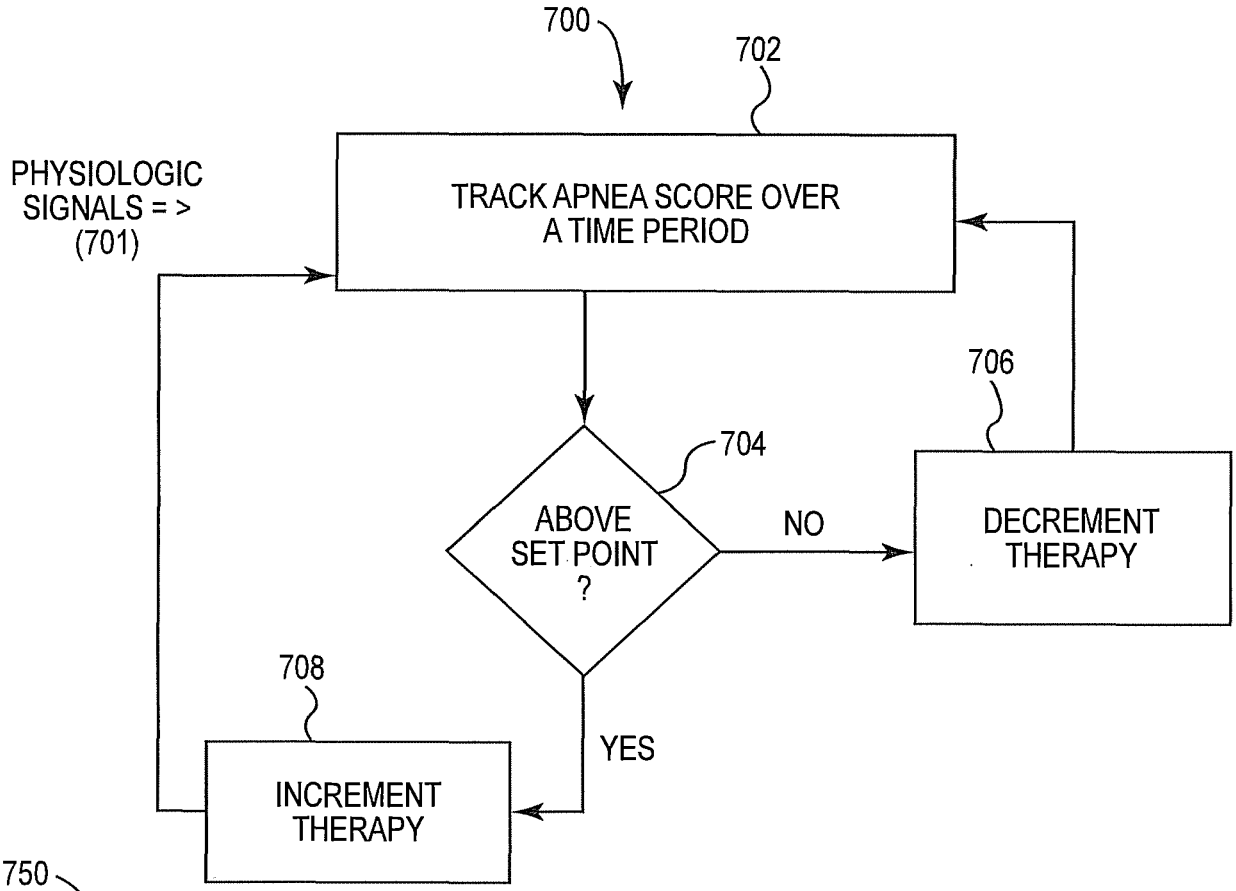

700
702
PHYSIOLOGIC SIGNALS = > (701)
TRACK APNEA SCORE OVER A TIME PERIOD
706
704
ABOVE SET POINT ?
NO
DECREMENT THERAPY
708
YES
INCREMENT THERAPY

Fig. 8A

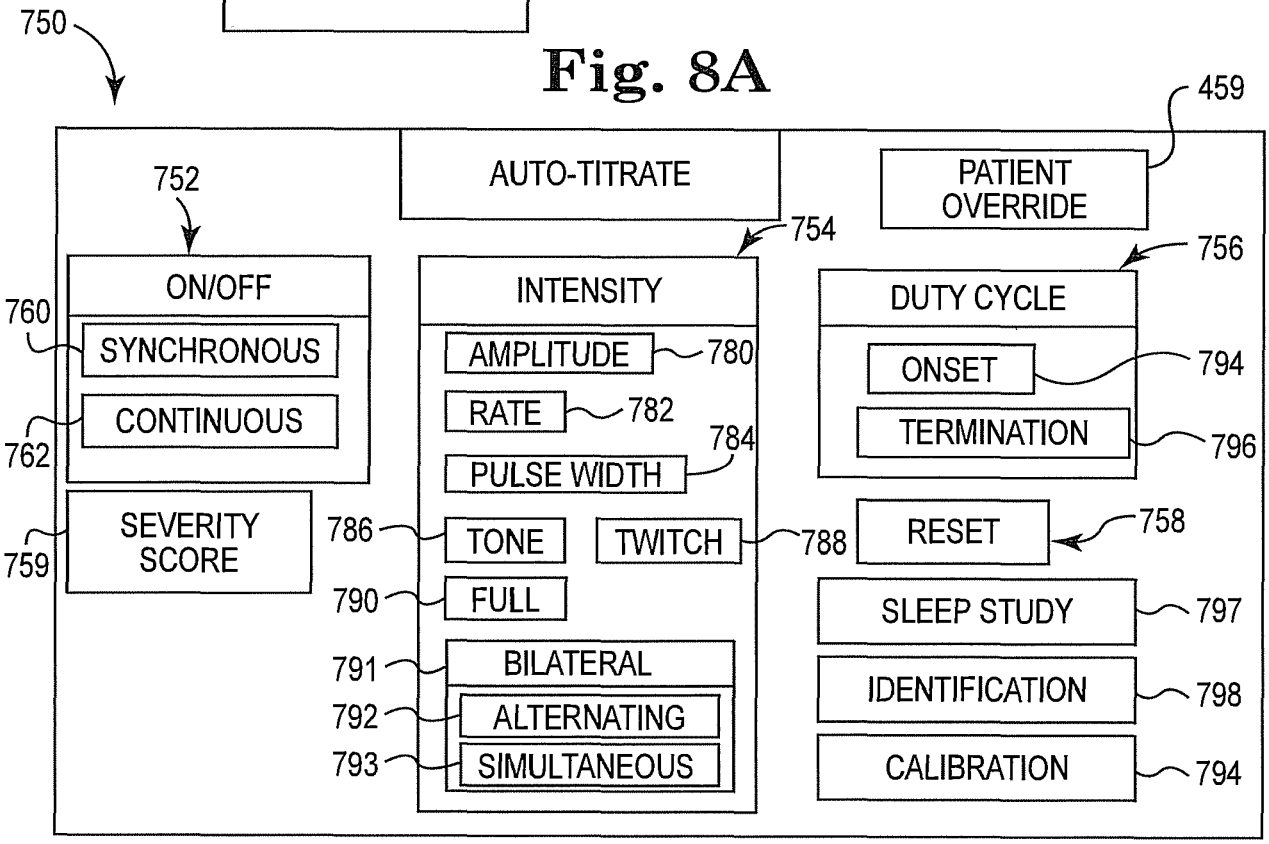

750
459
AUTO-TITRATE
PATIENT OVERRIDE
752
754
756
ON/OFF
INTENSITY
DUTY CYCLE
760
SYNCHRONOUS
AMPLITUDE
780
ONSET
794
CONTINUOUS
RATE
782
TERMINATION
796
762
784
PULSE WIDTH
SEVERITY SCORE
759
786
TONE
TWITCH
788
RESET
758
790
FULL
SLEEP STUDY
797
791
BILATERAL
IDENTIFICATION
798
792
ALTERNATING
793
SIMULTANEOUS
CALIBRATION
794

Fig. 9

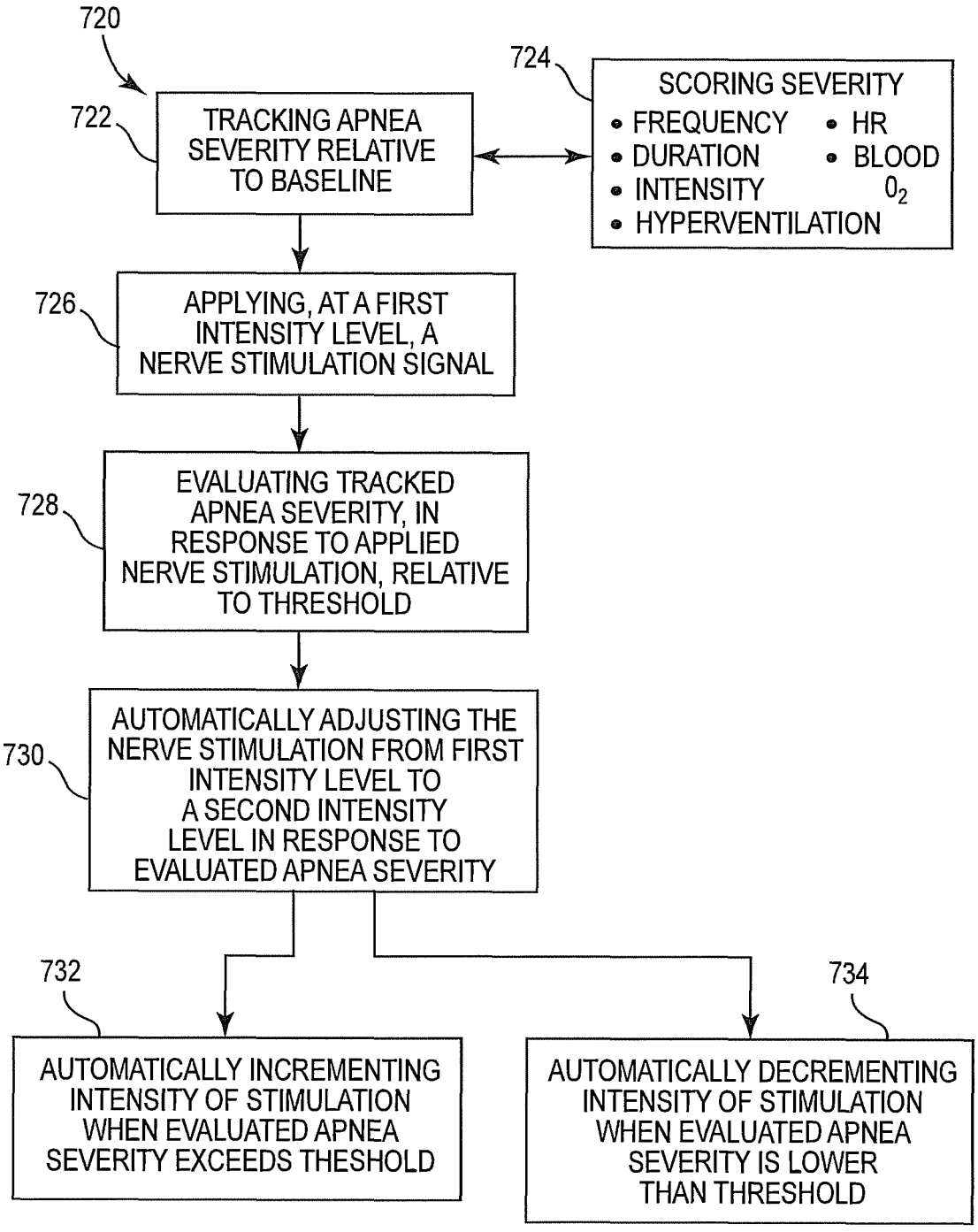

720
724
SCORING SEVERITY
• FREQUENCY
• DURATION
• INTENSITY
• HYPERVENTILATION
• HR
• BLOOD 0_2
722
TRACKING APNEA SEVERITY RELATIVE TO BASELINE
726
APPLYING, AT A FIRST INTENSITY LEVEL, A NERVE STIMULATION SIGNAL
728
EVALUATING TRACKED APNEA SEVERITY, IN RESPONSE TO APPLIED NERVE STIMULATION, RELATIVE TO THRESHOLD
730
AUTOMATICALLY ADJUSTING THE NERVE STIMULATION FROM FIRST INTENSITY LEVEL TO A SECOND INTENSITY LEVEL IN RESPONSE TO EVALUATED APNEA SEVERITY
732
AUTOMATICALLY INCREMENTING INTENSITY OF STIMULATION WHEN EVALUATED APNEA SEVERITY EXCEEDS THESHOLD
734
AUTOMATICALLY DECREMENTING INTENSITY OF STIMULATION WHEN EVALUATED APNEA SEVERITY IS LOWER THAN THRESHOLD

Fig. 8B

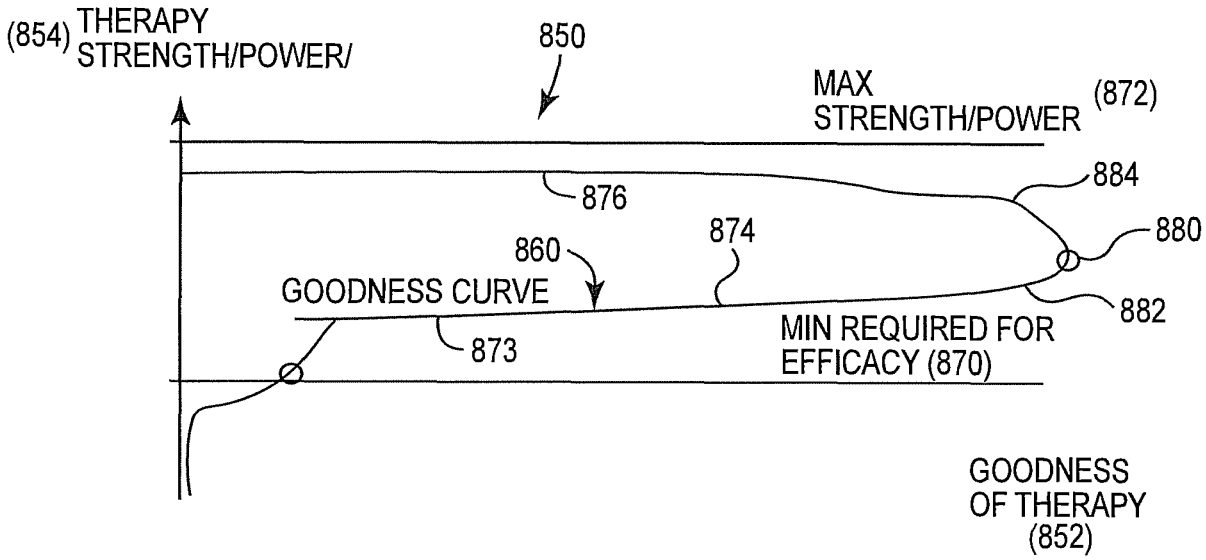

(854) THERAPY STRENGTH/POWER/
850
MAX STRENGTH/POWER
(872)
876
884
874
880
860
GOODNESS CURVE
882
873
MIN REQUIRED FOR EFFICACY (870)
GOODNESS OF THERAPY (852)

Fig. 10

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 October 2010 (14.10.2010)

PCT

(10) International Publication Number
WO 2010/117810 A1

(51) International Patent Classification:
A61N 1/05 (2006.01) *A61N 1/36* (2006.01)

(21) International Application Number:
PCT/US2010/029253

(22) International Filing Date:
30 March 2010 (30.03.2010)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/165,110 31 March 2009 (31.03.2009) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,

[Continued on next page]

(54) Title: PERCUTANEOUS ACCESS FOR SYSTEMS OF TREATING SLEEP-RELATED DISORDERED BREATHING

(57) Abstract: Systems and methods are described and illustrated for percutaneously implanting a stimulation lead for treating sleep-related disordered breathing.

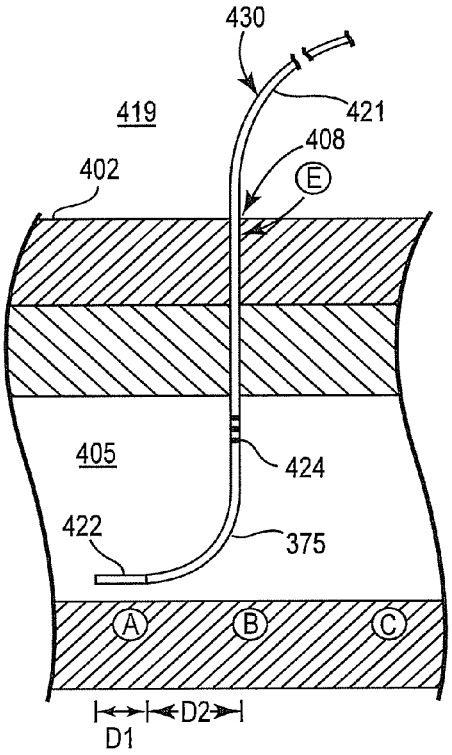


Fig. 7E

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CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

PERCUTANEOUS ACCESS FOR SYSTEMS OF TREATING SLEEP-RELATED DISORDERED BREATHING

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This PCT Patent Application claims priority to U. S. Provisional Patent Application Serial Number 61/165,110, filed on March 31, 2009, which is incorporated herein by reference.

BACKGROUND

[002] The present disclosure relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the present disclosure relates to systems and methods of using percutaneous delivery of a stimulation lead to treat sleep-related disordered breathing, such as obstructive sleep apnea and other disorders, and relates to various configurations of a stimulation electrode portion of a stimulation lead.

[003] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[004] One treatment for obstructive sleep apnea has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a cuff electrode placed around the hypoglossal nerve.

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BRIEF DESCRIPTION OF THE DRAWINGS

[005] Aspects and features of the present disclosure will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments of the present disclosure when considered in connection with the accompanying drawings, wherein:

[006] FIG. 1 is a schematic illustration of an implantable stimulation system, according to an embodiment of the present disclosure;

[007] FIG. 2 is a schematic illustration of a block diagram of an implantable stimulation system, according to an embodiment of the present disclosure;

[008] FIG. 3 is a schematic illustration of a block diagram of a sensing monitor, according to an embodiment of the present disclosure;

[009] FIG. 4 is a schematic illustration of a percutaneous access system including a site locator tool, a stimulation monitor, and a response evaluation array, according to an embodiment of the present disclosure;

[010] FIG. 5 is a schematic illustration of a method of identifying a stimulation site, according to an embodiment of the present disclosure;

[011] FIG. 6A is a side plan view schematically illustrating a stimulation lead introduction tool, according to an embodiment of the present disclosure;

[012] FIG. 6B is a sectional view as taken along lines 6B - - 6B of Figure 6A, according to an embodiment of the present disclosure;

[013] FIG. 6C is a side plan view schematically illustrating a stimulation lead introduction tool, according to an embodiment of the present disclosure;

[014] FIG. 7A is sectional view schematically illustrating insertion of a test locator tool, according to an embodiment of the present disclosure;

[015] FIG. 7B is sectional view schematically illustrating a configuration upon insertion of an introduction tool, according to an embodiment of the present disclosure;

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[016] FIG. 7C is sectional view schematically illustrating a configuration upon removal of a locator tool, according to an embodiment of the present disclosure;

[017] FIG. 7D is sectional view schematically illustrating a configuration upon insertion of a stimulation lead via the introduction tool, according to an embodiment of the present disclosure;

[018] FIG. 7E is sectional view schematically illustrating a configuration of the stimulation lead upon removal of the introduction tool, according to an embodiment of the present disclosure;

[019] FIG. 8A is a side plan view schematically illustrating a stimulation lead including a distal electrode portion, according to an embodiment of the present disclosure;

[020] FIG. 8B is a bottom plan view of the stimulation lead of FIG. 8A including a schematic illustration of a stimulation electrode portion, according to an embodiment of the present disclosure;

[021] FIG. 8C is a perspective view of the stimulation lead of FIGS. 8A-8B including a schematic illustration of an anchoring mechanism, according to an embodiment of the present disclosure;

[022] FIG. 8D is a perspective view of a distal portion of a stimulation lead introduction tool, according to an embodiment of the present disclosure;

[023] FIG. 8E is a sectional view of a distal portion of a stimulation lead introduction tool and a stimulation lead extending therethrough, according to an embodiment of the present disclosure;

[024] FIG. 8F is partial end view of a distal portion of a stimulation lead having convex-shaped electrode portion, according to an embodiment of the present disclosure;

[025] FIG. 8G is partial end view of a distal electrode portion of a stimulation lead having a concave-shaped electrode portion, according to an embodiment of the present disclosure;

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[026] FIG. 9 is a perspective view of a stimulation lead including an anchoring system, according to an embodiment of the present disclosure;

[027] FIG. 10 is a perspective view of an alternate anchoring system, according to an embodiment of the present disclosure;

[028] FIG. 11 is a sectional view schematically illustrating a method of percutaneous delivery of a stimulation lead, according to an embodiment of the present disclosure;

[029] FIG. 12 is a side plan view of an introduction tool employed in the method associated with FIG. 11, according to an embodiment of the present disclosure;

[030] FIG. 13 is a bottom plan view of a distal electrode portion of a stimulation lead, according to an embodiment of the present disclosure;

[031] FIG. 14A is an enlarged sectional view schematically illustrating a selectively deployable anchoring mechanism of the introduction tool of FIGS. 11-12, according to an embodiment of the present disclosure;

[032] FIG. 14B is an enlarged side view schematically illustrating the anchoring mechanism in a deployed state relative to the surrounding tissue, according to an embodiment of the present disclosure;

[033] FIG. 14C is a sectional view schematically illustrating a distal electrode portion of a stimulation lead secured relative to a nerve via an anchoring mechanism, according to an embodiment of the present disclosure;

[034] FIG. 15 is a perspective view schematically illustrating a bio-absorbable stimulation system prior to absorption, according to an embodiment of the present disclosure;

[035] FIG. 16 is a perspective view schematically illustrating the bio-absorbable stimulation system of FIG. 15 after absorption, according to an embodiment of the present disclosure;

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[036] FIG. 17A is an enlarged side plan view of an electrode portion of the stimulation system of FIGS. 15-16, according to an embodiment of the present disclosure;

[037] FIG. 17B is a sectional view as taken along lines 17B – 17B of FIG. 16, according to an embodiment of the present disclosure;

[038] FIG. 18 is a side plan view of a bio-absorbable, stent-electrode stimulation lead, according to an embodiment of the present disclosure;

[039] FIG. 19 is a side plan view schematically illustrating deployment of the stent-electrode stimulation lead of FIG. 18 relative to a nerve, according to an embodiment of the present disclosure;

[040] FIG. 20 is a sectional view schematically illustrating anchoring of an electrode against a nerve after absorption of the bio-absorbable stent portion of the stimulation lead, according to an embodiment of the present disclosure;

[041] FIG. 21 is a side plan view schematically illustrating the electrodes of the stimulation lead against the target nerve after absorption of the bio-absorbable stent portion of the stimulation lead, according to an embodiment of the present disclosure.

[042] FIG. 22 is a perspective view schematically illustrating a bio-absorbable electrode portion of a stimulation lead, according to an embodiment of the present disclosure;

[043] FIG. 23 is a perspective view schematically illustrating implanted electrodes of the stimulation lead of FIG. 22 prior to absorption, according to an embodiment of the present disclosure;

[044] FIG. 24 is a perspective view schematically illustrating the implanted electrodes of the stimulation lead of FIG. 22 after absorption, according to an embodiment of the present disclosure;

[045] FIG. 25 is a top plan view of an electrode portion of a stimulation lead, according to an embodiment of the present disclosure;

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[046] FIG. 26 is a top plan view schematically illustrating a stimulation system as deployed relative to a nerve, including the electrode portion of a stimulation lead and an insulator shield, according to an embodiment of the present disclosure;

[047] FIG. 27 is a sectional view as taken along lines 27 –27 of FIG. 26, according to an embodiment of the present disclosure;

[048] FIG. 28 is a top plan view of an electrode portion of a stimulation lead, according to an embodiment of the present disclosure;

[049] FIG. 29 is a side view schematically illustrating an insulator shield releasably connected, via a coupling mechanism, to an electrode portion of a stimulation lead, according to an embodiment of the present disclosure;

[050] FIG. 30 is a sectional view schematically illustrating one aspect of a method of percutaneous access for a stimulation system, according to an embodiment of the present disclosure;

[051] FIG. 31 is a top elevational view schematically illustrating one aspect of the method of percutaneous access, according to an embodiment of the present disclosure; and

[052] FIG. 32 is a sectional view schematically illustrating another aspect of the method of percutaneous access, according to an embodiment of the present disclosure.

DESCRIPTION OF EMBODIMENTS

[053] The following detailed description is merely exemplary in nature and is not intended to limit the present disclosure or the application and uses of the present disclosure. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, or the following detailed description.

[054] Embodiments of the present disclosure provide implantable medical devices, systems, and methods for treating sleep-related disordered breathing, such as but not limited to obstructive sleep apnea. In these methods and systems, stimulation is

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provided to the hypoglossal nerve (or another target nerve) through a lead system that is delivered percutaneously or delivered using other minimally invasive techniques. In addition, embodiments of the present disclosure include various configurations of the stimulation electrode portion of a stimulation lead.

[055] FIG. 1 is a schematic diagram of an implantable stimulation system that includes a percutaneously placed stimulation electrode, according to an embodiment of the present disclosure. As illustrated in FIG.1, an example of an implantable stimulation system 10 according to one embodiment of the present disclosure includes an implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 20, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes a stimulation electrode portion 65 and extends from the IPG 55 so that the stimulation electrode portion 65 is positioned in contact with a desired nerve, such as the hypoglossal nerve 53 of the patient 10, to enable stimulation of the nerve 53, as described below in detail. An exemplary implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., and which is incorporated herein by reference in its entirety. In one embodiment, the lead 52 further includes at least one sensor portion 60 (electrically coupled to the IPG 55 and extending from the IPG 55) positioned in the patient 10 for sensing respiratory effort, such as respiratory pressure.

[056] In some embodiments, the sensor portion 60 detects respiratory patterns (e.g., inspiration, expiration, respiratory pause, etc.) in order to trigger activation of an electrode portion to stimulate a target nerve. Accordingly, with this arrangement, the IPG 55 (Figure 1) receives sensor waveforms from the respiratory sensor portion 60, thereby enabling the IPG 55 to deliver electrical stimulation synchronously with inspiration (or another aspect of the respiratory pattern related to inspiration) according to a therapeutic treatment regimen in accordance with embodiments of the present disclosure. It is also understood that the respiratory sensor portion 60 is powered by the IPG 55 and the IPG 55 also contains internal circuitry to accept and process the impedance signal from the stimulation lead 52.

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[057] In some embodiments, the sensor portion 60 is a pressure sensor. In one aspect, the pressure sensor in this embodiment detects pressure in the thorax of the patient. In another aspect, the sensed pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow). With this configuration, the controller is configured to analyze this pressure sensing information to detect the respiratory patterns of the patient.

[058] In some other embodiments, the respiratory sensor portion 60 comprises a bio-impedance sensor or pair of bio-impedance sensors and can be located in regions other than the pectoral region. In one aspect, such an impedance sensor is configured to sense a bio-impedance signal or pattern whereby the control unit evaluates respiratory patterns within the bio-impedance signal. For bio-impedance sensing, in one embodiment, electric current will be injected through an electrode portion within the body and an electrically conductive portion of a case of the IPG 55 (Figure 3A) with the voltage being sensed between two spaced apart stimulation electrode portions (or also between one of the stimulation electrode portions and the electrically conductive portion of the case of IPG 55) to compute the impedance.

[059] In some embodiments, system 10 also comprises additional sensors to further obtain physiologic data associated with respiratory functions. For example, system 10 may include various sensors (e.g., sensors 67, 68, 69 in FIG. 1) distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals.

[060] In some embodiments, the sensing and stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. In other embodiments, one or more components of the system are not implanted in a body of the patient. A few non-limiting examples of such non-implanted components include external sensors (respiration, impedance, etc.), an external processing unit, or an external power source. Of course, it is further understood that the implanted portion(s) of the system provides a communication pathway to enable transmission of data and/or controls signals both to and from the implanted portions of the system relative to the external portions of the system. The communication pathway includes a radiofrequency (RF) telemetry link or other wireless communication protocols.

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[061] Whether partially implantable or totally implantable, the system is designed to stimulate the hypoglossal nerve during inspiration to thereby prevent obstructions or occlusions in the upper airway during sleep. In one embodiment, the implantable system comprises an implantable pulse generator (IPG), a peripheral nerve cuff stimulation lead, and a pressure sensing lead.

[062] Figure 2 is a block diagram schematically illustrating an implantable stimulation system 100, according to one embodiment of the present disclosure. In one embodiment, system 100 comprises at least substantially the same features and attributes as system 10 of Figure 1. As illustrated in Figure 2, system 100 includes a sensing module 102, a stimulation module 104, a therapy module 106, and a patient management module 108. In one embodiment, the IPG 109 of therapy module 106 comprises at least substantially the same features and attributes as IPG 55 of Figure 1.

[063] Via an array of parameters, the sensing module 102 receives and tracks signals from various physiologic sensors (such as a pressure sensor, blood oxygenation sensor, acoustic sensor, electrocardiogram (ECG) sensor, or impedance sensor) in order to determine a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. Such respiratory detection may be received from either a single sensor or any multiple of sensors, or combination of various physiologic sensors which may provide a more reliable and accurate signal.

[064] For example, in one embodiment, the sensing module 102 comprises a sensing monitor 120, as illustrated in Figure 3. The sensing monitor 120 includes a body parameter 130, which includes at least one of a position-sensing component 132 or a motion-sensing component 134. In one embodiment, the motion-sensing component 134 tracks sensing of "seismic" activity (via an accelerometer or a piezoelectric transducer) that is indicative of walking, body motion, talking, etc. In another embodiment, the position-sensing component 132 tracks sensing of a body position or posture via an accelerometer or other transducer. In some embodiments, body parameter 130 utilizes signals from both the position-sensing component 132 and the motion-sensing component 134.

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[065] In some embodiments, sensing monitor 120 additionally comprises one or more of the following parameters: an ECG parameter 136; a time parameter 138; a bio-impedance parameter 140; a pressure parameter 142; and a blood oxygen parameter 144. In one aspect, the pressure parameter 142 includes a respiratory pressure component 143. In one aspect, the time parameter 142 tracks time generally (e.g. time intervals, elapsed time, etc.) while in other aspects, the time parameter 142 tracks the time of day in addition to or instead of the general time parameters. In another aspect, the time parameter 142 can be used to activate or deactivate a therapy regimen according to a time of day.

[066] It is also understood that system 100 (Figure 2) would include, or be connected to, the analogous physiologic sensor (e.g., LED-type or optical tissue perfusion oxygen saturation) implanted within or attached to the body of the patient to provide data to each one of their respective parameters (e.g., blood oxygenation parameter 144) of the sensing monitor 120. In some embodiments, sensing monitor 120 also includes a target nerve parameter 146 which represents physiologic data regarding the activity of a nerve to be stimulated, such as the hypoglossal nerve, including specification of the trunk and/or one or more branches of the hypoglossal nerve. In yet other embodiments, sensing monitor 120 also includes an acoustic sensing parameter 147 which represents physiologic data from respiratory airflow or cardiac activity that is sensed acoustically and that is indicative of respiratory effort.

[067] In further reference to Figure 2, therapy manager 106 of system 100 is configured to automatically control initiation, termination, and/or adjustment of a sleep apnea therapy, in accordance with the principles of the present disclosure. Therapy manager 106 also tracks and applies various treatment parameters, such as an amplitude, pulse width, electrode polarity, duration, and/or frequency of a neuro-stimulation signal, in accordance with a treatment protocol programmed into the therapy manager 106.

[068] In one embodiment, therapy manager 106 comprises one or more processing units and associated memories configured to generate control signals directing the operation of system 100, including at least sensing module 102, therapy manager 106, stimulation module 104, and patient management module 108. In particular, in response to or based upon commands received via an input and/or instructions

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contained in the memory associated with the controller in response to physiologic data gathered via the sensing module 102, therapy manager 106 generates control signals directing operation of stimulation module 104 to selectively control stimulation of a target nerve, such as the hypoglossal nerve, to restore airway patency and thereby reduce or eliminate apnea events.

[069] With this in mind, therapy manager 106 acts to synthesize respiratory information, to determine suitable stimulation parameters based on that respiratory information, and to direct electrical stimulation to the target nerve. While any number of physiologic parameters can be used with varying success to detect an apnea, in one embodiment of the present disclosure, the sensing module 102 detects apneas via a thoracic bio-impedance parameter. In particular, a measurement of thoracic impedance is used to track the relative amplitude of the respiratory waveform. Physiologically speaking, the bio-impedance of the lungs varies as the lungs fill and empty with air. Accordingly, thoracic impedance increases during inspiration and decreases during expiration. In another aspect, a varying respiratory drive will also cause the amplitude of the bio-impedance to vary, with a larger respiratory drive increasing the signal amplitude of the bio-impedance.

[070] Upon obtaining the bio-impedance signal, the bio-impedance signal is further processed to identify an average peak amplitude over time. An apnea is detected by further identifying cyclic amplitude variations that occur for a duration substantially similar to the already known duration of a typical apnea event.

[071] For purposes of this application, the term "processing unit" shall mean a presently developed or future developed processing unit that executes sequences of instructions contained in a memory. Execution of the sequences of instructions causes the processing unit to perform steps such as generating control signals. The instructions may be loaded in a random access memory (RAM) for execution by the processing unit from a read only memory (ROM), a mass storage device, or some other persistent storage, as represented by a memory associated with the controller. In other embodiments, hard wired circuitry may be used in place of or in combination with software instructions to implement the functions described. For example, the controller may be embodied as part of one or more application-specific integrated circuits (ASICs). Unless otherwise specifically noted, the controller is not limited to

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any specific combination of hardware circuitry and software, nor limited to any particular source for the instructions executed by the processing unit.

[072] In general terms, the stimulation module 104 of system 100 is configured to generate and apply a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) 65) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager 106.

[073] In general terms, the patient management module 108 is configured to facilitate communication to and from the IPG 109 in a manner familiar to those skilled in the art. Accordingly, the patient management module 108 is configured to report activities of the IPG 109 (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG 109 from an external source, such as a patient programmer, clinician programmer, etc.

[074] In accordance with at least one embodiment of the present disclosure, a stimulation site locator tool 200 of a percutaneous delivery system 201 is schematically illustrated in the plan view of Figure 4. In general terms, the site locator tool 200 is configured to facilitate identifying a target or optimal stimulation site and/or a point of penetration to perform a percutaneous delivery of a stimulation lead near the target stimulation site. As shown in Figure 4, site locator tool 200 includes a needle 210 extending from a handle 212. The needle 210 includes a distal tip 214, needle body 216, and a series of depth markers 218 extending along the needle body 216. The needle 210 extends proximally from the distal tip 214 and through handle 212, terminating at proximal end 219. At proximal end 219, a connection port 236 provides releasable electrical connection between the needle 210 and a stimulation monitor (as later described in more detail), which provides an electrical stimulation signal at distal tip 214.

[075] Referring again to Figure 4, in one aspect, the needle body 216 includes a dielectric coating on its outer surface while a conductive surface of the distal tip 214 is exposed to allow electrical conductivity between the distal tip 214 and the tissue within the body. The depth markers 218 are visible to the eye and may in some

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embodiments, be formed of a material that is readily visible through radiographic and/or ultrasound visualization techniques, as later described in more detail.

[076] Moreover, it is understood that various surgical visualization techniques can be used in association with the embodiments of the present disclosure to assist in determining the location of the site locator tool 200, the stimulation electrode portion, and other components involved in percutaneous delivery of the stimulation lead.

[077] By inserting the site locator tool 200 percutaneously at various locations near or adjacent to the hypoglossal nerve (in cooperation with a stimulation monitor) the path of the hypoglossal nerve is identified based on the type and magnitude of neurogenic responses, such as neuromuscular responses, observed upon application of the test stimulation signal at those various test locations. In this way, those test locations that exhibit a neuromuscular response indicative of a quality nerve capture are used to identify the optimal or target site to place a stimulation electrode portion of a stimulation lead. These observed responses are also used to identify a skin insertion point at which the percutaneous access will be initiated.

[078] In some embodiments, the neuro-stimulation signal is applied at a single stimulation site along the hypoglossal nerve as illustrated in Figure 1 (see stimulation electrode portion 65). However, in other embodiments, the neuro-stimulation signal of a sleep apnea therapy is applied from two or more of multiple locations spaced longitudinally along the hypoglossal nerve. In such an arrangement, the separate, spaced apart stimulation electrode portions can be activated simultaneously or activated at different times. With this in mind, it is understood that the percutaneous access method can be applied to locate more than one site along the hypoglossal nerve to identify placement of several different stimulation electrode portions.

[079] In further reference to Figure 4, in cooperation with the site locator tool 200 a stimulation monitor, such as a nerve integrity monitor 250 (a stand alone monitor or a monitor integrated into a sleep apnea physician programmer 108, such as programmer 108 in Figure 2), is connected to the site locator tool 200 via connector 237. The stimulation monitor is used to aide the physician in determining proper electrode placement via stimulation applied via the site locator tool 200. In one embodiment, an IPG 55 (Figure 1) or IPG 109 (Figure 2) can be used as the

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stimulation monitor. In some embodiments, the stand-alone nerve integrity monitor 250 comprises at least substantially the same features and attributes as the nerve integrity monitor described in U.S. Patent 6,334,068, entitled INTRAOPERATIVE NEUROELECTROPHYSIOLOGICAL MONITOR, issued on December 25, 2001, and which is hereby incorporated by reference in its entirety. In other embodiments, other nerve integrity monitors or an equivalent array of instruments (e.g., a stimulation probe and electromyography system) are used to apply the stimulation signal and evaluate the response of the muscle innervated by the target nerve.

[080] As shown in Figure 4, in some embodiments nerve integrity monitor 250 comprises stimulation module 252 and a response module 254 that includes electromyography monitoring electronics (EMG) 256. In addition, Figure 4 further illustrates a response evaluation array 275, according to one embodiment of the present disclosure. The response evaluation array 275 provides one or more mechanisms to evaluate the effectiveness of a target site for stimulating a target nerve and to identify an entry point for percutaneous delivery of the stimulation electrode portion. In one embodiment, upon stimulation applied at a potential target site, the response array 275 includes: (1) observing or measuring the extent and location (an extension of the base of the tongue is preferred over extension of the tip) of tongue protrusion 278 (indicated by arrow P); (2) observing or measuring the extent of increased cross-sectional area (indicated by arrow W) of an upper respiratory airway 277, with the observation/measurement being performed via endoscopy, ultrasound, or other visualization techniques; and/or (3) measuring the extent of an EMG response 280 (measured via EMG electronics 256 of monitor 250) of one or more muscles.

[081] Accordingly, with this in mind, monitor 250 and one or more aspects of the response array 275 are used to evaluate the positioning of site locator tool 200 relative to a potential stimulation site on a target nerve. In one aspect, a repetitive stimulation pattern is applied from the stimulation module 252 of nerve integrity monitor 250 to the distal tip 214 of site locator tool 200, as the site locator tool 200 is percutaneously inserted into various locations adjacent to the target nerve and into the target nerve. In some embodiments, the applied stimulation pattern is a 1 second burst of stimulation every 3 seconds, a ramping stimulation pattern, and/or a

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physician controlled burst. In another aspect, electromyography (EMG) monitoring electronics 256 of the nerve integrity monitor 250 enables measuring a muscle response to the nerve stimulation applied during the iterative percutaneous insertion of the site locator tool 200. Accordingly, as further shown in Figure 4, fine wire electrodes 282 (or similar) are connected in electrical communication with EMG electronics 256 of the nerve integrity monitor 250 and are used to continuously monitor the muscle activity in response to the stimulation patterns applied via site locator tool 200. Using this arrangement, this closed loop feedback will allow the physician to obtain real-time feedback of a position of the site locator tool 200 (relative to the hypoglossal nerve) and feedback regarding the expected ability of a percutaneously implanted electrode lead to capture the target nerve.

[082] In one embodiment of the present disclosure, as illustrated in Figure 5, a method 300 of treating apnea includes identifying an optimal site to locate stimulation electrode portion 65 (Figure 1) along a length of the hypoglossal nerve that will result in a desired stimulation of the hypoglossal nerve and treatment of sleep apnea. In particular, as illustrated at 302 in Figure 5, the site locator tool 200 is inserted percutaneously (through the skin toward the target nerve) into various test stimulation sites at or around the hypoglossal nerve. For example, as further shown in the diagram 400 of Figure 7A, needle 210 extends through percutaneous access path 408 such that distal tip 214 becomes electrically coupled relative to nerve 410 at one of several potential stimulation sites (e.g., A, B, C) with proximal handle 212 external to skin surface 402. Via surgical navigation techniques, the graduation markers 218 enable measuring a depth of insertion through skin 402 and other subcutaneous tissues 404, 405 surrounding nerve 410. While Figures 4 and 7A illustrate just a few such markers 218 for illustrative purposes, it will be understood that markers 218 would extend along a length or substantial length of needle 210 and that the spacing of such markers 218 may vary from that shown in Figures 4 and 7A. It will be understood that various components of tool 200 and the surrounding tissues are enlarged and/or minimized for illustrative purposes.

[083] At each test site, a pre-determined profile of electrical stimuli is applied to identify one or more optimal or preferred target sites on the hypoglossal nerve. As illustrated at 304 in Figure 5, the optimal or preferred target site are identified from

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among the test sites based observing or measuring at least: (1) a degree of tongue protrusion; (2) the size of cross-sectional area of the upper airway; (3) a best EMG response indicative of maintaining airway patency; (4) a lack of response from non-target muscles; and/or (5) a twitch from the tongue muscle and/or laryngeal muscle. In one aspect, an optimal or preferred target stimulation site is correlated with the greatest impact on maintaining airway patency during inspiration. After identifying a target site, method 300 includes identifying a percutaneous access pathway to the target site. In one aspect, this identification includes identifying a skin entry site (such as D, E, F, or G), which may or may not be directly above the target stimulation site on the hypoglossal nerve. Finally, it is understood that these steps 302 - 306 can be repeated iteratively, as necessary, until all the optimal stimulation locations along the target nerve are identified.

[084] In one aspect, in evaluating various test stimulation sites, it will be understood that the magnitude of the measured response will be indicative how close the site locator tool 200 is to the hypoglossal nerve and/or which part of the hypoglossal nerve is being stimulated. For example, the distance between the site locator tool 200 and the hypoglossal nerve and the strength of the measured response is expressed in decreasing exponential relationship. In other words, as the distance away from the hypoglossal nerve increases, there is an exponential decrease in the magnitude of the measured response. In one aspect, the distance refers to a distance measured in three dimensions relative to the path of the hypoglossal nerve, as any given test site will involve: a lateral distance extending generally perpendicular relative to a longitudinal axis of the target nerve; (2) a vertical distance relative to the target nerve; and (3) a longitudinal distance extending generally parallel relative to a longitudinal axis of the target nerve. With this in mind, it is understood that as multiple potential sites are tested, a pattern is identified that highlights the best or optimal stimulation site(s) from among the test sites. In addition, other surgical navigation techniques can be used in cooperation with the application of the test stimulus to further pinpoint the optimal/preferred stimulation sites via visualizing the site locator tool 200 within the target anatomical environment at the time that the responses are measured.

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[085] In some embodiments, in evaluating multiple potential stimulation sites along the hypoglossal nerve, at each potential stimulation site the method 300 applies the pre-determined electrical stimuli as a stimulation signal with differing values for each signal parameter (e.g., pulse width, electrode polarity, frequency, duration, and amplitude) to determine which combination of values yields the best impact of the stimulation signal upon the target nerve at a potential site. In this way, each potential site is evaluated under conditions in which the stimulation signal would actually be applied were that potential site chosen as an optimal site for stimulation. In one embodiment, this determination of an optimal stimulation site via evaluating each of the stimulation parameters employs therapy module 106 (including IPG 109) in cooperation with stimulation module 104, a site locator tool 200, and patient programming module 108, as previously described in association with Figures 1-4.

[086] In one aspect, an optimal stimulation site identified via the site locator tool 200 is preserved to allow an accurate delivery of the stimulation electrode portion of the stimulation lead to that site. Accordingly, in some embodiments, while maintaining needle 210 in its inserted position in the optimal site along the hypoglossal nerve, handle 212 is removed from needle body 216 while maintaining the distal tip 214 in a coupled relationship to nerve 410, and then a lead introduction tool is slidably advanced over the proximal portion 219 of needle 210 of site locator tool 200 to produce the configuration shown in Figure 7B, as will be further described later.

[087] In general terms, a stimulation lead is inserted percutaneously to result in a distal portion of the stimulation lead being closely adjacent to a target stimulation site of a nerve. In some embodiments, an introducing mechanism is used to initiate and develop a percutaneous access pathway to the target stimulation site and facilitates introduction of the stimulation lead therethrough. While various different shapes and forms of lead introduction tools can be used, Figure 6A illustrates one exemplary embodiment of a lead introduction tool 350. As shown in Figure 6A, lead introduction tool 350 includes a cannula 360 extending through and supported by handle 362. Cannula 360 includes a curved distal portion 375 with a body portion 366 extending proximally from distal portion 375 to a proximal portion 369 within handle 362. In one aspect, cannula 360 includes a series of graduation depth markers 368 to permit measurement of the desired depth of insertion. While Figures

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6A and 7B illustrate just a few such markers 368 for illustrative purposes, it will be understood that markers 368 would extend along a length or substantial length of cannula 360 and that the spacing of such markers 368 may vary from that shown in Figures 6A and 7B. In some embodiments, at least some of the depth markers 368 are also formed of a radiopaque material to enable visualization under fluoroscopy or other visualization techniques to ensure a proper orientation, position, and placement of the cannula 360 relative to a target nerve and/or other tissues, structures, etc. It also will be understood that at least some conductive portions of cannula 360, needle 210 will be visualized under fluoroscopy or other visualization techniques to further aid ensuring proper placement, orientation, and/or position of those respective elements.

[088] As shown in the sectional view of Figure 6B, cannula 360 defines a lumen 370 that extends throughout body portion 366. In general terms, cannula 360 is a generally tubular structure with electrically conductive properties. Accordingly, as shown in Figure 6B, in one aspect, body portion 366 has a dielectric or insulative coating 367 on its outer surface while distal tip 364 of cannula 360 omits a dielectric coating.

[089] In one embodiment, distal tip 364 includes an end opening 390 sized and shaped to facilitate passage of a stimulation lead therethrough. Moreover, curved distal portion 372 is formed of a generally resilient, flexible material. Accordingly, upon slidably advancing cannula body 366 over a pre-placed site locator tool 200, as illustrated in Figures 4 and 7A, curved distal portion 372 assumes a generally straight shape to aid its insertion percutaneously through skin 402 and tissues 404, 405 at an angle generally perpendicular to the hypoglossal nerve, as shown in Figure 7B. In addition, in this position, the proximal portion and/or handle 362 of tool 350 remains external to skin surface 402. It will be understood that in some embodiments, in the absence of site locator tool 200, a stiffener or stylet, as known to those skilled in the art, can be used to maintain the cannula body 366 in a straight configuration during its insertion percutaneously. One generally example of such stylets is described and illustrated in Buckberg U.S. Patent 5,226,427, which is hereby incorporated by reference in its entirety.

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[090] In its straightened shape, cannula 310 has a shape substantially similar to that shown for tool 380 that is later described in association with Figure 6C. Referring again to Figure 6A, once the distal tip 364 is located at a desired depth, the locator tool 200 (or other stiffener) is removed causing the curved distal portion 372 to relax and resume its generally curved shape, as shown in Figure 7C. This relaxation, in turn, orients distal end opening 378 to be generally parallel to the hypoglossal nerve 410 as shown in Figure 7C, thereby assuming a position suitable to direct a stimulation lead to be slidably advanced along the hypoglossal nerve to a desired stimulation site. In some embodiments, upon such relaxation, the distal end opening 378 is oriented at a generally obtuse angle relative to the generally straight proximal portion of the cannula 310.

[091] In some embodiments, as will be understood by those skilled in the art, when identifying the optimal stimulation site (A) from among multiple potential sites (e.g. A, B, C, etc.), the site locator tool 200 would also be used to identify a corresponding entry point (e.g., D, E, F, G, etc.) of the lead introduction tool that is distal or proximal to the optimal stimulation site (e.g., A), as illustrated in Figures 7A-7E. In one embodiment, the spacing (along an axis generally parallel to the hypoglossal nerve) between the entry point at the skin surface (e.g., E) and the optimal stimulation site (A) on the hypoglossal nerve is substantially equal to the distance (D1) that distal end opening 378 extends from the generally perpendicular (relative to the hypoglossal nerve) orientation of cannula body portion 366 when inserted.

[092] In another embodiment, the spacing between the skin entry point and the optimal stimulation site is configured to further account for the length (represented by D2 in Figure 6A) of the stimulation lead (including the electrode portion as represented by dashed lines 395) that would extend out of end opening 378 to deliver the electrode portion of the stimulation lead at the target stimulation site. This arrangement further insures that the final placement of the electrode portion of the stimulation lead accurately corresponds to the previously identified optimal or target stimulation site (e.g. A in Figures 7A-7E). However, it will be further understood that in some embodiments, the distal end of the stimulation lead is positioned to extend beyond the target stimulation site marked at distance D2 to ensure that the target stimulation site remains generally centered along the length of the electrode portion

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(e.g., electrode array 442 of portion 440 as later described in relation to Figure 8A-8C) of the stimulation lead. In such embodiments, the distance D2 corresponds to a length no more than a length of the electrode portion and likely less than (e.g. about one-quarter, one-half, or three-quarters) a length of the electrode portion (e.g. electrode array 442 of portion 440 in Figures 8A-8C).

[093] Accordingly, in this embodiment the total spacing (along an axis generally parallel to a longitudinal axis of the hypoglossal nerve in this region) between the skin entry point and the optimal stimulation site would be the combination of the distances D1 and D2. With this in mind, in one embodiment, after the optimal stimulation site (e.g. A from among A, B, C, etc.) is identified via the site locator tool 200, the site locator tool 200 is used to trace the path of the hypoglossal nerve (or other suitable anatomical landmark) to identify a skin entry point (e.g. E in Figure 7A-7B) for the lead introduction tool 350 that spaced apart from the optimal stimulation site (e.g. A in Figures 7A-7B) by a distance of D1 plus D2.

[094] In one aspect, tracking these distances D1 and D2 greatly enhances the introduction of the stimulation lead to arrive at the optimal stimulation site because of the relative absence of significant anatomical structures (e.g., bone canals, protuberances, etc.) in the region of the hypoglossal nerve that is to be stimulated.

[095] In another embodiment, a lead introduction tool 380 (shown in Figure 6A) includes substantially the same features and attributes as lead introduction tool 350 of Figures 6A-6B, except for including a straight distal portion 382 with a side opening 390 instead of the curved distal portion 372 and end opening 378 shown in Figure 6A. Accordingly, in this embodiment, straight distal portion 382 includes the side opening 390 sized and shaped to facilitate passage of a distal portion of a stimulation lead therethrough. In one aspect, opening 390 is configured as a side-directed, non-coring opening for lumen 370. With this arrangement, upon insertion percutaneously, the cannula body 360 of tool 380 is oriented generally perpendicular relative to the skin and relative to the hypoglossal nerve, with the distal side opening 390 enabling a stimulation lead to exit cannula body 360 in a path extending at a generally obtuse angle relative to the orientation of body 360 (as it percutaneously extends through a skin surface and tissues) and generally parallel to the hypoglossal nerve to be advanced generally parallel to the hypoglossal nerve.

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[096] When using lead introduction tool 380, the distance D1 shown in Figure 6A and Figures 7C-7E is generally not tracked because of the straight shape of distal portion 382 (including tip 384) and because the lead introduction tool 380 is oriented generally perpendicular to the hypoglossal nerve over the optimal stimulation site. However, in one aspect, one can optionally account for the length of the electrode portion of a stimulation lead as it would extend generally outward and away from the distal tip 384 through opening 390 (and generally perpendicular to a longitudinal axis of the cannula body 360). Accordingly, in the embodiment of lead introduction tool 380, in addition to identifying the optimal stimulation site (e.g. A in Figures 7A-7E) with the site locator tool 200, the operator would also identify a skin entry point (e.g. G in Figure 7C) that is spaced by the distance D2 from the optimal stimulation site. The distance D2 generally corresponds to the length of the stimulation lead (including the electrode portion) that would extend out of distal side opening 390 to deliver the electrode portion of the stimulation lead at the target stimulation site. In this way, the operator insures that the electrode portion of the stimulation lead is accurately delivered to the identified target stimulation site (e.g. A). As noted previously, the distance D2 would have a length no more than, and likely less than, a length of the electrode portion (such as electrode array 442 in Figure 8B) to ensure centering the electrode portion relative to the target stimulation site.

[097] In some embodiments, the stimulation lead (e.g., stimulation lead 430 as will be described in association with at least Figures 8A-8E) is configured to be cooperable with a removably attachable stylet to facilitate advancing the stimulation lead through cannula 380 and through the tissue surrounding the target stimulation site. In particular, as the distal portion of the stimulation lead exits the distal side opening 410, the distal portion 436 will have to be advanced via tunneling through the surrounding tissue. With this in mind, the stylet will provide rigidity as the stimulation lead is tunneled to the target stimulation site and once the stimulation lead is properly positioned, the stylet is removed from its connection to the stimulation lead. Moreover, in some embodiments, this stylet is also used to selectively deploy an anchoring mechanism associated with the electrode portion of the stimulation lead.

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[098] In some embodiments, the cannula of lead introduction tool 350 or 380 is generally non-conductive and the conductive elements of the site locator tool 200 and/or of the stiffener are used as an electrically conductive pathway to confirm the location of the target stimulation site and/or the location of the skin entry point spaced from the target stimulation site.

[099] In some embodiments, other types of introducing mechanisms are used to establish a percutaneous access pathway for a stimulation lead. For example, one introducing mechanism includes a guide wire and a needle having a cannula and a stylet. With this arrangement, the needle cannula is percutaneously inserted to establish a percutaneous pathway with aid from the stylet to steer, guide, and/or stiffen the needle cannula. After a path is established by the combination of the cannula and stylet, the stylet is removed. With the cannula still in place, a guide wire is inserted into a proximal portion of the cannula and advanced through the cannula until a distal portion of the guide wire is adjacent the target stimulation site. Next, with the guide wire still in place, the cannula portion of the needle is removed proximally over the guide wire, leaving just the guide wire in place. Using known techniques, a stimulation lead is releasably coupled to the guide wire and advanced, via the guide wire, through the established percutaneous access pathway until an electrode portion of the stimulation lead is adjacent the target stimulation site. With the stimulation lead remaining in place, the guide wire is then removed. Finally, the stimulation lead is anchored to maintain the electrode portion in an electrically coupled relationship with the target stimulation site of the nerve.

[0100] While various different shapes and forms of leads can be used in the methods and systems of the present disclosure, Figures 8A-8C illustrate one exemplary embodiment of a stimulation lead 430 is that is configured to be deployed percutaneously. In one embodiment, the stimulation lead 430 is delivered via the tools 200, 350, 380 (as previously described in association with Figures 4-7) while in other embodiments, the stimulation lead 430 is delivered via other minimally invasive delivery techniques. Various aspects of the delivery of stimulation lead 430 will be described herein in further detail.

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[0101] As shown in Figures 8A-8C, stimulation lead 430 includes a front side 432 and a back side 434 with the lead 430 extending between a distal portion 436 and a proximal portion 438.

[0102] At distal portion 436, the front side 432 supports an electrode portion 440 including a first array 442 of electrodes 444. In general terms, substantially the entire length of the electrode portion 440 comprises a generally flat surface and when the back side 434 also forms a generally flat surface, then the entire distal portion 436 defining the electrode portion 440 comprises a generally flat or planar member (with the exception of the to-be-described protrusions 464 on back side 434).

[0103] This generally flat or planar configuration of distal portion 436 (including stimulation electrode portion 440) provides a low profile topography, thereby facilitating its advancement through the tissue surrounding the hypoglossal nerve. In addition, by having at least a generally flat surface of the front side 432 of distal portion 436, a much closer and effective interface between the stimulation electrode portion 440 and the surface of the hypoglossal nerve can be achieved. However, in some other embodiments, the front side 432 of the distal portion 436 is not generally flat, but has at least some curved portion or undulating portion. In one example, as illustrated in Figure 8F, the curved portion of the front side 432 of the distal portion 436 forms a generally concave shape configured to accentuate the extent to which the electrode portion 440 reciprocally conforms to the generally arcuate shape of the outer surface of the hypoglossal nerve. In another example, as illustrated in Figure 8G, the front side 432 of the distal portion 436 forms a generally convex shape. In one aspect, this generally convex shape is configured to accentuate slidable passage of the distal portion through the tissue surrounding the hypoglossal nerve to arrive at the optimal stimulation site

[0104] Likewise, in some embodiments, the back side 434 of the distal portion 436 is not generally flat, but has at least some curved portion which can be concave or convex. In one aspect, a generally convex shape on the back side 436 is configured to accentuate slidable passage of the distal portion through the tissue surrounding the hypoglossal nerve to arrive at the target stimulation site.

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[0105] In another aspect, because the front side 432 carries electrode portion 440, the back side 434 of the distal portion 436 is generally made or coated with an electrically insulative material. With this arrangement, back side 434 effectively acts as a shield to prevent the stimulation signal from affecting the sensory nerves and skin overlying the stimulation site.

[0106] In another aspect, at proximal portion 438 of stimulation lead 430, a second array 450 of electrodes 452 is formed on both the front side 432 and the back side 434 of stimulation lead 430. The first array 442 of electrodes 444 are electrically connected to the second array 450 of electrodes 452 with the second array 450 of electrodes 452 configured to provide electrical connection to the IPG (55 in Figure 1 or 109 in Figure 2). Via control from the IPG 55, each electrode 444 of stimulation electrode portion 440 is independently programmable to apply a stimulation signal that has a selectively controllable polarity, amplitude, frequency, pulse width, and/or duration.

[0107] In one embodiment, the first array 442 of electrodes 444 includes a lateral component (i.e., extending along a width W1) or a longitudinal component (i.e., extending along a length L1) of at least three electrodes in a guarded cathode electrode polarity arrangement. This guarded cathode electrode polarity arrangement hyperpolarizes tissues near the hypoglossal nerve while providing for complete depolarization of the volume of the hypoglossal nerve adjacent the electrode portion 440 of the stimulation lead 430. However, as shown in Figure 8B, in some embodiments, the first array 442 includes a multitude of electrodes 444 (substantially greater than three) extending along the width and along the length of the electrode portion 440. This arrangement permits selection of different combinations of electrodes 444 from among the first array 442, thereby optimizing the stimulation of the hypoglossal nerve via an optimal combination of electrodes 444 within the first array 442. Moreover, in some embodiments, one or more of the electrodes 444 are varied in shape and/or pitch, or varied by staggering of the rows of electrodes 444.

[0108] In some embodiments, with the assumption that a diameter of the target nerve in the region of the target stimulation site is about 3 millimeters, the electrode portion 440 will have a width (W1 in Figure 8B) of at least about 5 millimeters. Accordingly,

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in these embodiments, the width (W1) of the electrode portion 440 is at least substantially equal to or substantially greater than the diameter of the target nerve in the region of the target stimulation site. This relationship insures that the electrical stimulation signal (for treating sleep apnea) will affect the full cross-section of the nerve so that substantially all the axons of the target nerve will potentially be activated (depending upon the parameters of the applied stimulation signal).

[0109] A body portion 437 extends between the electrode portion 440 (at the distal portion 436) and the proximal portion 438. With the exception of electrodes 444, the body portion 437 is a generally insulative member devoid of electrodes on the front side 432 and back side 434. It is understood, of course, that wires extend through an interior of the body portion 437 to connect electrodes 444 to the IPG (55 in Figure 1 or 109 in Figure 2). In general terms, the body portion 437 has a length sufficient to extend from the electrode portion 440 to the IPG 55 (Figure 1).

[0110] In some embodiments, the distal portion 436 of stimulation lead 430 includes an anchoring mechanism 462 located on back side 434, i.e. on an opposite side relative to the stimulation electrode portion 440. In one aspect, the anchoring mechanism 462 provides a cuff-less arrangement to secure the electrode portion 440 in close proximity to the nerve with the anchoring mechanism being disposed on an opposite side of the electrode portion 440 so that the anchoring mechanism 462 faces away from the nerve. This arrangement secures the electrode portion independently of the nerve and in a desired position relative to the nerve without placing any pressure or other mechanical effects on the nerve that might otherwise be used to secure an electrode relative to a nerve.

[0111] In one aspect, the anchoring mechanism 462 includes at least one array of protrusions 464. In one embodiment, the protrusions 464 are flaps formed of a resilient material while in other embodiments, the protrusions 464 are barbs, prongs, or other anchoring components. In some of these embodiments, the protrusions are sized and shaped to induce fibrotic growth at and near the protrusions to cause further anchoring of the distal portion 436 of the stimulation lead 430. In one aspect, within about one month, the protrusions 464 become ingrown with fibrotic tissue. Accordingly, while the protrusions 464 act to provide some long-term stability to the position of stimulation lead 430 within the body, one purpose of the protrusions 464

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is to provide such stability for at least about one month, which generally corresponds to the amount of time for fibrotic tissue growth to effect a more permanent, long term stabilization of electrode portion 440 at the target site within the body.

[0112] In one aspect, the protrusions 464 extend generally outward at an angle (e.g., 30, 45, 60 degrees) from a surface of the back side 434 of the distal portion 436 of the stimulation lead 430. As shown in Figures 8A and 8B, in some embodiments, at least one pair of the protrusions 464 are provided in a divergent orientation which enhances the stability of the stimulation lead 430 by reducing the likelihood of the stimulation lead 430 from migrating away from its placed location. In particular, once implanted, the divergent orientation of the protrusions 464 enhance maintaining the electrode portion 440 of the stimulation lead 430 in its target location regardless of the direction of applied forces on the stimulation lead. In one aspect, the protrusions 464 have a length and width configured to engage or integrate with the tissues surrounding the hypoglossal nerve. However, in another aspect, the protrusions 464 form a generally tab-like structure made of a flexible polymer that can collapse upon application of a sufficiently high force, thereby enabling adjustment of the position of the electrode portion 440 of the stimulation lead 430 and/or removal of the stimulation lead 430.

[0113] In some embodiments, the protrusions 464 are sized and shaped to facilitate their disengagement from the surrounding tissues (via the use of a tool) to enable removal of the electrode portion 440 of the stimulation lead 430 from its implanted location adjacent the hypoglossal nerve. Such removal would take place in the event that a trial treatment plan was ineffective or in the event that the stimulation lead 430 was malfunctioning.

[0114] However, in the event that only some of the electrodes 444 were malfunctioning, the stimulation lead 430 need not be removed because the IPG 55 of Figure 1 (or IPG 109 in Figure 2) can be used to activate a different set of electrodes 444 within the first array 442 to produce a new combination of electrodes 444 arranged to apply a therapeutic regimen for treating sleep apnea. Moreover, an adjustment of the stimulation parameters (e.g., amplitude, pulse width, frequency, duration, and electrode polarity) via the IPG 55, 109 can compensate for the different position of the electrodes in the new combination of activated electrodes 444 for

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applying the stimulation signal. In this embodiment, the many varied positions of the electrodes 444 both along the length of the distal portion 436 of the electrode portion 440 of the lead 430 and transversely across the distal portion 436 enables precise activation of selective groups of electrodes 444 (at their various spaced apart locations) to produce an effective stimulation signal. Likewise, in the event that some inadvertent migration of the stimulation lead 430 occurs distally or proximally relative to the optimal stimulation site after the stimulation lead 430 has been considered to be properly placed, then the IPG 55 (or IPG 109 in Figure 2) is used to activate a different set of electrodes 444 of the first array 442 to achieve a stimulation signal that compensates for the migration to maintain a proper stimulation signal at the target stimulation site.

[0115] The stimulation lead 430 is configured to balance various parameters including optimal electrode orientation, patient comfort, anchor strength, preventing migration of the lead, and providing for removability of the lead, as well as facilitating subcutaneous tunneling of the stimulation lead 430 to the site of the IPG. As such, this stimulation lead 430 provides several advantageous features, including providing for stimulation of the entire cross-sectional volume of the hypoglossal nerve volume in a manner comparable with cuff electrodes. Moreover, by facing the electrodes 444 away from the skin and by backing the electrodes 444 with an insulative layer (body portion 437), the stimulation lead 430 minimizes stimulation of nearby sensory nerves. In addition, by having an array 442 of multiple electrodes 444 that are independently programmable or controllable relative to each other via operation of IPG 55, the therapy can be adjusted in a non-invasive manner in the event that the stimulation lead 430 migrates from its original placement. In other words, the stimulation can be shifted from one combination of electrodes 444 in the array 442 to a different combination of electrodes 444 in the array 442 to account for the shift in the overall position of the electrode portion 440 of the stimulation lead 430 relative to the hypoglossal nerve. Of course, it will be understood that different combinations of electrodes 444 can be activated simply to achieve a different therapy regimen, even in the absence of migration or malfunction of electrode array 442.

[0116] In use, the stimulation lead 430 is delivered percutaneously via feeding the distal portion 436 into a proximal portion 369 of the cannula 360 of lead introduction

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tool 350 or 380 and slidably advancing the distal portion 436 therethrough until the distal portion 436 of stimulation lead 430 exits the distal opening (390 or 410, respectively) of the lead introduction tool 350, 380 to be oriented generally parallel and closely adjacent to the hypoglossal nerve at a target stimulation site (e.g. A) with the electrode portion 440 facing toward the nerve and away from the skin (and underlying sensory nerves), as illustrated in Figure 7D. Next, while maintaining the position of the distal portion 422 (e.g. electrode array 442 in Fig. 8B) stimulation lead 430, the tool 350 is withdrawn proximally from tissues 404, 405 to leave just stimulation lead 430 in place, as illustrated in Figure 7E. From this configuration, the proximal portion 421 of stimulation lead 430 is tunneled and/or maneuvered subcutaneously to extend from the neck region to a pectoral region, to achieve a general configuration similar to that shown in Figure 1 for lead 52.

[0117] In some embodiments, as shown in perspective view of Figure 8D and the sectional view of Figure 8E, a distal tip 364A of a lead introduction tool 350A includes a shell-like cover 480 protruding distally outward from the cannula body 360A and is configured with a wall 482 to control the deployment of the protrusions 464 of the anchoring mechanism 462 of stimulation lead 430. In particular, the wall 482 of cover 480 acts as a barrier to maintain the protrusions 464 in a collapsed position against or close too the back side 434 of the distal portion 436 of the stimulation lead 430 so that the protrusions 464 do not engage the surrounding tissue prior to proper positioning of the stimulation electrode portion 440 against the hypoglossal nerve. At the same time, the distal portion 364 continues to define an opening 365A generally opposite the cover 480 to enable exposing the electrode array 442 to the target nerve to allow testing or confirming positioning over the target stimulation site prior to deploying the anchor mechanism 462. In some embodiments, the cover 480 defines a half-circular cross-sectional shape having a diameter (D3) generally corresponding to a diameter of cannula 360. Once proper positioning of the stimulation electrode 440 has been achieved and upon proximally withdrawing the tool 350A, the cover 480 is withdrawn from its position over anchoring mechanism 462, thereby releasing protrusions to engage surrounding tissues. Likewise, in the event that the stimulation lead 430 must be removed, the cover 480 of the lead introduction tool 350 will force the collapse of the protrusions 464 (against the body of the distal portion 436 of the stimulation lead 430) as the

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distal portion 436 of the stimulation lead 430 is withdrawn proximally into the lead introduction tool 350A.

[0118] In another aspect, once implanted, a stimulation system for automatically treating obstructive sleep apnea will preferably remain in a stable position to endure the normal activities of the patient. For example, the neck of a patient moves through a wide range of motion through many different positions. To counteract the potential for a stimulation lead to move back and forth along the hypoglossal nerve (relative to a desired stimulation site), the anchoring mechanism 462 anchors the distal portion 436 of the stimulation lead 430 at the target stimulation site of the nerve. Accordingly, this anchoring mechanism insures that proper placement of the stimulation lead is maintained despite the dynamic motion and varying positions of the neck, which could otherwise cause inadvertent repositioning of the stimulation lead (relative to the target nerve) if the distal anchoring mechanisms were not present.

[0119] In addition, as previously noted, the anchoring mechanism 462 maintains this stable position without encircling the nerve (as a conventional cuff would) via an anchoring mechanism located on a directly opposite side of the distal portion 436 of the stimulation lead 430 with the anchoring mechanism 462 engaging the surrounding tissue instead of engaging the nerve. Nevertheless, to the extent that the electrode portion 440 of the distal portion 436 remains in close proximity or contact with the nerve, this relationship also contributes to the stability of the distal portion 436 because the anchoring mechanism 462 (on the opposite side from the electrode portion 440) is simultaneously securing the distal portion 436 in its desired position.

[0120] Accordingly, in some embodiments, as shown in Figure 9, a second anchoring mechanism 502 and/or third anchoring mechanism 504 is deployed to further stabilize the position of the stimulation lead 430 in addition to the first anchoring mechanism 462. As shown in Figure 9, body portion 437 of stimulation lead 430 extends proximally from the electrode portion 440 and from the first anchoring mechanism 462 while the second anchoring mechanism 502 is positioned at a first distance (D3) away from the first anchoring mechanism 462. The third anchoring mechanism 504 is spaced proximally by a second distance (D4) from the second

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anchoring mechanism 502. As further shown in Figure 9, a first region 510 (including portion 437) of simulation lead 430 extends between first anchoring mechanism 462 and second anchoring mechanism 502 while a second region 512 extends between second anchoring mechanism 502 and third anchoring mechanism 504. Finally, a third region 514 of lead 430 extends proximally from third anchoring mechanism 504 for passage toward the IPG (55 in FIG. 1 or 109 in FIG. 2).

[0121] In some embodiments, both the first region 510 and the second region 512 of the lead body 437 are pre-shaped into a serpentine or S-shaped configuration prior to deployment. In this pre-shaped configuration, first region 510 has a first length (D3) while second region 512 has a second length (D4). Once deployed via tunneling subcutaneously in a pathway proximally from the stimulation site, the S-shaped first and second regions 510, 512 provide strain relief mechanisms that act in concert with the first, second, and third anchoring mechanisms 462, 502, 504 to stabilize the position of the stimulation lead 430 while compensating for movements of the body as described above.

[0122] Figure 10 is a side plan view of a stimulation lead including a dynamic anchoring system 525, according to an embodiment of the present disclosure. As shown in Figure 10, system 525 includes a first anchor 530, second anchor 532, and a third anchor 534 with portions 510 and 512 of a stimulation lead interposed between the respective anchors. In one embodiment, one, two, or three of the anchors 530, 532, 534 include a biomediating mechanism, that is, a mechanism to induce fibrotic growth in the surrounding tissue at which the respective anchor is located and thereby further anchor the distal portion of a stimulation lead. As shown at 540 in Figure 10, the anchors 530-534 comprise one or more of tines, mesh (e.g. Dacron mesh), barbs, flaps, and the like that are configured to mechanically engage the surrounding tissue.

[0123] In addition, in some embodiments, one or more of the anchors 530, 532, 534 are configured to provide a surface sized or treated (coated) to induce fibrotic growth to further secure the anchor. The "biomediating" anchors are particularly advantageous in a method of percutaneous delivery because the anchors do not require suturing, and therefore, regions 514, 512, and 510 of the stimulation lead can be tunneled toward the IPG 55 in FIG. 1 (or IPG 109 FIG.2) without having to apply

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sutures when the anchors 530, 532, 534 arrive at their intended positions. However, it is understood that in some embodiments, minimally invasive suturing techniques can be applied as desired to further secure the respective anchors in place (during the initial period of fibrotic growth) to supplement the securing strength of the mechanical component (e.g., barbs, flaps, etc.) of the respective anchors.

[0124] Figures 11-14 schematically illustrate a method 550 of percutaneously delivering an electrode portion of a stimulation lead to a target nerve, according to an embodiment of the present disclosure. In viewing the Figures 11-14, it will be understood that sizes and/or relative spacing of various components of the anatomy (e.g., a size or width of incision, nerves, muscles, skin layer, etc.) and/or components of the tools (e.g., barbs, rods, etc.) have been exaggerated for illustrative clarity to highlight application of the tool. This method achieves placement of the electrode portion without the generally disruptive, and more time consuming, conventional cut-down implantation procedure (which would typically include a full dissection around the target nerve). Moreover, it is understood that prior to deployment of method 550, one or more optimal stimulation sites on the hypoglossal nerve have been identified via a site locator tool (e.g. site locator tool 200) or via other tools. It is also understood that one or more surgical navigation techniques are used to: (1) employ the site locator tool to identify the optimal stimulation site; (2) make an incision to provide a skin entry point generally over the optimal stimulation site; and (3) guide the distal portion of an introduction tool or implantation instrument to that optimal stimulation site.

[0125] As shown in Figure 11, method 550 includes making an incision 553 through the skin 552 and through first muscle layer 554 to provide access to the previously identified optimal stimulation site at target nerve 558, such as the hypoglossal nerve. The incision is relatively small, such as 2 centimeters wide, so that the access to the nerve 558 is considered minimally invasive. Next, via use of an implantation instrument 560, an electrode portion 565 of a stimulation lead 568 is inserted through the incision 553 and guided to the nerve 558. As shown in Figure 12, the implantation instrument 560 includes a distal tip 562 from which a selectively deployable, engagement mechanism 570 protrudes and a barrel 563 extending proximally between a handle 564 and distal tip 562. The barrel 563 is configured to

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support deployment of the engagement mechanism 570. A trigger 561 mounted at handle 564 is connected to a proximal end of the engagement mechanism 570 and controls selective deployment of the engagement mechanism 570.

[0126] Moreover, in one embodiment, as shown in Figure 13, the electrode portion 565 comprises an insulative carrier 580 supporting an array of spaced apart electrodes 582 aligned in series. The carrier 580 also includes an array of securing elements 584A, 584B, 584C, 584D extending outward from the sides and/or ends of the carrier 580 to facilitate securing the carrier 580 relative to the surrounding tissues adjacent the hypoglossal nerve. The securing elements 584A-584D can be loops or any other structure to which a suture or fastener is securable relative to the surrounding tissue. In this way, the electrodes 582 of the electrode portion 565 become secured relative to nerve 558 with the electrodes 582 facing the nerve 558. In one embodiment, the electrodes 582 are aligned with a longitudinal axis of the electrode portion 565 and/or of the stimulation lead supporting the electrode portion 565. As previously noted, the electrode portion 565 is implanted so that the electrodes 582 also face away from the skin 552 (with carrier 580 acting as a shield) to minimize stimulation of sensory nerves at or near the skin 552.

[0127] In one aspect, as shown in Figure 13, the electrodes 582 have a width W2 (at least 3-5 millimeters) generally equal to or greater than a diameter of the target nerve (e.g., 3 millimeters) while carrier 580 has a width (W3) substantially greater than the width W2 of the electrodes 582 to insure shielding of the skin from the stimulation signal emitted from electrodes 582.

[0128] Referring again to Figure 11, once the electrode portion 565 is properly positioned over the nerve 558, the implantation instrument 560 secures the electrode portion 565 in position relative to the nerve 558 via enagement mechanism 570. While the engagement mechanism 570 can take many different forms, in one embodiment shown in Figure 14, the anchoring mechanism 570 protrudes from the distal portion 562 of barrel 563 of implantation instrument 560.

[0129] In particular, the anchoring mechanism 570 includes one or more small diameter rods 572 extending longitudinally within a conduit formed by barrel 563 with each rod 572 supporting a needle 574 configured to selectively extend distally from

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an end of each respective rod 572. In one embodiment, barrel 563 includes a generally hollow, elongate tubular member, and the rods 572 extend through a length of the barrel 563 while being longitudinally movable within the barrel 563.

[0130] Each needle 574 includes a barb 576 removably mounted at a distal end 575 of the needle 574. In one embodiment, barbs 576 are made from a stainless steel material or a plastic material while having a relatively small length and/or diameter (e.g., 1 -3 millimeters) to avoid patient discomfort. In addition, a suture 575 includes a first end connected to the barb 576 and a second end connected to securing elements 584 of electrode portion 565 of the stimulation lead. In a pre-deployment state, the respective sutures 575 are in a relaxed state without tension. In one embodiment, needles 574 are formed of a metal, such as a Nitonol material.

[0131] Accordingly, with the electrode portion 565 positioned over an optimal stimulation site of the nerve 558, trigger 561 activates anchoring mechanism 570 to automatically cause the rods 572 to force the needles 574 to protrude distally outward and penetrate into surrounding tissues adjacent the nerve 558 and electrode portion 565, and then the trigger 561 is subsequently relaxed causing retraction of rods 572 and their respective needles 574. However, the barbs 576 remain fixed in the surrounding tissues because they detach from the needles 574 (at a point of detachment represented by dashed lines 579) as the needles 574 are retracted. At this point, the implantation instrument 560 is removed from the incision site, leaving the electrode portion 565 in place.

[0132] In one aspect, as the needles 574 are advanced to place the barbs 576 into the tissue the sutures 575 become under tension, and as the needles 574 are retracted into barrel 563 with the barbs 576 remaining in the tissue, the sutures 575 remain under tension which effectively exerts tension on the carrier 580 to urge electrodes 582 into pressing contact against the nerve. For example, as schematically illustrated in the side view of Figure 14B, with barbs 576 deployed in tissue 590, securing elements 584B, 584D (and their respective sutures 575) are under tension, thereby urging electrode portion 565 (and particularly electrodes 582) against the nerve 592. This arrangement provides longitudinal stability to the secured position of the electrode portion 565 relative to the nerve. While not shown it is understood that the securing elements 584A, 584C on the opposite side of the

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electrode portion 565 also would be deployed via sutures 575 and barbs 576 so that all four securing elements 584A, 584B, 584C, 584D of electrode portion 565 are deployed. Accordingly, when secured under tension relative to the tissue 592 (via sutures 575 and barbs 576), securing elements 584A and 584C also provide longitudinal stability to the position of the electrode portion 565 relative to the nerve 590.

[0133] Moreover, in such an arrangement, securing element 584A and securing element 584B are positioned on opposite sides of the electrodes 582 to straddle the nerve 592, thereby insuring lateral stability of the electrode portion 565. Likewise, securing element 584C and securing element 584D are positioned on opposite sides of the electrodes 582 to straddle the nerve 592, thereby insuring lateral stability of the electrode portion 565.

[0134] In some embodiments, as shown in Figure 14B, the securing elements 584 are made of a flexible material to permit their bending toward the tissue to facilitate securing the barbs 576 and sutures 575 under tension. In these embodiments, the carrier 580 supporting the securing elements 584 can be either substantially rigid as shown in Figure 14B or can be generally flexible as shown in Figure 14C. In particular, as shown in the schematic sectional view of Figure 14C, an electrode portion 565 includes a flexible carrier 581 supporting electrodes 582 with the carrier 581 configured to flexibly conform to the arcuate shape of the cross-section of the nerve 558. This arrangement insures close contact of the electrode 582 relative to the nerve 558 and accentuates the application of tension on sutures 575 when barbs 576 are anchored into the surrounding tissue 590. In another aspect, it will be clear from a consideration of both Figures 14B and 14C, the securing elements include a first array of barbs for deployment on one side of the electrode portion 565 and a second array of barbs for deployment on an opposite side of electrode portion 565.

[0135] After securing the electrode portion 565, the implantation instrument 560 is removed and the lead body 567 of the stimulation lead 568 is delivered subcutaneously, via a tunneling tool, from the anchored site of the electrode portion 565 to the IPG 55 (Figure 1).

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[0136] Various configurations of stimulation electrode portions of a stimulation lead are described and illustrated in association with the embodiments of Figures 15-27. These various stimulation electrode portions can be delivered percutaneously or via other suitable delivery techniques. In some embodiments, the electrode portions and/or supporting proximal portions of the stimulation lead are configured to have a minimal mechanical impact on the nerve and the surrounding tissues and/or are configured to be implanted via minimally invasive techniques.

[0137] Figures 15-17B schematically illustrate stimulation system including a bio-absorbable electrode portion 601 of a stimulation lead 600, according to an embodiment of the present disclosure. It is understood that prior to deployment of electrode portion 600, one or more optimal stimulation sites on the hypoglossal nerve have been identified via a site locator tool (e.g. site locator tool 200 shown in Figure 3) or via other tools. It is also understood that one or more surgical navigation techniques are used to: (1) employ the site locator tool to identify the optimal stimulation site; and (2) place the electrode portion at that optimal stimulation site.

[0138] As shown in Figure 15, stimulation lead 600 comprises an electrode portion 601 including cuff 602 and electrodes 610, as well as wires 612, anchor 614, and non-absorbable portion 620 of stimulation lead 600. In one embodiment, the cuff 602 comprises a generally elongate tubular member that carries electrodes 610 and is configured to wrap around nerve 625 in a releasably secured manner with a generally cylindrical shape, thereby maintaining electrodes 610 in close contact against nerve 625. A wire 612 extends proximally through the cuff 602 from each of the respective electrodes 610 and has a length extending further to anchor 614 and non-absorbable portion 620 so that the wires 612 are in electrical communication with IPG 55 (Figure 1).

[0139] In some embodiments, as shown in Figure 17A, each electrode 610 includes a conductive contact portion 616 and an electrically insulative cover 618. The electrically insulative cover 618 extends over the top portion 639 of the contact portion 616, extends beyond all four sides of contact portion 616, including sides 635, 637 viewable in Figure 17A. At a proximal end 634 of the electrode 610, a strain relief member 636 connects wire 612 to contact portion 616 via wire 611. In

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one embodiment, electrodes 610 are embedded in the cuff 602 with bottom portion 638 exposed at inner surface of cuff 602. In some embodiments, electrodes 610 are aligned such that a longitudinal axis of each electrode 610 is generally perpendicular to a longitudinal axis of the cuff 602 and the respective electrode 610 are spaced apart from each other along a length of the cuff 610.

[0140] In one aspect, cuff 602 is made of a bio-absorbable material so that over a period of several weeks following the implantation of electrode portion 601, the cuff 602 is absorbed by the body, thereby leaving the electrodes 610 in their desired position relative to nerve 625. At the same time that the cuff 602 is being absorbed, tissue growth occurs at and around the wires 612 and occurs at and around the electrodes 610 as they become exposed from absorption of cuff 602. In some embodiments, wires 612 are arranged with several coiled portions 613 (highlighted in the enlarged caption in Figure 15) to further induce fibrotic tissue growth at and around the wires 612 such that tissue growth at each coiled portion acts as a separate anchor. After the absorption process for cuff 602 (and any other bio-absorbable components) is complete, the fibrotic tissue growth is sufficient to act as an anchoring mechanism to maintain the position of the electrodes 610 in their generally spaced apart relationship at the intended stimulation site and to secure the wires 612 to further maintain the position of electrodes 610. The resulting arrangement is illustrated in Figures 16 and Figure 17B. In the sectional view of Figure 17B, fibrotic tissue growth 642 surrounds the electrode 610 and wires 612 to mechanically secure the electrodes 610 in position over nerve 625 beneath skin/muscle portion 640. As further shown in Figure 17B, insulative cover 618 protects each electrode 610 from the tissue growth 642. In one aspect, the insulative cover 618 covers a top portion and sides of each electrode 610 while a bottom portion of each electrode element 610 remains exposed to nerve 625. In some embodiments, the outer surface of insulative cover 618 includes a coating configured to induce the fibrotic tissue growth.

[0141] In one aspect, by employing a bio-absorbable cuff and inducing tissue growth to secure electrodes 610, this system provides minimal long-term impact at the implantation site. In particular, the implanted, cuff-less set of electrodes 610 will be comfortable for the patient because of the absence of the relatively bulky size of a

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conventional cuff. This cuff-less arrangement also will be less likely to induce inadvertent mechanical effects on the target nerve (as compared to a conventional cuff electrode system), which can affect nerve function and comfort.

[0142] In some embodiments, anchor 614 is also made of bio-absorbable material and is absorbed over time within the body. Accordingly, tissue growth also would occur in this region to further secure wires 612 in place.

[0143] However, in some embodiments, as shown in Figures 15-16, the stimulation lead 600 includes a non-absorbable fastener 622 configured to maintain the separate wires 612 in a grouped arrangement. In one aspect, fastener 622 insures an orderly transition of the separate wires 622 to the permanent lead portion 620 that extends to the IPG 55 (Figure 1). In another aspect, fastener 622 also provides strain relief to prevent inadvertent pulling of wires 612 on the target nerve. However, in other embodiments, this fastener 622 is omitted or is made of a bio-absorbable material.

[0144] Figures 18-21 schematically illustrate a bio-absorbable electrode portion 650 of a stimulation lead, according to an embodiment of the present disclosure. It is understood that prior to deployment of electrode portion 650, one or more optimal stimulation sites on the hypoglossal nerve have been identified via a site locator tool (e.g. site locator tool 200) or via other tools. It is also understood that one or more surgical navigation techniques are used to: (1) employ the site locator tool to identify the optimal stimulation site; and (2) place the electrode portion at that optimal stimulation site. Finally, it is also understood that the electrodes 660 of electrode portion 650 would be electrically connected via wires and a lead body to an IPG 55 (Figure 1) and that this general arrangement is omitted in Figures 18-21 for illustrative clarity.

[0145] Figures 18-19 are plan views of an electrode portion 650 of a stimulation lead in which the electrode portion 650 includes a generally flexible coil member 651 and electrodes 660. In general terms, the coil member 651 wraps around a nerve 663 and defines a stent-like insulative member that maintains electrodes 660 in close contact against nerve 663. However, unlike a conventional cardiovascular stent which is deployed within a blood vessel via expanding the stent outward against the

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wall of the blood vessel, the coil member 651 is configured to wrap around an outer surface of a nerve 663 in a self-sizing relationship and is not configured to expand radially when deployed in the desired position.

[0146] In some embodiments, the coil member 651 forms a generally helical shape and includes a pair of spaced apart rails 652 with numerous struts 654 extending between and interconnecting the rails 652. In one embodiment, the rails 652 and struts 654 are made of non-conductive materials. In one aspect, electrodes 660 are sized and shaped to extend between a pair of rails 652, as shown in Figures 18-19, in a manner similar to the struts 654. In one embodiment, the electrodes 660 are in general alignment with a longitudinal axis of the coil member 651. However, it will be understood that the coil member 651 is not strictly limited to the arrangement of rails 652 and struts 654 shown in Figures 18-19 because numerous variations and arrangements of struts can be used to form the helically shaped coil member.

[0147] As shown in its pre-deployment state in Figure 18, coil member 651 has an inner diameter (D6) that is substantially less than a diameter (D5) of the target nerve 663 (see also Figure 19). Accordingly, when coil member 651 is placed about the larger diameter nerve 663, the coil member 651 wraps about the nerve 663 in a self-sizing manner such that the inner diameter of the coil member 651 substantially matches the diameter of the target nerve 663, as shown in Figure 19. To the extent that any spacing is shown between the coil member 651 and nerve 663 in Figure 19, this spacing is provided for illustrative clarity to clearly define the components of the coil member 651 separately from nerve 663.

[0148] In some embodiments, the coil member 651 attracts tissue growth at rails 652 and struts 654 with the combination of the tissue growth and the rails 652 and struts 654 acting as an anchoring mechanism to maintain the electrodes 660 in close contact against nerve 663.

[0149] In some other embodiments, the coil member 651 forms a bio-absorbable material so that after absorption of rails 652 and struts 654 takes place, electrodes 660 remain in close contact to nerve 663 with tissue growth 670 on and around the electrodes 660 holding the electrodes 660 in place relative to the nerve 663, as shown in Figures 20-21. The various components (struts and rails) of the coil

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member 651 form a latticework or frame configured to induce fibrotic tissue growth in a pattern generally matching the structure of the coil member 651 so that the induced tissue growth forms in a mechanically advantageous framework holding the electrodes 660 in place relative to the nerve 663. In one aspect, this framework of fibrotic growth forms a bio-cuff in which tissues produced within the body form a cuff to maintain the electrodes 610 in the desired position relative to the nerve.

[0150] It is understood that tissue growth also would occur at and around the wires (not shown) extending proximally from the electrodes 660 toward the IPG 55 (Figure 1). It is further understood, that similar to previous embodiments, an outer portion of the electrode 660 (the portion that does not contact the nerve 663) would include an insulative cover to act as a barrier between the contact portion of the electrode 660 and the surrounding tissue.

[0151] Moreover, in one embodiment, each electrode 660 is connected to a respective one of an array of wires with each respective wire connected to, and extending to, a stimulation lead body configured for electrical communication with an IPG 55 (Figure 1). In one embodiment, the array of wires includes substantially the same features and attributes as the array of wires 612, as previously described and illustrated in association with Figures 15-16.

[0152] Figures 22-24 schematically illustrate an electrode portion 700 of a stimulation lead, according to an embodiment of the present disclosure. It is understood that prior to deployment of electrode portion 700, one or more potential stimulation sites on the hypoglossal nerve have been identified via a site locator tool (e.g. site locator tool 200) or via other tools. It is also understood that one or more surgical navigation techniques are used to: (1) employ the site locator tool to identify the optimal stimulation site; and (2) place the electrode portion at that optimal stimulation site.

[0153] As shown in Figures 22-23, electrode portion 700 includes a carrier 702 supporting generally spike-shaped electrodes 710 that are spaced apart from each other along a length of the carrier 702. The carrier 702 includes a distal end 704 and a proximal end 706 while each electrode 710 forms a conductive member including an exposed distal tip 714 and an insulative covered base portion 712. While just two electrodes 710 are shown, it will be understood that in other embodiments, carrier

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702 supports more than two electrodes 710. In one embodiment, the carrier 702 comprises a generally flat member having a first side and a second side (opposite the first side), with the electrodes 710 extending generally outward from the first side of the generally flat member.

[0154] In another aspect, for each electrode 710, a separate wire 720 extends through the carrier 704 (shown as dashed lines in Figure 23) and is electrically connected to the base portion 712 of each respective electrode 710. It is further understood that the electrodes 710 are formed of ultra fine wires, as known to those skilled in the art, and that the electrodes 710 are shown in Figures 22-24 in an exaggerated, enlarged form strictly for illustrative purposes.

[0155] Once the electrode portion 700 is delivered to the intended stimulation site, pressure is applied to insert the distal tips 714 of the respective electrodes 710 into the nerve 730. Because of the small dimensions of the ultra fine wire forming each electrode 710, the electrodes 710 are maintained in this position via the tissue of the nerve effectively capturing the electrodes 710. With this arrangement, close contact of the electrodes 710 to the nerve 730 is insured, resulting in effective stimulation of the nerve 730.

[0156] In some embodiments, once the electrode portion 700 is secured in place, the electrode portion 700 attracts tissue growth (not shown) about carrier 702 and base portion 712 of needles 710 with the combination of the tissue growth and the carrier 702 and base portions 712 acting as an anchoring mechanism to maintain the electrode tips 714 in penetrating engagement (i.e. inserted engagement) relative to nerve 730.

[0157] In some other embodiments, the carrier 702 forms a bio-absorbable material so that carrier 702 is absorbed over time, leaving just electrodes 710 and wire portions 721, 720 in place at nerve 730, as shown in Figure 24. As the absorption of carrier 702 occurs, electrodes 710 are held in inserted engagement relative to nerve 730 because of tissue growth (not shown) forming on and around the base portion 712 of electrodes 710 (as the carrier is absorbed) to hold the electrodes 710 in penetrating engagement relative to the nerve 730. It is understood that a similar

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tissue growth would occur at and around the wire portions 721 and 720 extending proximally from the electrodes 660 toward the IPG 55 (Figure 1).

[0158] Figures 25-32 schematically illustrate stimulation system 800 and a method of implanting components of system 800, according to an embodiment of the present disclosure. As shown in Figures 25-27, the stimulation system 800 includes at least an electrode portion 801 of a stimulation lead 802 and a shield 804. It is understood that prior to deployment of electrode portion 801, one or more optimal stimulation sites on the hypoglossal nerve have been identified via a site locator tool (e.g. site locator tool 200 shown in Figure 1) or via other tools. It is also understood that one or more surgical navigation techniques are used to: (1) employ the site locator tool to identify the optimal stimulation site; and (2) place the electrode portion at that optimal stimulation site.

[0159] As shown in Figure 25, stimulation lead 803 includes electrode portion 801 and lead body 808 with the electrode portion 801 including a generally elongate carrier body extending between a distal end 817 and a proximal end 816, and an electrode strip 815, which includes an array 818 of electrodes 820 spaced apart along a length of the carrier body. The lead body 808 extends proximally from electrode portion 801 and includes an anchor 810 with a proximal lead portion 812 configured for extension to and electrical connection to an IPG (55 in FIG. 1 or 109 in FIG. 2).

[0160] The electrode strip 815 has a length (L2) substantially greater than a diameter of a nerve, and sufficient to extend across a diameter of a nerve 840 and outward from both sides of the nerve 840, as shown in at least Figures 26-27. In one embodiment, the length (L2) is at least twice the diameter of the nerve. In another embodiments, the length (L2) is at least three times the diameter of the nerve, such that with an expected nerve diameter of about 3 millimeters, the electrode strip 815 has a length (L2) of about 9 millimeters. In this embodiment, about 3 millimeters of the full length of the electrode strip 815 would be in close proximity or contact with the nerve 840 while about 3 millimeters of the length of the electrode strip 815 would extend outward from each side of the nerve 840, as schematically illustrated in Figures 26-27. In some embodiments, electrode strip 840 has a width (W4) of about 3 millimeter, which facilitates a minimally invasive implantation method in some

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embodiments (as will be later described in more detail in association with Figures 30-32). In comparison, a conventional cuff electrode might typically have a width of about 9 millimeters.

[0161] In use, the electrode portion 801 is delivered to an intended stimulation site along the hypoglossal nerve 840 and with the electrode strip 815 having a generally perpendicular orientation relative to a longitudinal axis (represented by line A) of the nerve 840 (in the region of the intended stimulation site), as shown in Figure 26. In one embodiment, as illustrated in the sectional view of Figure 27, the electrode portion 801 is positioned so that the electrodes 820 of electrode strip 815 faces toward nerve 840 to apply the stimulation signal onto the nerve 840. Moreover, in some embodiments, each electrode 582 is independently programmable or controllable via IPG 55 (Figure 1) in a manner substantially similar to previously described embodiments to allow control and adjustment over the stimulation signal without re-positioning the electrode strip 815. In addition, an insulative shield 804 is interposed between the nerve 840 and skin 830 (and underlying muscle 832) such that the shield 804 permits application of the stimulation signal on the nerve 840 while preventing application of the stimulation signal on the skin 830.

[0162] In this arrangement, nerve 840 is sandwiched between the electrode strip 815 and insulative shield 804 and the electrode portion 801 is deployed so that at least a portion of the electrode strip 806 extends, in close proximity to or in close contact with, about the outer surface of the nerve 840, as shown in the sectional view of Figure 27. However, in this sandwiched arrangement, each of the electrode strip 815 and shield 804 are secured independently relative to the surrounding tissue such that neither electrode strip 815 nor shield 804 are secured to the nerve 840. For example, in one embodiment, electrode strip 815 is secured at each of its ends, via anchors (represented by x 878 and x 879 in Figure 26), relative to the surrounding tissue and independent of nerve 840. With the generally perpendicular orientation of both the electrode strip 815 and the shield 804, this configuration permits movement of the nerve 840 in a lateral direction (represented by arrow M) relative to both the electrode strip 815 and the shield 804, thereby accommodating shifting of the nerve 840 as the neck of the patient moves through a wide range of motion through many different positions.

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[0163] With this in mind, upon lateral movement of nerve (along arrow M), both the electrode strip 815 and shield 804 remain stationary such that the sandwiched arrangement is maintained even when nerve 840 moves. Accordingly, because of the electrode strip 815 has a length (L2) that is substantially longer than the diameter of nerve 840, in any lateral position of the nerve 840 (within a natural, limited range of motion) the electrode strip 815 remains in a position to apply an efficacious stimulation signal to nerve 840. Similarly, because the shield 804 has length (L3) substantially longer than the diameter of nerve 840 and substantially longer than the length (L2) of the electrode strip 815, the shield is always positioned to block application of the stimulation signal to the skin 830 (and underlying sensory nerves). In one embodiment, shield 804 defines an area substantially greater than an area of an electrical field produced by electrodes 820 toward a skin surface.

[0164] While the electrode portion 801 extends generally perpendicular to the longitudinal axis of the nerve 840 (at the stimulation site), in some embodiments the lead body 808 extends generally parallel to the longitudinal axis of the nerve 840 to follow a path toward the IPG 55 (Figure 1). As previously noted, the lead body 808 includes an anchor 810 to permit securely anchoring the lead body 808 (and therefore the electrode portion 801 as well) relative to the anatomical structures and tissues nearby to the nerve 840. From the anchor 810, a proximal portion 812 of the lead body 808 extends further toward the IPG 55 (Figure 1) via a subcutaneous tunnel.

[0165] In some embodiments, the application of a perpendicular orientation of an electrode strip (e.g. electrode strip 815) relative to nerve 840 is used with other cuff-less electrode configurations. For example, embodiments associated with Figures 11-14C can be deployed to orient the electrode portion 565 to be generally perpendicular to the nerve such that the series of electrodes 582 are aligned transverse to a longitudinal axis of the target nerve without a cuff encircling the circumference of the nerve 840. It will be understood that the number of electrode contacts will be adjusted, as appropriate, in the electrode portion 565 to insure capture of the nerve throughout a full cross-section (or diameter) of the nerve.

[0166] In further reference to Figures 25-29, in some embodiments, electrode portion 801 includes one or more anchoring mechanisms. Accordingly, Figure 28 is a top

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plan view of an electrode portion 850 including a series of electrode contacts 820, a distal end 852, and a proximal end 854. At distal end 852, one or more loops (or other securing elements) 860 are provided to enable suturing or otherwise fastening the distal end 852 relative to surrounding tissue adjacent the nerve 840. Similarly, at proximal end 854, one or more loops (or other securing elements) 870, 872 are provided to enable suturing or otherwise fastening the proximal end 854 relative to surrounding tissue adjacent the nerve 840. In this way, the electrode strip 850 is securable in a stable position close to nerve 840 (but independently of the nerve) without being secured to the nerve 840 itself and/or without encircling the nerve 840.

[0167] In some other embodiments, as schematically illustrated in the sectional view of Figure 29, electrode strip 815 and shield 804 are secured together. In these embodiments, the sandwiched configuration of electrode strip 815 and shield 804 is maintained relative to nerve 840 to thereby permit lateral movement (directional arrow M) of nerve 840 while still providing electrical stimulation of nerve 840 via electrode strip 815 and while still protecting skin 830 via shield 804. In particular, fastening mechanism 870 includes a first component 872 and a second component 874, with each respective component 872, 874 sized to extend between the electrode strip 815 and the shield 804. In one non-limiting aspect, by providing first component 872 on one lateral side of nerve 840 (connected to the first ends of the respective strip and shield) and by providing second component 874 on an opposite lateral side of nerve 840 (connected to the second ends of the respective strip and shield), the fastening mechanism 870 provides a lateral boundary or barrier to insure that nerve 840 will remain between electrode strip 815 and shield 804 while permitting lateral movement of nerve 840. In other embodiments, only one end of the respective electrode strip 815 and the shield 804 are secured together, leaving the other end open.

[0168] In one embodiment, the first component 872 of securing mechanism 870 comprises a buckle-belt mechanism that is connectable to the distal end 817 of electrode strip 815 and connectable to the distal end 805 of the shield 804. Likewise, the second component 874 comprises a buckle-belt mechanism that is connectable to the proximal end 816 of electrode strip 815 and connectable to the proximal end 807 of the shield 804.

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[0169] In some embodiments, the combination of the shield 804 and the electrode strip 815 are delivered percutaneously in a minimally invasive implantation method, as schematically illustrated in Figures 30-32. In particular, because the electrode strip 815 is quite narrow (e.g., 3 millimeters wide as shown in Figures 25-27), the procedure begins via making two small incisions 880, 882 in the skin 830 (and underlying tissues/muscles 832) on opposite lateral sides of the underlying nerve 840, as shown in Figure 31. At least one of the incisions 880, 882 will have a width (W6) generally corresponding to the width (W4 in Figure 25) of the electrode strip 815. Using a forceps (not shown), the electrode strip 815 is maneuvered through incision 880 and via incision 882 (as represented via arrows E and R) until the electrode strip 815 is in position underneath nerve 840 with electrode contacts 820 in close contact with the nerve 840 and facing skin 830, as shown in Figure 30. Next, using a similar technique involving incisions 880 and/or 882, the shield 804 is introduced into a position interposed between nerve 840 and skin 830. If necessary, either incision 880, 882 can be widened slightly to accommodate introduction of the larger width (W5) of shield 804 through the respective incision. With this minimally invasive method of implantation, the sandwiched configuration of the electrode strip 815 and the shield 804 relative to the nerve 840 is achieved with minimal disruption to the skin and tissues above and near the nerve 840. Accordingly, the combination of the electrode strip 815 and the shield 804 enable a minimally invasive method of implanting those elements while also providing a stimulation system that minimally impacts the natural state of the nerve by acting as a cuff-less electrode.

[0170] Several different embodiments have been described in association with Figures 1-14, in which an IPG 55 is implanted in a pectoral region and in which a sensor electrode(s) and a stimulation electrode(s) (extending from the IPG 55) are delivered percutaneously to sense respiratory patterns and to apply a stimulation signal, respectively. In addition, several embodiments of stimulation electrode arrays (and associated anchor mechanisms) have been described in association with Figures 15-32. Moreover, it is understood that in some of these embodiments, a lead is percutaneously placed in each side of the body (left and right) such that bilateral (simultaneous or alternating) stimulation takes place on the left and/or right hypoglossal nerve (or other target nerve). With these various embodiments in mind, it is further understood that among those embodiments, several configurations are

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provided in which at least two electrodes are spaced apart in the body in the vicinity of the upper airway such that an impedance is measurable between the two spaced apart electrodes to provide an indication of airway patency (e.g., opening and/or closing of the upper airway). In some configurations, the spaced electrodes are both stimulation electrodes, while in other configurations, the spaced apart electrodes comprise one stimulation electrode and one respiratory sensor electrode. In yet other configurations, the two spaced apart electrodes (used for measuring an impedance indicative of airway patency) include one of the electrodes comprising at least one of a stimulation electrode and a respiratory sensor electrode and the other one of the electrodes comprising an electrode formed by an electrically conductive portion of a case or housing of the IPG 55.

[0171] Moreover, in some embodiments, the respective electrode portions provide a dual function in that each electrode provides a respiratory sensing function or a stimulation function as well as acting as a part of a pair of impedance sensing electrodes. On the other hand, in other embodiments, at least one electrode of the pair of impedance sensing electrodes does not also act to sense respiration (e.g. inspiration) or to stimulate but rather is dedicated for use in sensing impedance to detect or indicate a degree of airway patency.

[0172] At least some embodiments of the percutaneously-delivered electrode portions (described herein) enable precise location of an electrode portion adjacent to an optimal neurostimulation site because the percutaneous approach enables the surgeon to vary the position of an electrode portion of a stimulation lead along the length of the hypoglossal nerve. In addition, this precise placement is performed in a minimally invasive manner unlike the anatomically disruptive conventional cut-down procedure for placing stimulation leads. The methods and systems of the present disclosure allows the surgeon to identify a precise optimal stimulation site that causes contraction of one or more specific muscles (suited to restore airway patency) prior to fixing the location of the electrode portion relative to the target nerve.

[0173] Embodiments of the present disclosure provide an implantable system to provide therapeutic solutions for patients diagnosed with obstructive sleep apnea.

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The system is designed to stimulate the hypoglossal nerve during inspiration thereby preventing occlusions in the upper airway during sleep.

[0174] While at least one exemplary embodiment has been presented in the foregoing detailed description, it should be appreciated that variations exist. It should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope, applicability, or configuration of the present disclosure in any way. Rather, the foregoing detailed description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the present disclosure as set forth in the appended claims and the legal equivalents thereof.

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Claims

1. A method of implanting a stimulation lead to treat sleep-related disordered breathing, comprising:

percutaneously inserting a distal portion of an introducing mechanism and positioning the distal portion to be adjacent to a target nerve stimulation site while maintaining a proximal portion of the introducing element external to a skin surface; and

releasably engaging a stimulation lead relative to the proximal portion of the introducing mechanism, and slidably advancing the stimulation lead via the introducing mechanism to percutaneously insert the stimulation lead until a distal portion of the stimulation lead is positioned at the target stimulation site.

2. The method of claim 1,

removing the introducing mechanism while maintaining the position of the distal portion of the stimulation lead at the target stimulation site.

3. The method of claim 2, wherein maintaining the position of the distal portion of the stimulation lead includes:

deploying an anchor mechanism to maintain the position of the distal portion at the target stimulation site.

4. The method of claim 3, wherein deploying the anchor mechanism includes:

locating the anchor mechanism at the distal portion of the stimulation lead.

5. The method of claim 4, wherein the stimulation lead includes a first side and a second side opposite the first side, and wherein locating the anchor mechanism includes:

locating the anchor mechanism on the second side of the distal portion of the stimulation lead.

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6. The method of claim 5, comprising:

arranging the first side of the distal portion of the stimulation lead to include at least one stimulation electrode configured to releasably contact the nerve at the target stimulation site; and

arranging the second side of the distal portion of the stimulation lead to include an insulating element to interpose the insulating element between the nerve and the skin surface.

7. The method of claim 5, wherein deploying the anchor mechanism comprises:

selectively releasing an array of members from a first storage position against a body of the distal portion of the stimulation lead to a second deployment position to extend generally outward from a body of the distal portion of the stimulation lead.

8. The method of claim 7, comprising:

providing at least a portion of the introducing mechanism as a cannula and wherein slidably advancing the stimulation lead via the introducing mechanism includes slidably advancing the stimulation lead into and through the cannula;

during advancement of the distal portion of the stimulation lead through the cannula, maintaining the respective member in the first storage position via engagement of the distal portion against an inner surface of the cannula; and

releasing the respective members of the stimulation lead from the first storage position into the second deployment position upon removal of the cannula from the target stimulation site.

9. The method of claim 8, wherein maintaining the respective flaps in the first storage position comprises:

releasably covering the members with a distal extension of the cannula, wherein the distal extension defines an opening to expose the electrode portion of the stimulation lead.

10. The method of claim 7, comprising:

arranging the members as at least one of barbs or flaps

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11. The method of claim 1, comprising:

removing the cannula while maintaining the distal portion of the stimulation lead at the target stimulation site.

12. The method of claim 1, wherein percutaneously inserting a distal portion of an introducing mechanism comprises:

providing at least a portion of the introducing mechanism as a cannula and wherein slidably advancing the stimulation lead via the introducing mechanism includes slidably advancing the stimulation lead into and through the cannula;

arranging the cannula to include a flexible distal portion having a generally curved shape such that in a deployment position, an end of cannula is oriented in a direction oriented at a generally obtuse angle relative to a longitudinal axis of a proximal portion of the cannula and in an insertion position, the flexible distal portion is configurable to assume an orientation generally parallel to the longitudinal axis of the proximal portion of the cannula.

13. The method of claim 12, comprising:

upon positioning the distal portion of the stimulation lead at the target stimulation site, causing the distal flexible portion to assume the generally curved shape;

slidably advancing the distal portion of the stimulation lead out of the end of the cannula until the distal portion is at the target stimulation site;

removing the cannula while maintaining the distal portion of the stimulation lead at the target stimulation site.

14. The method of claim 13, comprising:

locating an entry point of the cannula into the skin surface at a first distance away from the target stimulation site, wherein the first distance is generally equal to a sum of:

a second distance between the end of the cannula and a longitudinal axis of the proximal portion of the cannula when the distal portion is in the deployment position; and

a third distance corresponding to at most a length of an electrode portion of the stimulation lead.

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15. The method of claim 13, comprising:

via a percutaneous access, advancing a proximal portion of the stimulation lead from the target stimulation site to a pectoral region of a patient.

16. The method of claim 1, percutaneously inserting a distal portion of an introducing mechanism comprises:

providing at least a portion of the introducing mechanism as a cannula and arranging the cannula to include a generally rigid, straight distal portion having an opening oriented generally perpendicular to a longitudinal axis of the cannula;

wherein slidably advancing the stimulation lead via the introducing mechanism includes slidably advancing the stimulation lead into and through the cannula to cause the distal portion of the stimulation lead to extend out of the end of the opening until the distal portion of the stimulation lead is at the target stimulation site and in an orientation at a generally obtuse angle relative to the proximal portion of the cannula; and

removing the cannula while maintaining the distal portion of the stimulation lead at the target stimulation site.

17. The method of claim 16, comprising:

locating an entry point of the cannula into the skin surface at a first distance away from the target stimulation site, wherein the first distance is generally equal to a second distance corresponding to at most a length of an electrode portion of the stimulation lead.

18. The method of claim 1, comprising:

upon advancing the cannula, measuring a depth of insertion of the distal portion via graduation markings spaced apart along a length of the cannula.

19. The method of claim 1, wherein percutaneously inserting a test needle comprises:

percutaneously inserting the test needle at a plurality of test stimulation sites, including the target stimulation site;

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determining the target stimulation site from among the plurality of test stimulation sites via applying, at each respective test stimulation site, a stimulation signal;

monitoring, during application of the stimulation signal, at least one of:

occurrence of a tongue protrusion or tongue retraction;

change in a cross-sectional area of an upper airway;

a lack of response in non-target muscles;

a twitch in a tongue muscle or laryngeal muscle; or

strongest electromyography response for a target muscle.

20. The method of claim 19, comprising:

identifying, based on the determined target stimulation site, a percutaneous access pathway to the target stimulation site.

21. The method of claim 19, wherein determining the target stimulation site comprises:

varying an array of stimulation parameters at each test stimulation site, the respective stimulation parameters including at least one of an amplitude parameter, a frequency parameter, a pulse width parameter, a polarity parameter, and a duration parameter.

22. A percutaneous access system for implanting a stimulation lead to treat sleep-related disordered breathing, the method comprising:

a test needle including a distal portion and a proximal portion, the proximal portion including a handle releasably secured relative to the proximal portion, wherein the handle is sized to remain external to a skin surface and the needle has a length configured to percutaneously access a nerve;

a cannula defining a generally tubular member having a distal portion, a proximal portion, and configured to be slidably advanceable over the test needle; and

a stimulation lead including a distal portion having a first side defining an electrode array and a second side opposite the first side, the second side defining a selectively deployable anchoring mechanism and the stimulation lead configured to

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be slidably advanced through the cannula and having a length greater than a length of the cannula.

23. The system of claim 22, wherein the cannula includes a distal extension that extends from the distal portion and is configured to maintain the anchoring mechanism in a storage mode when the distal extension covers the anchor mechanism and a deployment mode when the distal extension permits exposure of the anchor mechanism.

24. The system of claim 23, wherein the distal extension defines an opening to expose the electrode portion of the stimulation lead while the distal extension is in both of the respective storage and deployment modes.

25. The system of claim 22, comprising at least one of:

an intermediate portion of the cannula including a series of graduation markings spaced apart along a portion of a length of the cannula and positioned to gauge a depth of insertion of the cannula percutaneously; or

an intermediate portion of the test needle including a series of graduation markings spaced apart along a portion of a length of the test needle and positioned to gauge a depth of insertion of the test needle percutaneously.

26. The system of claim 22, wherein at least one of the test needle, the cannula, or the stimulation lead include at least one radiopaque marker configured to identify, under fluoroscopy, an orientation and position of the respective test needle, cannula, or stimulation lead.

27. The system of claim 22, wherein the distal portion of the cannula is flexible and has a generally curved shape to orient a distal end of the cannula in a direction generally perpendicular to a longitudinal axis of a proximal portion of the cannula, and

wherein the system includes a stiffener releasaby engageable relative to the cannula and in an installed position within the cannula, the stiffener causes the flexible distal portion to assume an orientation generally parallel to the longitudinal

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axis of the proximal portion of the cannula and in a removed position, the stiffener causes the flexible distal portion to assume its generally curved shape.

28. An electrode implantation instrument for establishing percutaneous access to a nerve, the instrument comprising:

a handle;

a barrel extending from the handle and having a length configured to provide percutaneous access to a nerve; and

an engagement mechanism supported by the barrel and including at least one selectively deployable barb to secure an electrode body relative to a nerve via penetrating engagement of the at least one barb into tissue adjacent the nerve,

wherein the electrode body is sized and shaped for percutaneous insertion for placement adjacent a target nerve.

29. The instrument of claim 28 wherein the barrel includes a generally hollow, elongate tubular member, and the engagement mechanism includes at least one rod extending through, and longitudinally movable within, the barrel,

wherein the at least one barb is releasably coupled to a distal end of the at least one rod.

30. The instrument of claim 29, wherein the handle includes a release trigger coupled via the barrel to a proximal end of the rod, and wherein the release trigger is configured to cause forward movement of the at least one rod out of a distal end of the barrel to align the at least one barb for penetration into the tissue adjacent the nerve.

31. The instrument of claim 30, wherein the distal end of the at least one rod includes a needle and the at least one barb is releasably coupled to the needle.

32. The instrument of claim 30, and further comprising:

an electrode body releasably coupled to the distal end of the at least one rod via the at least one barb.

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33. The instrument of claim 32, wherein the instrument includes at least one suture member interposed between, and connecting, the electrode body to the at least one barb such that upon release of the at least barb from the distal end of the rod, the at least one barb remains connected to the electrode body.

34. The instrument of claim 32, wherein the at least one barb includes a first array of barbs and a second array of barbs, the first array disposed on a first side portion of the electrode body and the second array disposed on a second side portion of the electrode body wherein the first array and the second array are laterally spaced apart by a width greater than a width of a nerve.

35. The instrument of claim 34, wherein the electrode body includes a series of electrode elements aligned in longitudinal axis of stimulation lead and interposed between the first array of barbs and the second array of barbs.

36. A percutaneously implantable electrode system comprising:

a cuff configured to be releasably fittable about a nerve and made of a bio-absorbable material;

an array of electrode elements embedded in the cuff, wherein a longitudinal axis of each electrode element is generally perpendicular to a longitudinal axis of the cuff and the respective electrode elements are spaced apart from each other along a length of the cuff; and

an array of wires, a respective one of the wires connected to, and extending from, a respective one of the electrode elements,

wherein the array of wires extends distally from a stimulation lead body, and

wherein the cuff is sized and shaped to be percutaneously insertable adjacent a target nerve.

37. The electrode system of claim 36, wherein each wire is arranged as a series of coils along a length of the respective wire.

38. The electrode system of claim 37, comprising:

a fastener body to which each wire connected, the fastener body spaced apart from distal end of wires.

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39. The electrode system of claim 36, wherein each electrode element includes:

a conductive portion having a bottom portion exposed at inner surface of the cuff and a top portion opposite the bottom portion; and

an insulation cover connected to, and generally surrounding both the top portion of the conductive portion and sides of the conductive portion,

wherein the bio-absorbable material of the cuff generally surrounds at least the insulation cover and the sides of each respective electrode element.

40. The electrode system of claim 39, wherein the conductive portion of each electrode element is configured to contact the nerve and the insulation cover is configured to be interposed between the nerve and a skin surface.

41. A percutaneoulsy implantable electrode system comprising:

an elongate stent made of a bio-absorbable material and configured to self-sizingly collapse about a nerve to become coupled to the nerve;

an array of electrode elements carried by the stent, wherein the respective electrode elements are spaced apart from each other along a length of the tubular member; and

an array of wires, a respective one of the wires connected to, and extending from, a respective one of the electrode elements,

wherein the array of wires extends distally from a stimulation lead body, and

wherein the elongate stent is sized and shaped to be percutaneously insertable adjacent a target nerve.

42. The electrode system of claim 41, wherein each electrode element is generally parallel to a longitudinal axis of the elongate tubular member.

43. The electrode system of claim 42, wherein the stent comprises a pair of interconnected helical struts, wherein each respective electrode element is supported between the respective helical struts.

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44. The electrode system of claim 41, wherein the bio-absorbable material is configured to cause absorption of the stent within a patient's body upon a predetermined time period.

45. A percutaneously implantable electrode system comprising:

an elongate carrier made of a bio-absorbable material;

an array of electrode spikes supported by the carrier, wherein the respective electrode spikes extend generally outward from a surface of the carrier and the respective spikes are spaced apart from each other along a length of the carrier; and

an array of wires, a respective one of the wires connected to, and extending from, a respective one of the electrode spikes,

wherein the array of wires extends distally from a stimulation lead body, and

wherein the elongate carrier is sized and shaped for percutaneous insertion adjacent a target nerve.

46. The electrode system of claim 45, wherein the carrier comprises a generally flat member having a first side and a second side, with the electrode spikes extending upward from the first side of the generally flat member.

47. The electrode system of claim 46, wherein each electrode spike defines a conductive element having a first distal portion and a second proximal portion, the second proximal portion including an insulative covering on top of the conductive element and the first distal portion defining an exposed conductive region sized to make penetrating contact into the nerve.

48. The electrode system of claim 45, wherein the bio-absorbable material is configured to cause absorption of the carrier within a patient's body upon a predetermined time period.

49. A percutaneous electrode system comprising:

a stimulation unit including:

an elongate carrier having a distal end, a proximal end, and a body extending between the distal and proximal ends;

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an array of electrode elements spaced apart along a length of the elongate carrier and configured to produce an electrical field; and

a stimulation lead in electrical communication with the respective electrode elements; and

an insulation shield defining an area substantially greater than an area of the electrical field produced by the electrode elements; and

a fastening mechanism configured to connect the carrier to the insulation shield to arrange the stimulation unit and the insulation shield on opposite sides of the nerve and with the insulation shield closer to a skin surface than the stimulation unit,

wherein each of the stimulation unit, the insulation shield, and the fastening mechanism are sized and shaped for percutaneous insertion adjacent the nerve.

50. The electrode system of claim 49, wherein the fastening mechanism includes a pair of fasteners, one of the fasteners coupling a distal end of carrier to a distal end of the shield, and the other of the fasteners coupling a proximal end of the carrier to a proximal end of the shield.

51. The electrode system of claim 49, wherein the body of the elongate carrier has a length at least twice a diameter of the nerve.

52. The electrode system of claim 49 wherein the stimulation lead includes a plurality of wires, wherein a respective one of the wires is electrically connected to a respective one of the electrode elements independent of the other respective wires and other respective electrode elements.

53. A method of percutaneously implanting a stimulation electrode, the method comprising:

percutaneoulsy creating a pair of incisions through a skin-muscle layer on opposite sides of a nerve;

percutaneously inserting a stimulation unit into and through one of the incisions and advancing the stimulation unit through tissues to a position behind the nerve such that an electrode array of the stimulation unit faces the nerve and a skin surface; and

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percutaneously inserting an insulation shield into and through one of the incisions and advancing the insulation shield through the tissues to a position about the nerve opposite the electrode array of the stimulation unit such that the shield is interposed between the nerve and the skin surface.

54. The method of claim 53, comprising:

coupling the insulation shield relative to the stimulation unit while maintaining space between the shield and the stimulation unit.

55. The method of claim 54, wherein coupling the insulation shield comprises:

securing a first fastener between a first end of the stimulation unit and a first end of the shield and securing a second fastener between a second end of the stimulation unit and a second end of the shield with the nerve interposed between the first fastener and the second fastener.

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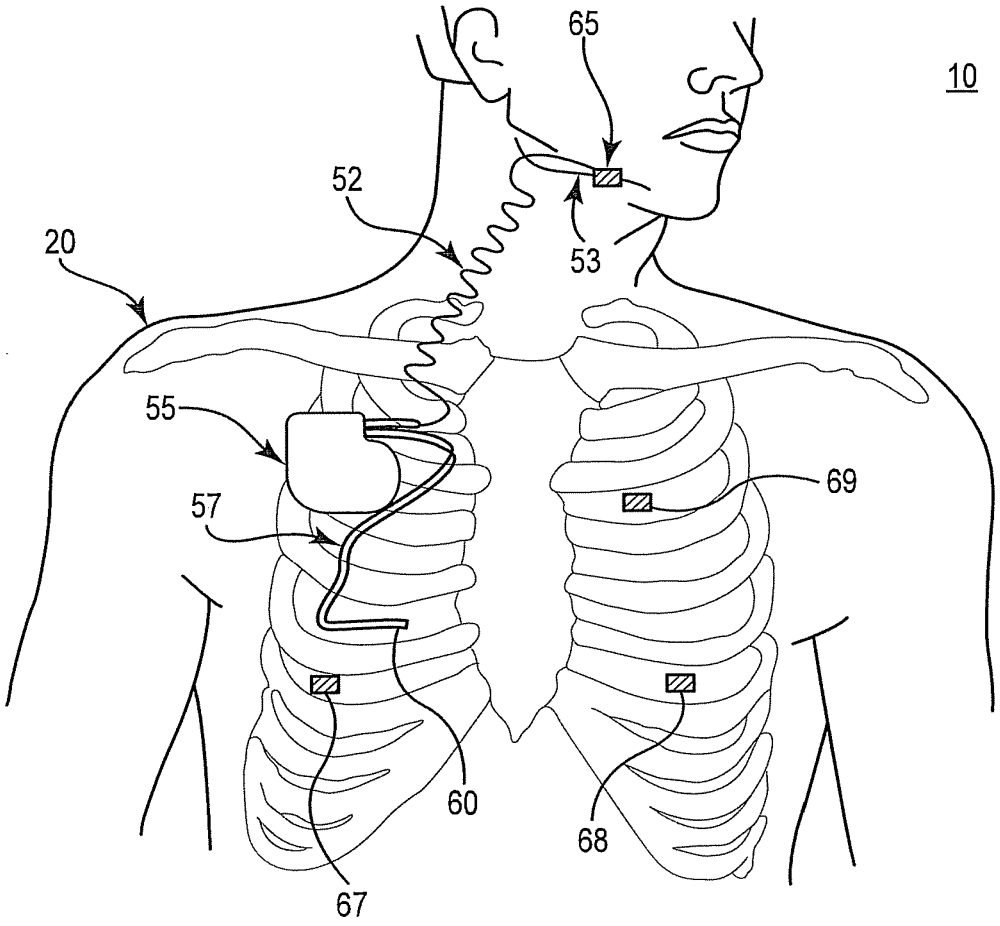


Fig. 1

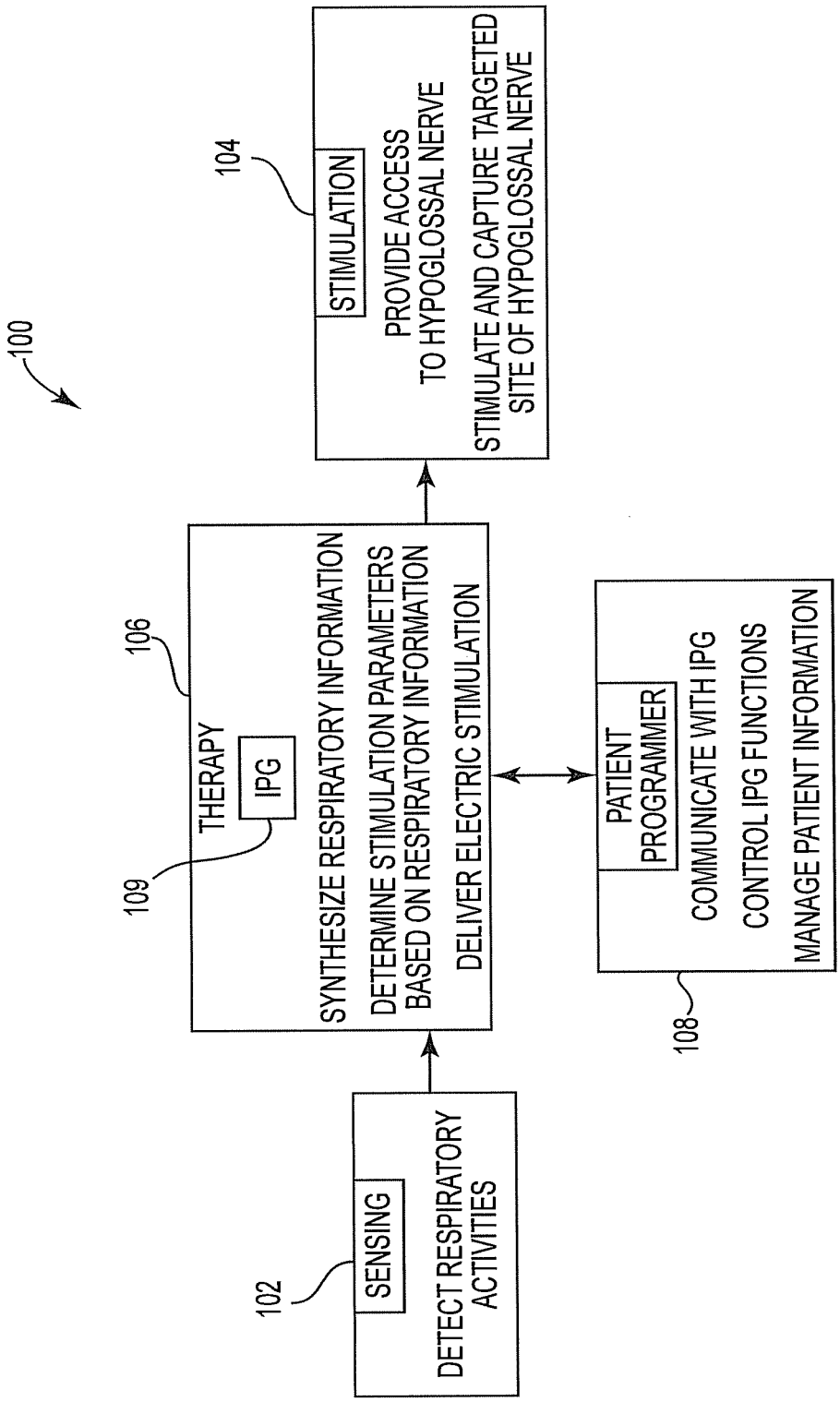

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PATIENT PROGRAMMER
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MANAGE PATIENT INFORMATION

Fig. 2

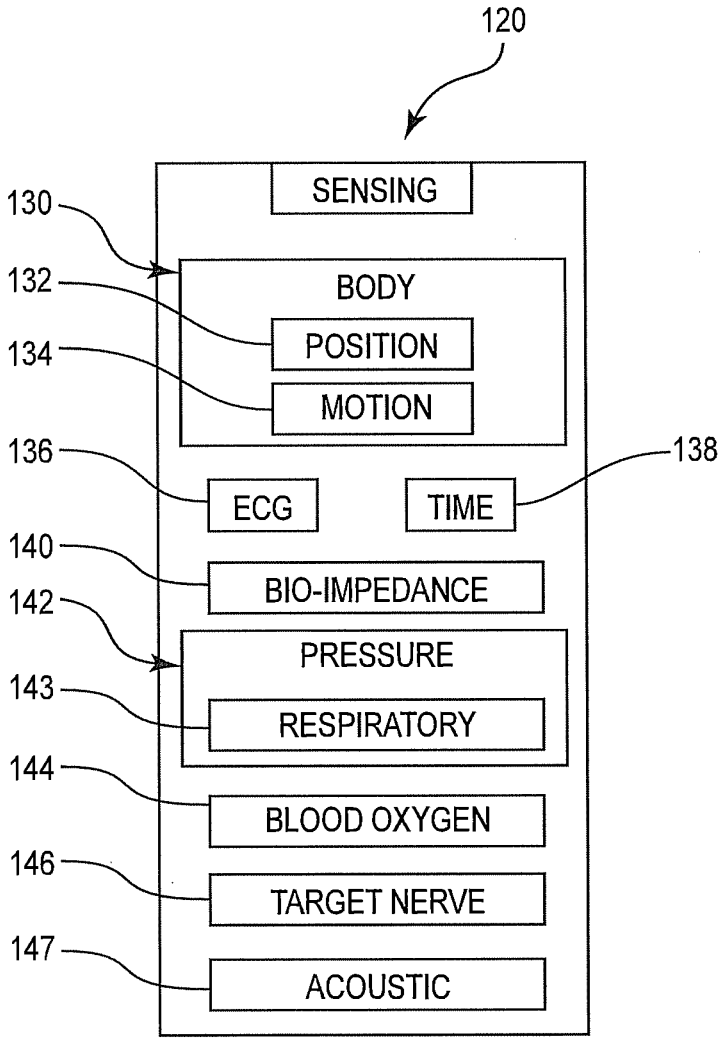

120
SENSING
130
BODY
132
POSITION
134
MOTION
136
138
ECG
TIME
140
BIO-IMPEDANCE
142
PRESSURE
143
RESPIRATORY
144
BLOOD OXYGEN
146
TARGET NERVE
147
ACOUSTIC

Fig. 3

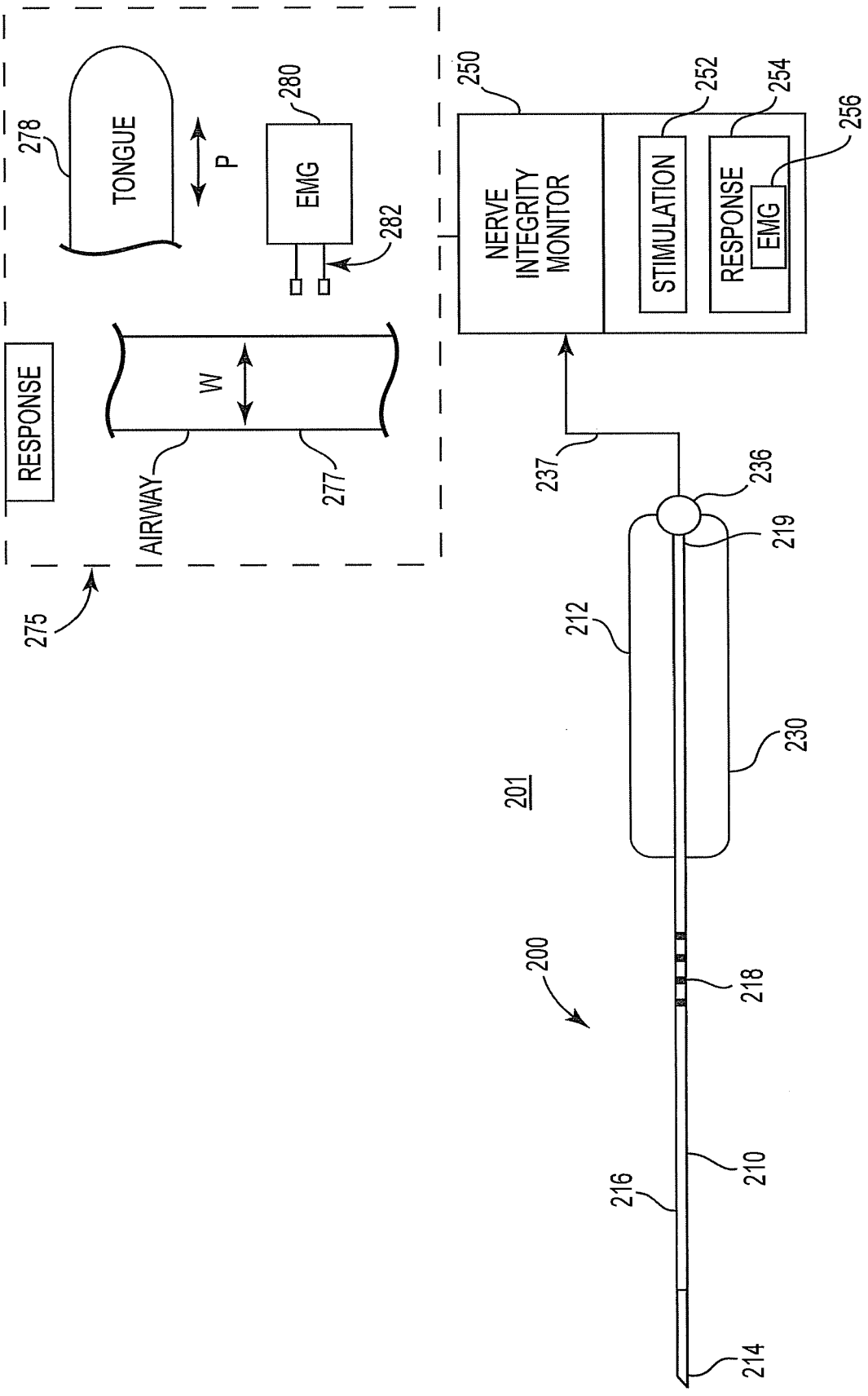

RESPONSE
275
AIRWAY
277
W
278
TONGUE
P
280
EMG
282
250
NERVE INTEGRITY MONITOR
252
STIMULATION
254
RESPONSE
EMG
256
237
236
219
212
230
201
200
218
216
210
214

Fig. 4

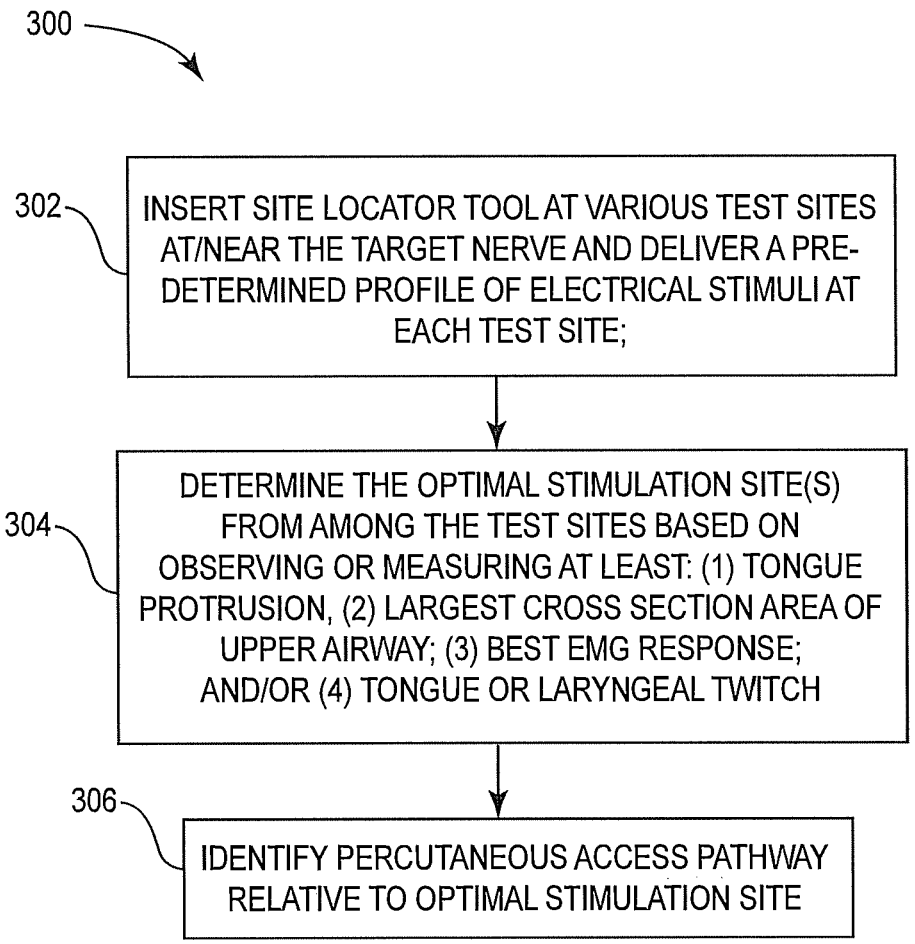

300
302
INSERT SITE LOCATOR TOOL AT VARIOUS TEST SITES AT/NEAR THE TARGET NERVE AND DELIVER A PRE-DETERMINED PROFILE OF ELECTRICAL STIMULI AT EACH TEST SITE;
304
DETERMINE THE OPTIMAL STIMULATION SITE(S) FROM AMONG THE TEST SITES BASED ON OBSERVING OR MEASURING AT LEAST: (1) TONGUE PROTRUSION, (2) LARGEST CROSS SECTION AREA OF UPPER AIRWAY; (3) BEST EMG RESPONSE; AND/OR (4) TONGUE OR LARYNGEAL TWITCH
306
IDENTIFY PERCUTANEOUS ACCESS PATHWAY RELATIVE TO OPTIMAL STIMULATION SITE

Fig. 5

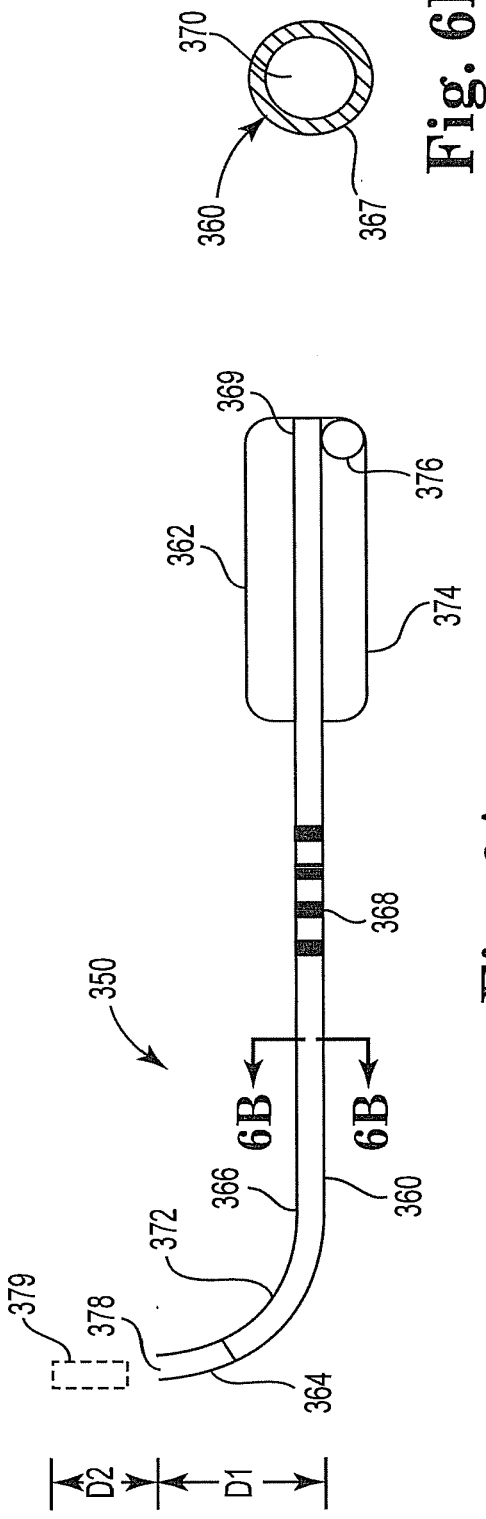


Fig. 6A

Fig. 6B

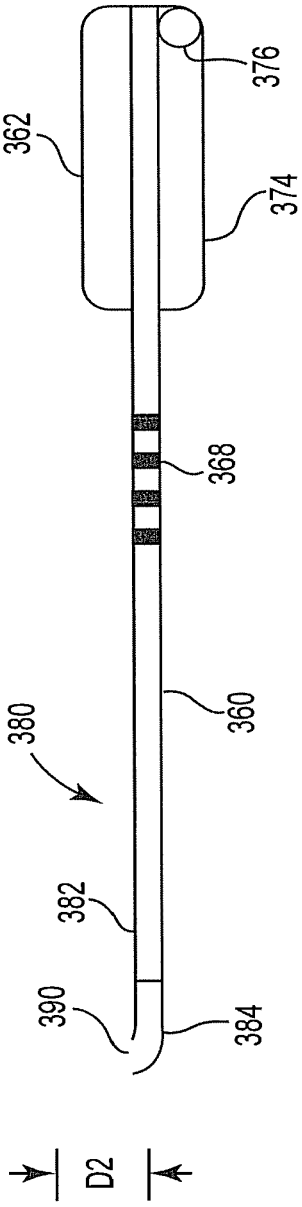


Fig. 6C

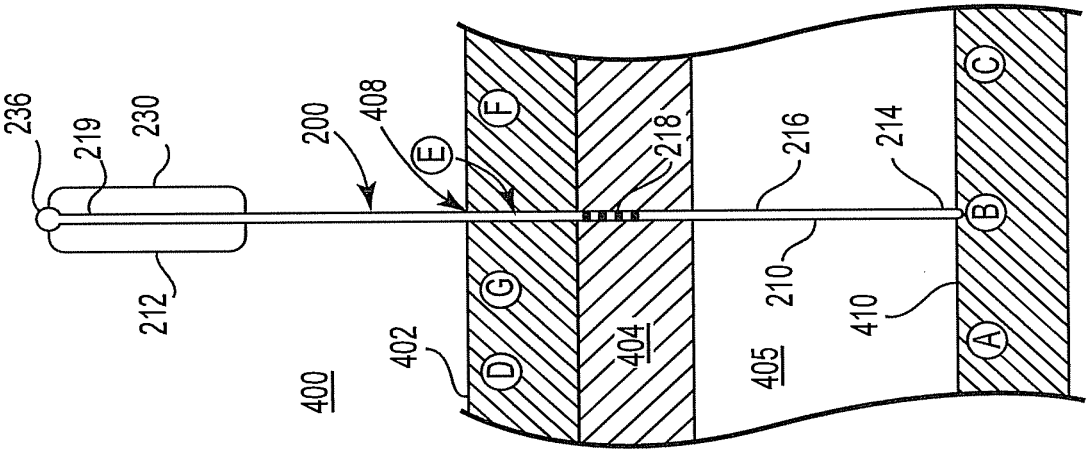


Fig. 7A

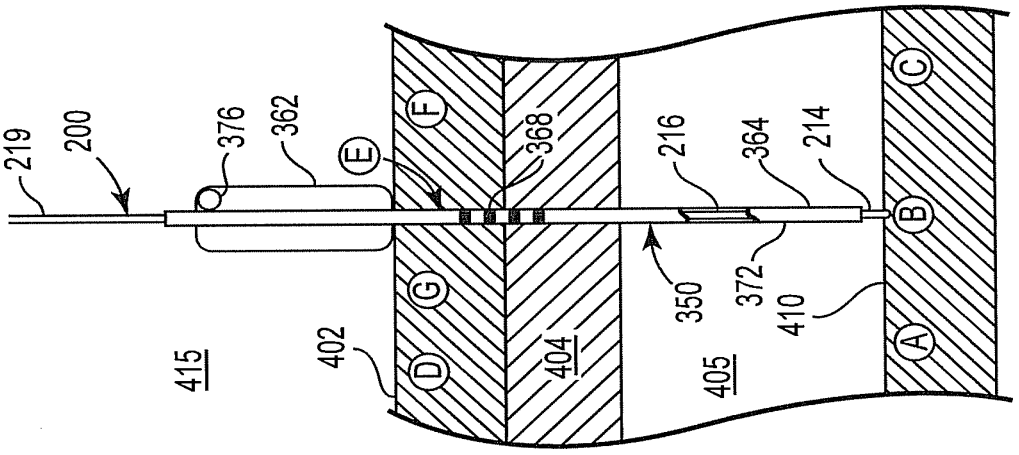


Fig. 7B

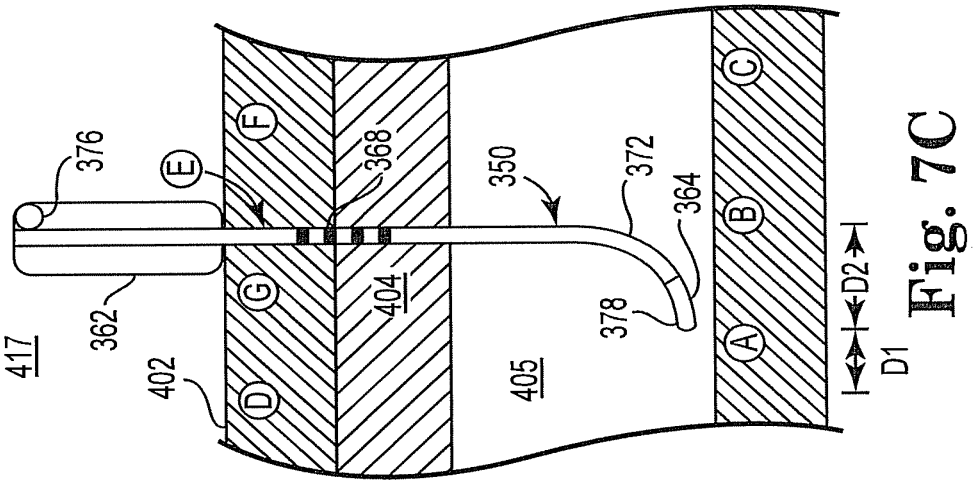


Fig. 7C

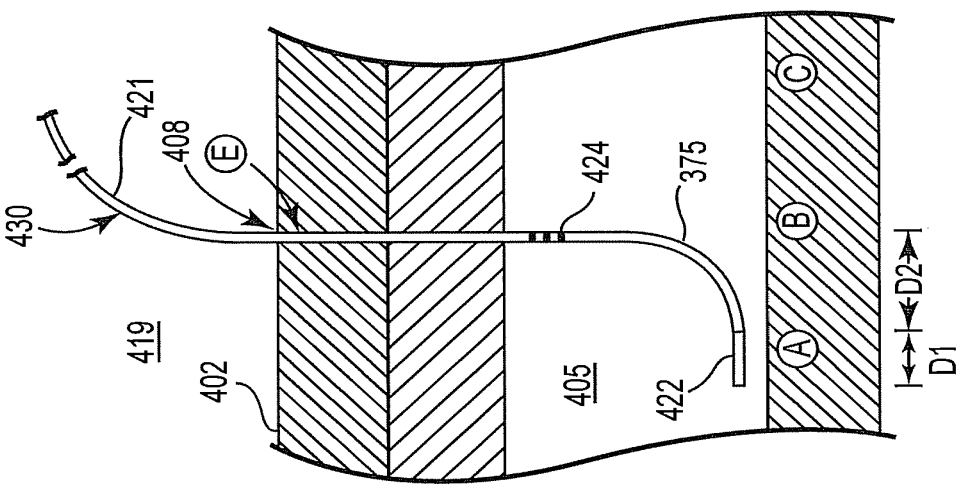

421
408
E
430
424
375
C
B
A
D2
D1
419
402
405
422

Fig. 7E

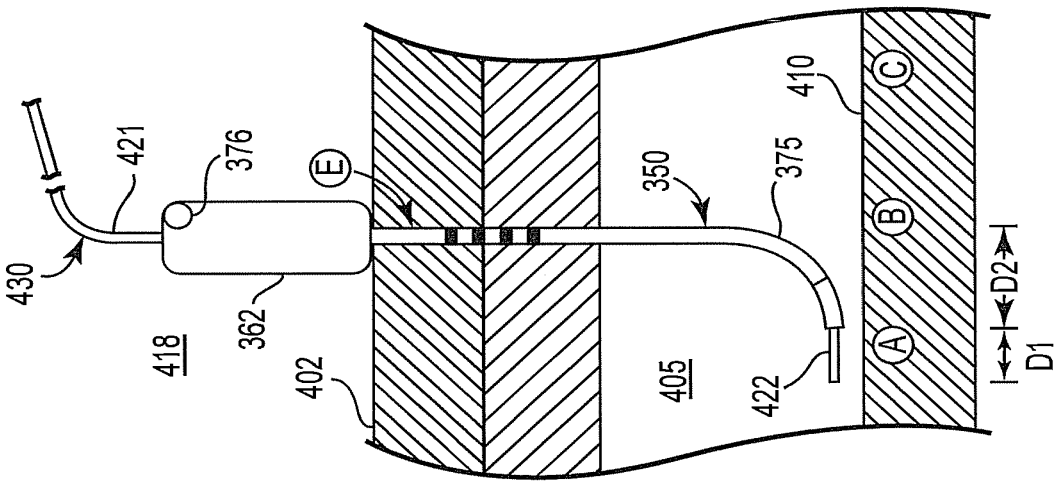
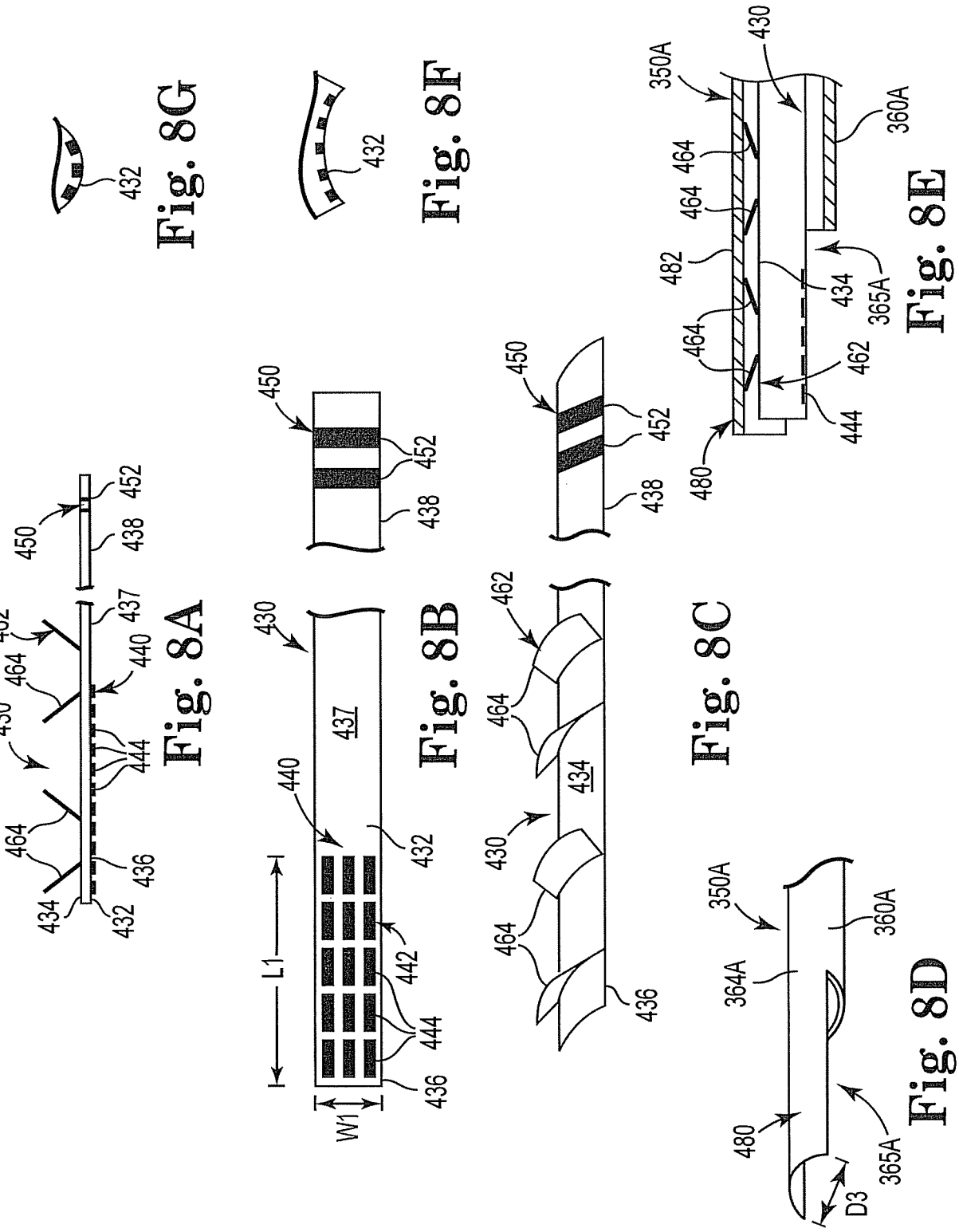

421
376
E
430
350
375
410
C
B
A
D2
D1
418
362
402
405
422

Fig. 7D


432
Fig. 8G
432
Fig. 8F
350A
430
360A
464
464
482
434
365A
464
462
444
480
Fig. 8E
450
452
438
462
462
464
464
434
430
464
436
Fig. 8C
450
452
438
430
437
440
432
L1
442
444
436
W1
Fig. 8B
462
464
437
440
444
434
436
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452
438
Fig. 8A
350A
360A
364A
480
365A
D3
Fig. 8D

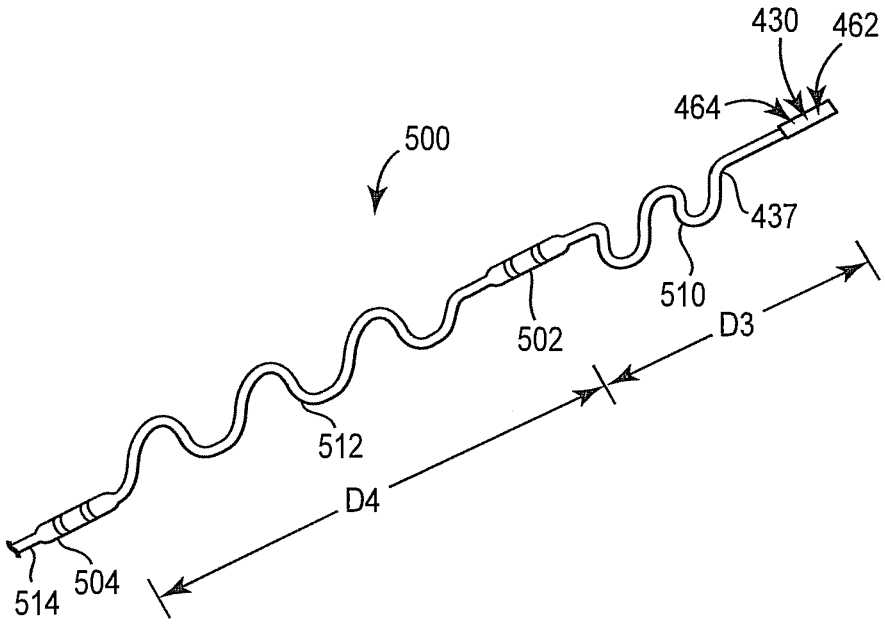

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502
D3
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D4
504
514

Fig. 9

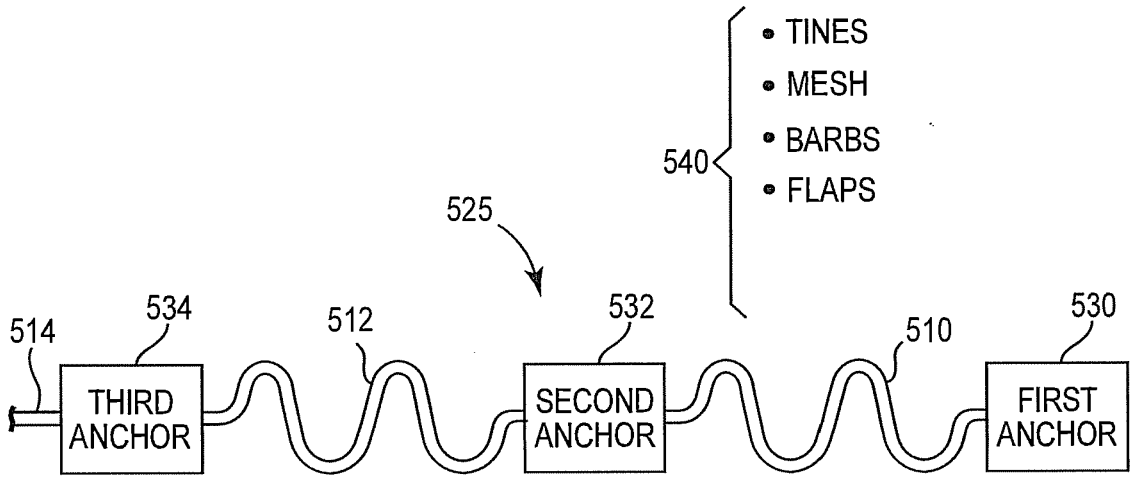

• TINES
• MESH
• BARBS
• FLAPS
540
525
514
534
512
532
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530
THIRD ANCHOR
SECOND ANCHOR
FIRST ANCHOR

Fig. 10

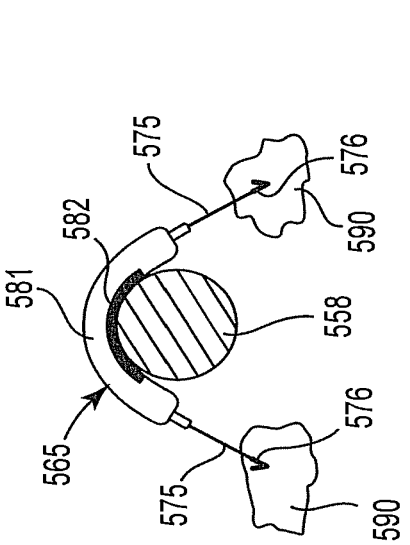


Fig. 14C

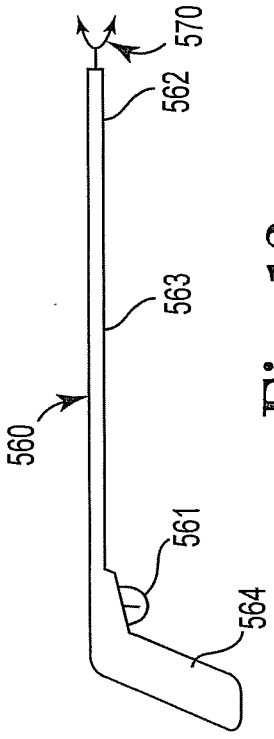


Fig. 12

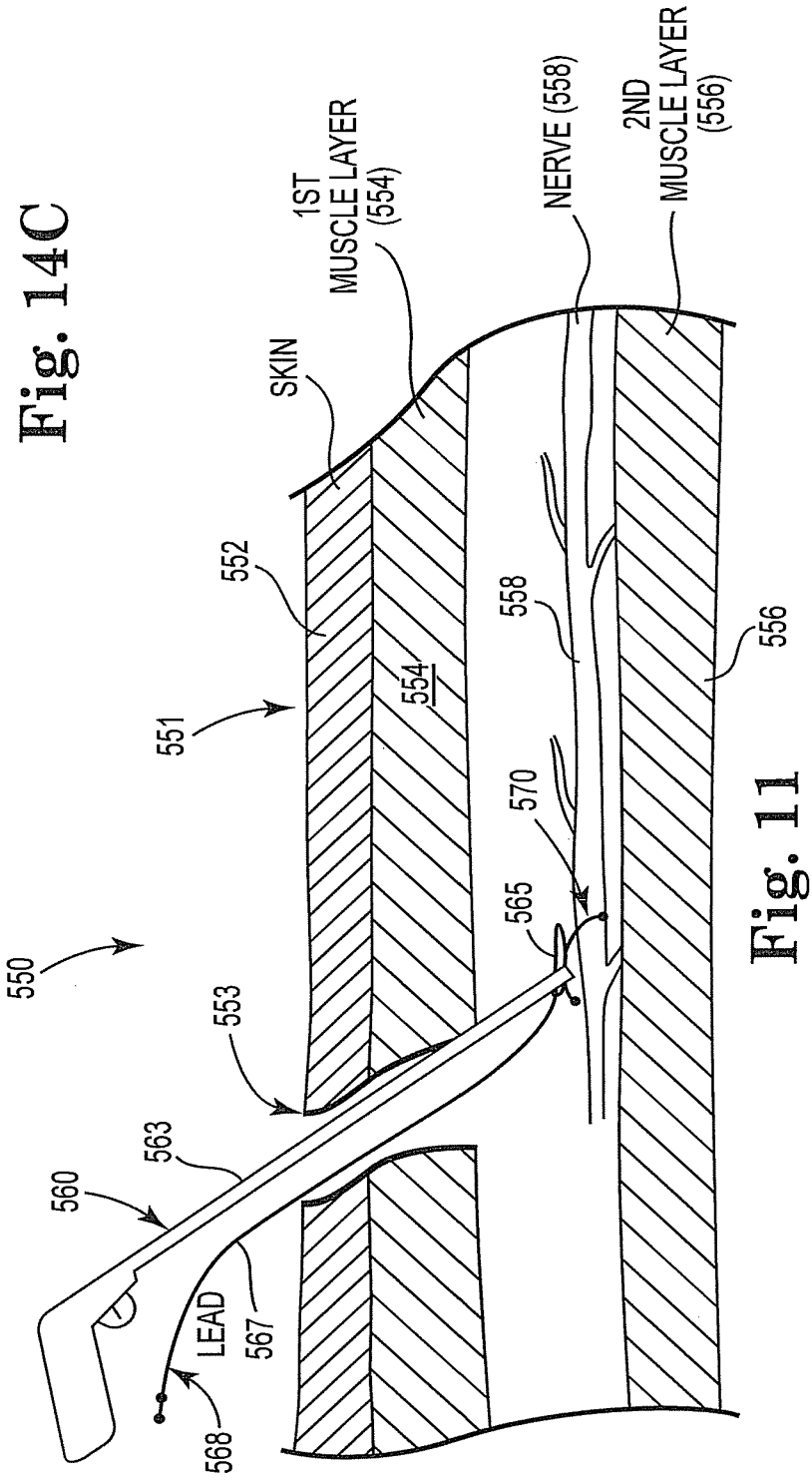


Fig. 11

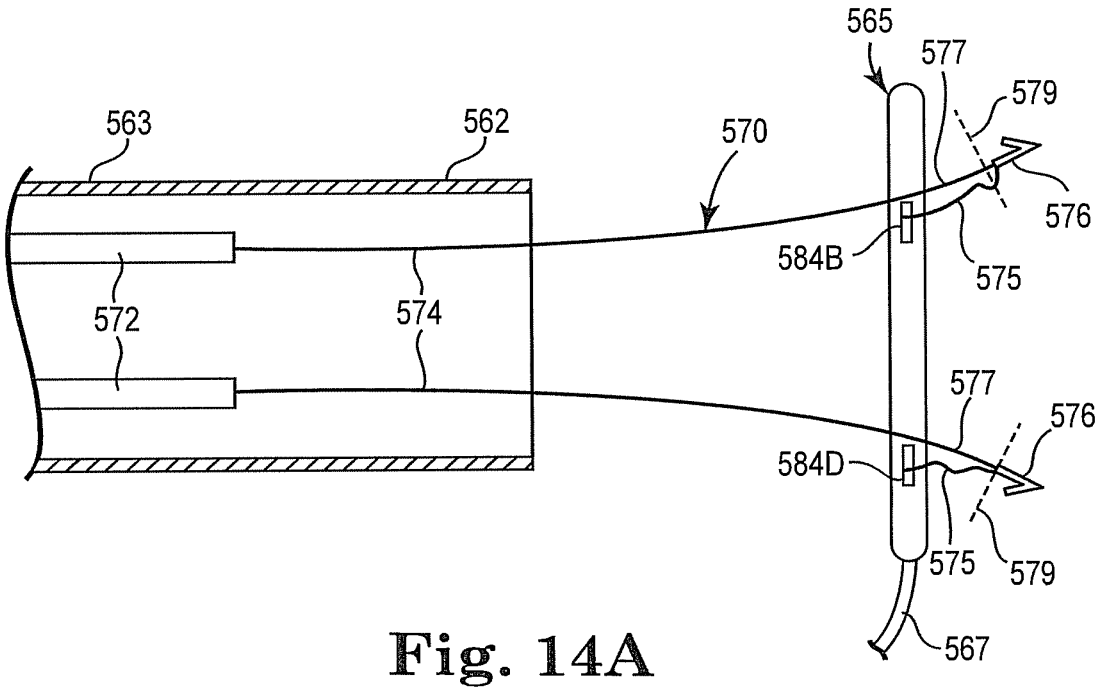


Fig. 14A

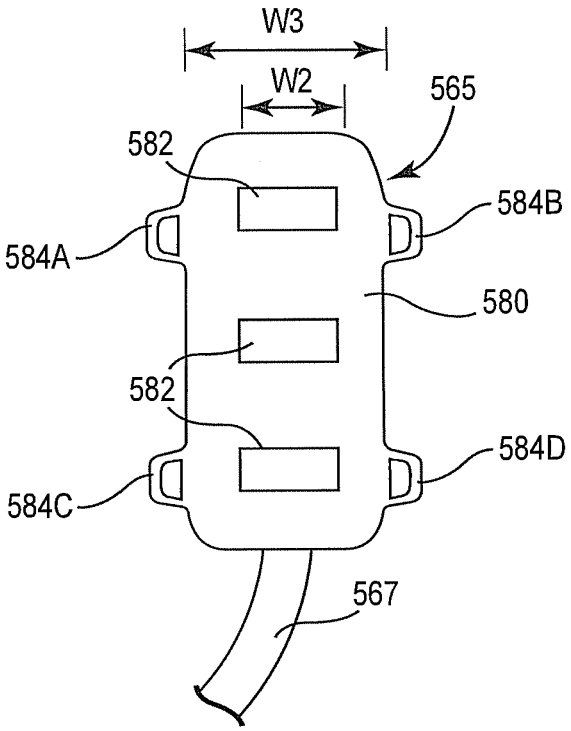


Fig. 13

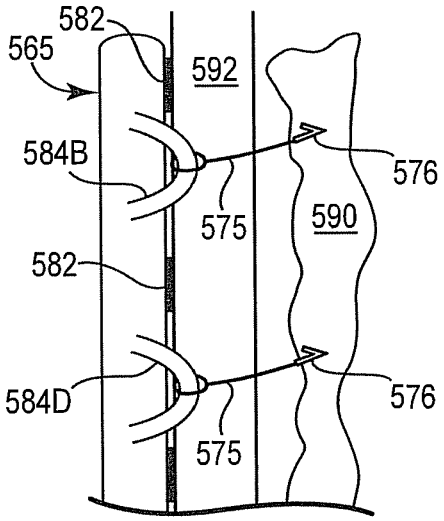


Fig. 14B

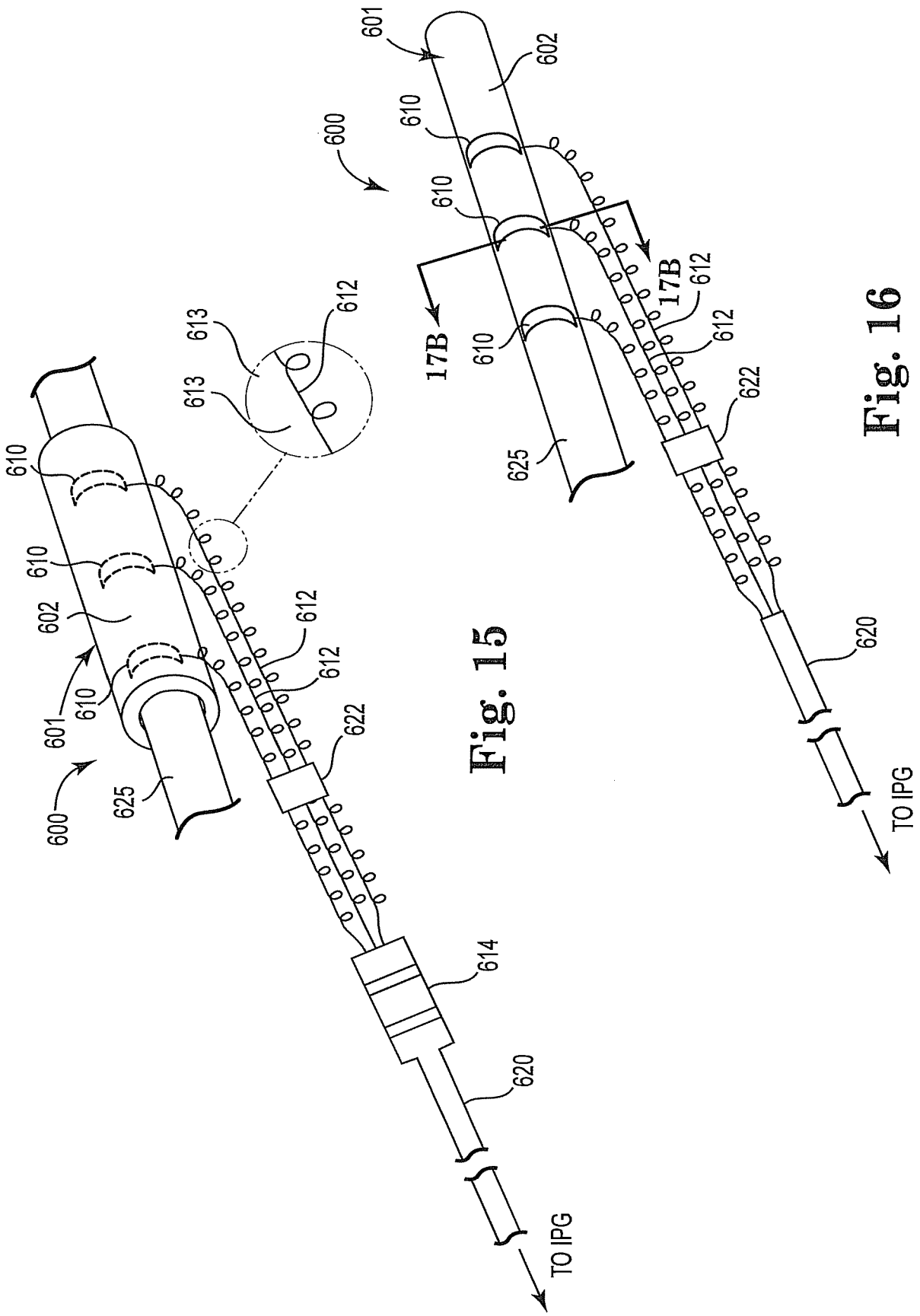

600
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613
17B
17B
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TO IPG
TO IPG

Fig. 15

Fig. 16

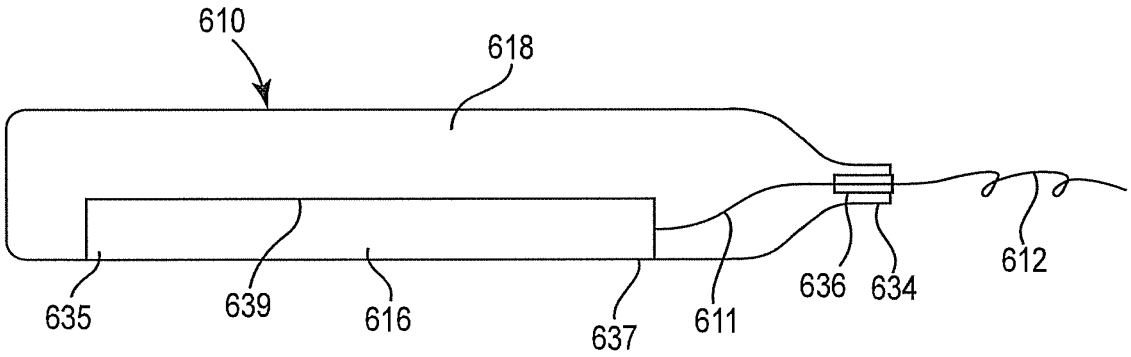


Fig. 17A

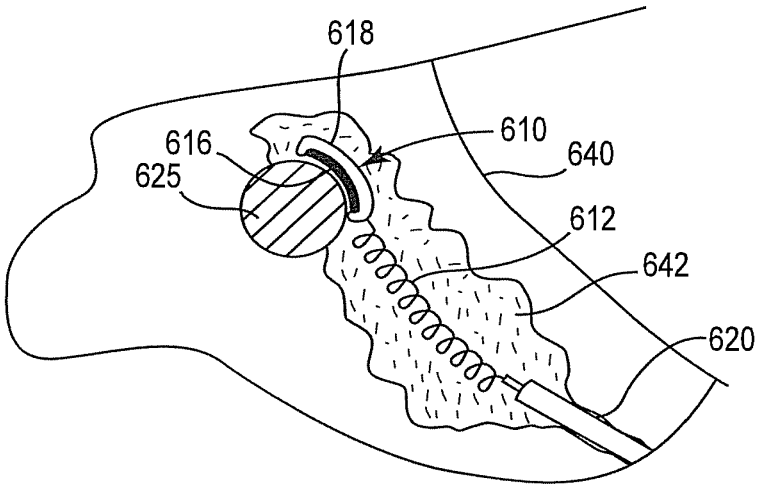


Fig. 17B

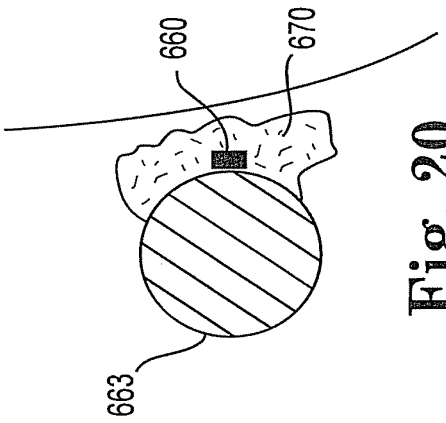


Fig. 20

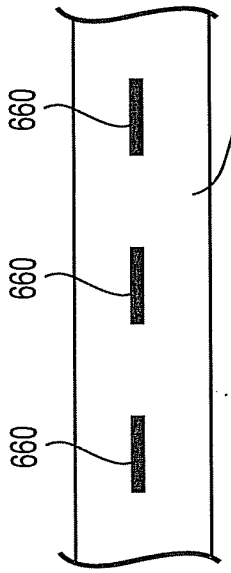


Fig. 21

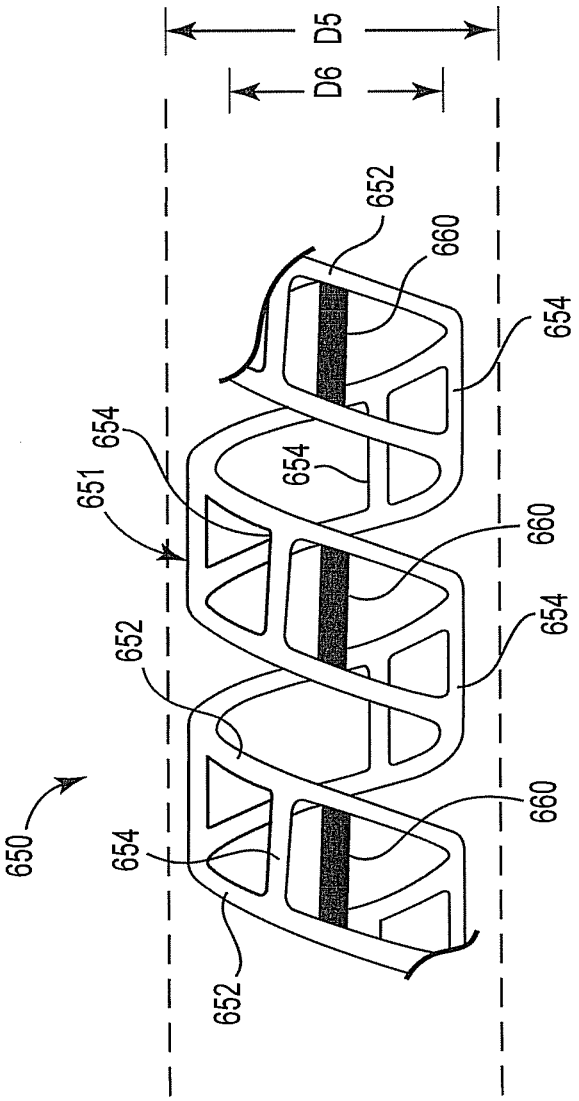


Fig. 18

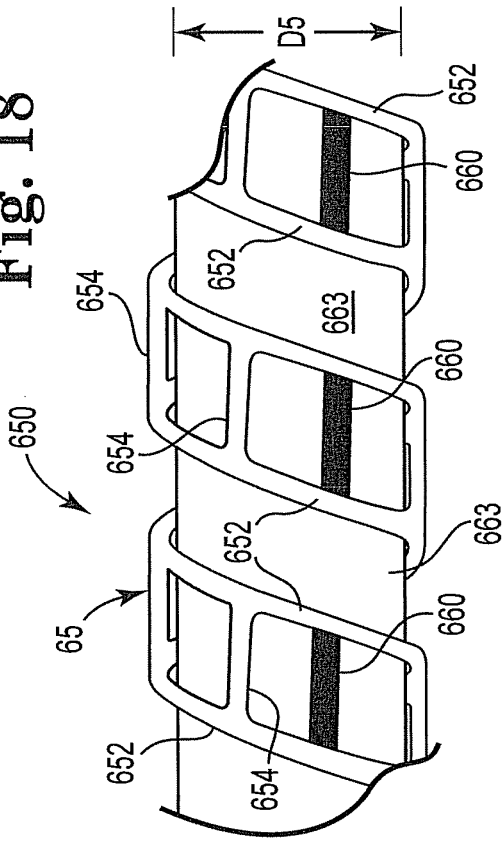


Fig. 19

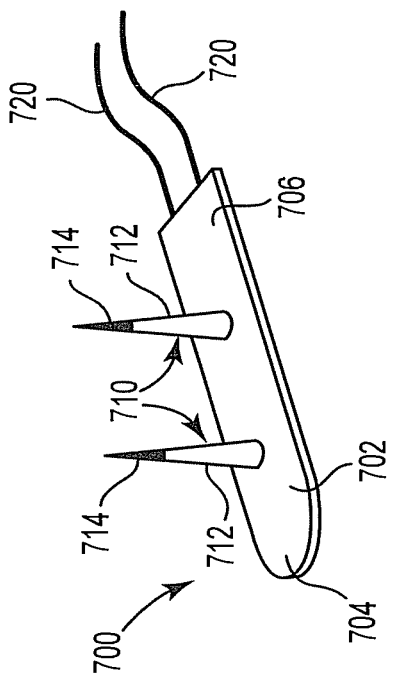


Fig. 22

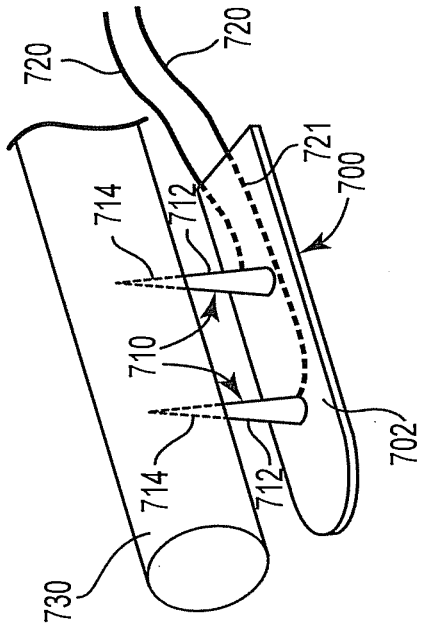


Fig. 23

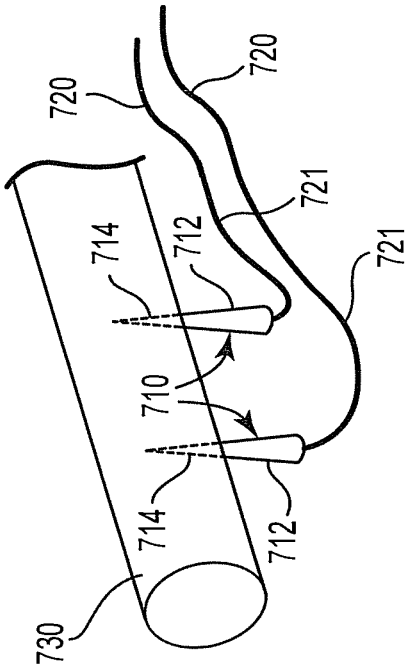


Fig. 24

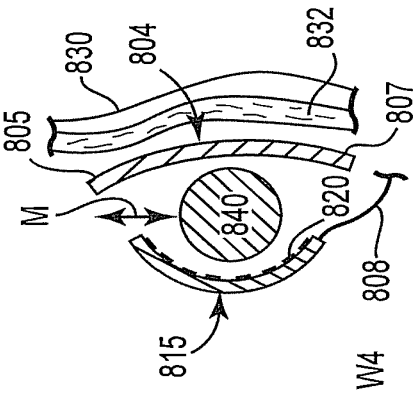


Fig. 27

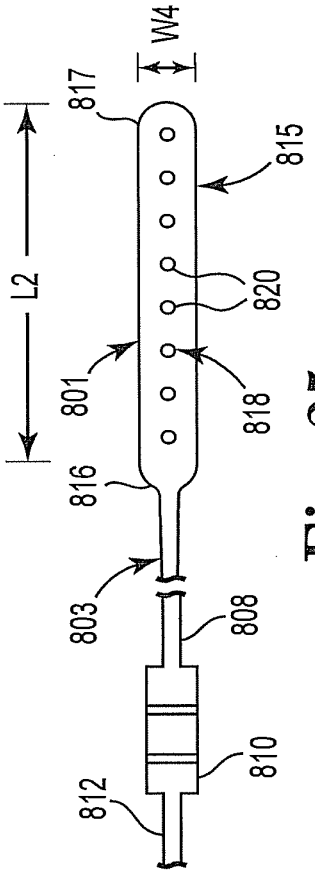


Fig. 25

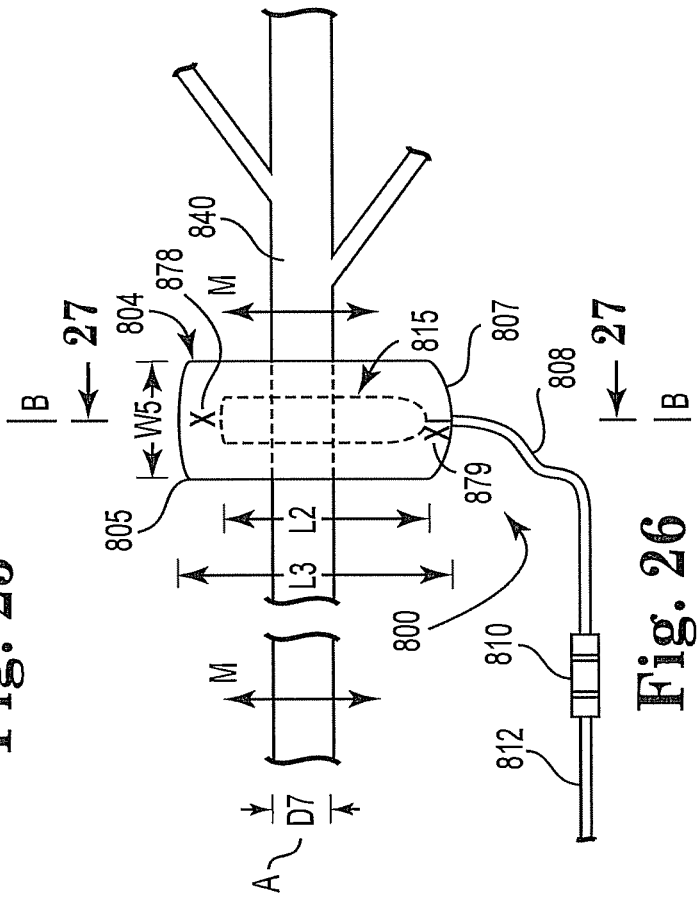


Fig. 26

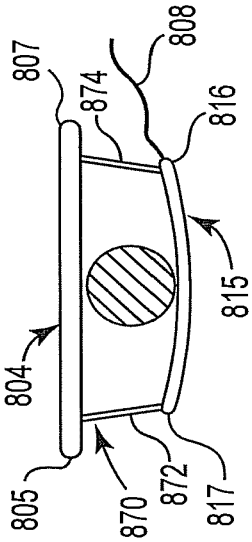


Fig. 29

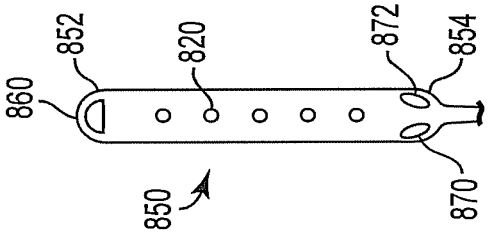


Fig. 28

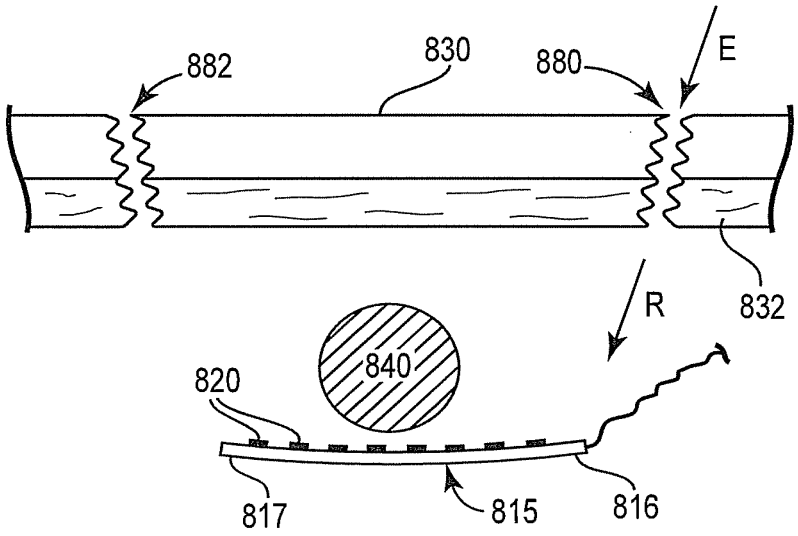


Fig. 30

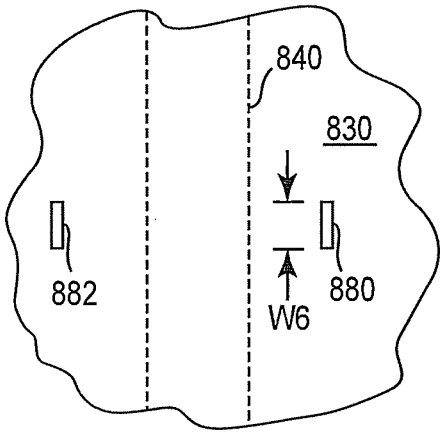


Fig. 31

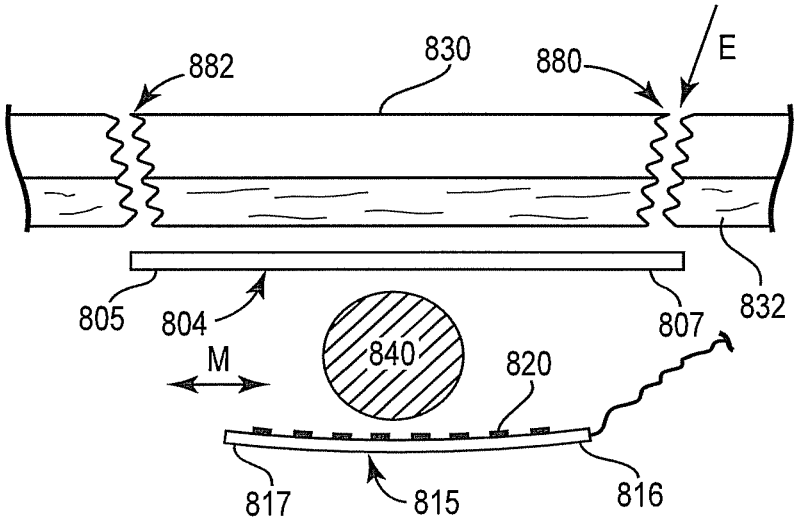


Fig. 32

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/029253

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/05 A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2008/183187 A1 (BLY MARK J [US]) 31 July 2008 (2008-07-31) abstract; figures 1,2 paragraphs [0020] - [0027]	22-27
Y	US 2008/103545 A1 (BOLEA STEPHEN L [US] ET AL) 1 May 2008 (2008-05-01) abstract; figures 2,24 paragraphs [0002], [0083] - [0085], [0121]	22-27
Y	US 4 512 351 A (POHNDORF PETER J [US]) 23 April 1985 (1985-04-23) the whole document	22-27
A	US 2005/234439 A1 (UNDERWOOD RONALD A [US]) 20 October 2005 (2005-10-20) the whole document	22-27

-/--

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 June 2010	24/09/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Fax: (+31–70) 340–3016	Pereda Cubián, David

Form PCT/ISA/210 (second sheet) (April 2005)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01399

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2010/029253

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2005/182457 A1 (THROPE GEOFFREY B [US] ET AL) 18 August 2005 (2005-08-18) the whole document	22-27
A	US 2005/171576 A1 (WILLIAMS JEFFREY M [US] ET AL WILLIAMS JEFFREY M [US] ET AL) 4 August 2005 (2005-08-04) the whole document	22-27
A	US 2005/159637 A9 (NELSON LIONEL M [US] ET AL NELSON LIONEL M [US] ET AL) 21 July 2005 (2005-07-21) the whole document	22-27
A	US 2003/139789 A1 (TVINNEREIM MAGNE [NO] ET AL) 24 July 2003 (2003-07-24) the whole document	22-27
A	DE 101 03 288 A1 (SCHAUERTE PATRICK [DE]) 1 August 2002 (2002-08-01) the whole document	22-27

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01400

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2010/029253

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-21, 53-55
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

22-27

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01401

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 22-27

   Invention I: Percutaneous system for the access of electrode(s) to a nerve: Access system for treating sleep-related disordered breathing

   ---

2. claims: 28-35

   Invention II: Percutaneous sytem for the access of electrode(s) to a nerve: Electrode implantation instrument

   ---

3. claims: 36-48

   Invention III: Percutaneous system for the access of electrode(s) to a nerve: Implantable electrode system

   ---

4. claims: 49-52

   Invention IV: Percutaneous system for the access of electrode(s) to a nerve: Stimulation unit, with insulation shield and fastening mechanism

   ---

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2010/029253

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2008183187 A1	31-07-2008	WO 2008094350 A1	07-08-2008
US 2008103545 A1	01-05-2008	AU 2007313319 A1	24-04-2008
		CA 2666529 A1	24-04-2008
		EP 2116274 A2	11-11-2009
		US 2008103407 A1	01-05-2008
		WO 2008048471 A2	24-04-2008
US 4512351 A	23-04-1985	NONE	
US 2005234439 A1	20-10-2005	NONE	
US 2005182457 A1	18-08-2005	AU 2005214041 A1	01-09-2005
		CA 2554676 A1	01-09-2005
		EP 1720606 A2	15-11-2006
		JP 2007531562 T	08-11-2007
		JP 4125357 B2	30-07-2008
		JP 2007268293 A	18-10-2007
		WO 2005079295 A2	01-09-2005
US 2005171576 A1	04-08-2005	AU 2002349957 A1	28-04-2003
		CA 2463936 A1	24-04-2003
		EP 1444004 A2	11-08-2004
		WO 03033068 A2	24-04-2003
US 2005159637 A9	21-07-2005	AU 2004224331 A1	07-10-2004
		CA 2519154 A1	07-10-2004
		EP 1613251 A2	11-01-2006
		JP 2006523121 T	12-10-2006
		JP 2007229485 A	13-09-2007
		US 2004149290 A1	05-08-2004
		US 2007186936 A1	16-08-2007
		US 2005004417 A1	06-01-2005
		WO 2004084709 A2	07-10-2004
US 2003139789 A1	24-07-2003	NONE	
DE 10103288 A1	01-08-2002	WO 02058785 A1	01-08-2002
		EP 1353724 A1	22-10-2003

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
14 February 2013 (14.02.2013)

WIPO | PCT

(10) International Publication Number
WO 2013/023218 A1

(51) **International Patent Classification**:
A61N 1/36 (2006.01) *A61B 5/08* (2006.01)

(21) **International Application Number**:
PCT/US2012/050615

(22) **International Filing Date**:
13 August 2012 (13.08.2012)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
61/522,426 11 August 2011 (11.08.2011) US

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) **Title**: SYSTEM FOR SELECTING A STIMULATION PROTOCOL BASED ON SENSED RESPIRATORY EFFORT

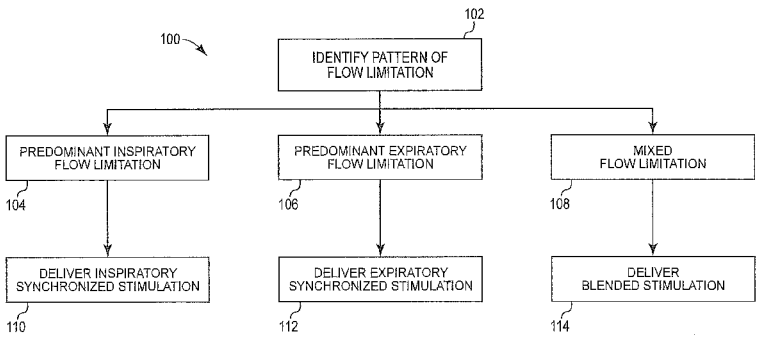


Fig. 1C

(57) **Abstract**: A stimulation protocol determination system (74) includes an input module (76) and a selector module (78). The input module is provided to receive an indication of an upper airway flow limitation via sensed respiratory effort (82) information. The selection module is provided to automatically select, based on the indicated upper airway flow limitation, a stimulation protocol (86).

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SYSTEM FOR SELECTING A STIMULATION PROTOCOL BASED ON SENSED RESPIRATORY EFFORT

Cross-Reference to Related Application

This application is a Non-Provisional Application of Provisional U.S. Patent Application Serial Number 61/522,426, entitled "Method and System for Applying Stimulation in Treating Sleep Disordered Breathing," filed August 11, 2011, incorporated herein by reference.

Background

In cases in which sleep disordered breathing is caused by upper airway obstructions, one form of treatment includes stimulating one or more nerves that affect upper airway dilation. In a conventional technique, the stimulation is applied continuously or synchronized to the respiratory cycle. However, in some instances, continuous stimulation may not desirable because of any potential long-term effects of over-stimulating the nerve.

Brief Description of the Drawings

The accompanying drawings are included to provide a further understanding of embodiments and are incorporated in and constitute a part of this specification. The drawings illustrate embodiments and together with the description serve to explain principles of embodiments. Other embodiments and many of the intended advantages of embodiments will be readily appreciated as they become better understood by reference to the following detailed description. The elements of the drawings are not necessarily to scale relative to each other. Like reference numerals designate corresponding similar parts.

Figure 1A is a schematic diagram of an at least partially implantable stimulation system relative to a patient, according to an example of the present disclosure.

Figure 1B is a block diagram schematically illustrating a pulse generator, according to one example of the present disclosure.

Figure 1C is flow diagram schematically illustrating a method of treating an upper airway flow limitation, according to one example of the present disclosure.

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Figure 2 is a diagram schematically illustrating respiratory cycles in one example breathing pattern, according to one example of the present disclosure.

Figure 3 is a diagram schematically illustrating a first respiratory cycle exhibiting a flow limitation that occurs predominantly during an inspiratory phase and schematically illustrating a second respiratory cycle exhibiting mitigation of the flow limitation in response to a nerve stimulation protocol, according to one example of the present disclosure.

Figure 4 is a diagram schematically illustrating a first respiratory cycle exhibiting a flow limitation that occurs predominantly during an expiratory phase and schematically illustrating a second respiratory cycle exhibiting mitigation of the flow limitation in response to a nerve stimulation protocol, according to one example of the present disclosure.

Figure 5A is a diagram schematically illustrating a first respiratory cycle exhibiting a mixed flow limitation that overlaps a portion of an inspiratory phase and a portion of an expiratory phase and schematically illustrating a second respiratory cycle exhibiting mitigation of the flow limitation in response to one example nerve stimulation protocol, according to one example of the present disclosure.

Figure 5B is a diagram schematically illustrating portions of a generally continuous stimulation period relative to portions of the respective inspiratory and expiratory phases of a respiratory cycle, according to one example of the present disclosure.

Figure 6 is a diagram schematically illustrating a first respiratory cycle exhibiting a mixed flow limitation that overlaps a portion of an inspiratory phase and a portion of an expiratory phase and schematically illustrating a second respiratory cycle exhibiting mitigation of the flow limitation in response to one example nerve stimulation protocol, according to one example of the present disclosure.

Figures 7A-7B are a pair of diagrams with each diagram schematically illustrating a series of respiratory cycles during which one example nerve stimulation protocol is applied, according to one example of the present disclosure.

Figures 8-13 are a series of diagrams with each diagram schematically illustrating a respiratory cycle during which one example nerve stimulation protocols is applied, according to one example of the present disclosure.

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Detailed Description

In the following Detailed Description, reference is made to the accompanying drawings which form a part hereof, and in which is shown specific examples of the present disclosure which may be practiced. In this regard, directional terminology, such as "top," "bottom," "front," "back," "leading," "trailing," etc., is used with reference to the orientation of the Figure(s) being described. Because components of examples of the present disclosure can be positioned in a number of different orientations, the directional terminology is used for purposes of illustration and is in no way limiting. It is to be understood that other examples may be utilized and structural or logical changes may be made without departing from the scope of the present disclosure. The following detailed description, therefore, is not to be taken in a limiting sense.

At least some examples of the present disclosure are directed to methods of treating obstructive sleep apnea via applying stimulation in intervals or periods during targeted portions of the respiratory cycle. By doing so, upper airway patency is maintained and/or increased while preventing collapse of the upper airway. At the same time, by using targeted stimulation, one can limit the overall volume of stimulation applied to a given nerve or set of nerves.

Figure 1A is a schematic diagram of an at least partially implantable stimulation system, according to an example of the present disclosure. As illustrated in Figure 1A, in one example system 10 an implantable pulse generator (IPG) 35, capable of being surgically positioned within a pectoral region of a patient 20, and a stimulation lead 32 electrically coupled with the IPG 35 via a connector (not shown) positioned within a connection port of the IPG 35. The lead 32 includes a stimulation electrode portion 45 and extends from the IPG 35 so that the stimulation electrode portion 45 is positioned in contact with a desired nerve, such as the hypoglossal nerve 33 of the patient 10, to enable stimulation of the nerve 33, as described below in detail. An exemplary implantable stimulation system in which lead 32 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., and which is incorporated herein by reference in its entirety. In one embodiment, the lead 32 further includes at least one

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sensor portion 40 (electrically coupled to the IPG 35 and extending from the IPG 35) positioned in the patient 10 for sensing respiratory effort, such as respiratory pressure.

In some embodiments, the sensor portion 40 detects respiratory effort including respiratory patterns (e.g., inspiration, expiration, respiratory pause, etc.) in order to trigger activation of an electrode portion to stimulate a target nerve. Accordingly, with this arrangement, the IPG 35 (Figure 1) receives sensor waveforms from the respiratory sensor portion 40, thereby enabling the IPG 35 to deliver electrical stimulation synchronously with inspiration (or synchronized relative to another aspect of the respiratory cycle) according to a therapeutic treatment regimen in accordance with examples of the present disclosure. It is also understood that the respiratory sensor portion 40 is powered by the IPG 35 and the IPG 35 also contains internal circuitry to accept and process the impedance signal from the stimulation lead 32.

In some embodiments, the sensor portion 60 is a pressure sensor. In one example, the pressure sensor in this embodiment detects pressure in the thorax of the patient. In other examples, the sensed pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow). With this configuration, the controller is configured to analyze this pressure sensing information to detect the respiratory patterns of the patient.

In some other embodiments, the respiratory sensor portion 40 comprises a bio-impedance sensor or pair of bio-impedance sensors and can be located in regions other than the pectoral region. In one aspect, such an impedance sensor is configured to sense a bio-impedance signal or pattern whereby the control unit evaluates respiratory patterns within the bio-impedance signal. For bio-impedance sensing, in one embodiment, electric current will be injected through an electrode portion within the body and an electrically conductive portion of a case of the IPG 35 (Figure 3A) with the voltage being sensed between two spaced apart stimulation electrode portions (or also between one of the stimulation electrode portions and the electrically conductive portion of the case of IPG 35) to compute the impedance.

In some embodiments, system 10 also comprises additional sensors to further obtain physiologic data associated with respiratory functions. For example, system 10 may include various sensors (e.g., sensors 47, 48, 49 in FIG. 1) distributed about the chest area

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for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals.

In some embodiments, the sensing and stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. In other embodiments, one or more components of the system are not implanted in a body of the patient. A few non-limiting examples of such non-implanted components include external sensors (respiration, impedance, etc.), an external processing unit, or an external power source. Of course, it is further understood that the implanted portion(s) of the system provides a communication pathway to enable transmission of data and/or controls signals both to and from the implanted portions of the system relative to the external portions of the system. The communication pathway includes a radiofrequency (RF) telemetry link or other wireless communication protocols.

Whether partially implantable or totally implantable, the system is designed to stimulate the hypoglossal nerve during some portion of the repeating respiratory cycle to thereby prevent obstructions or occlusions in the upper airway during sleep. In one embodiment, the implantable system comprises an implantable pulse generator (IPG), a peripheral nerve cuff stimulation lead, and a pressure sensing lead.

Figure 1B is a block diagram schematically illustrating an implantable pulse generator (IPG) 60, according to one example of the present disclosure. In one embodiment, IPG 60 generally includes at least substantially the same features and attributes as IPG 35 of Figure 1A. As illustrated in Figure 1B, in one example, implantable pulse generator 60 includes controller 62, memory 64, sensing module 66, stimulation module 68, patient management module 70, and a therapy manager 72.

Via an array of parameters, the sensing module 66 receives and tracks signals from various physiologic sensors (such as a pressure sensor, blood oxygenation sensor, acoustic sensor, electrocardiogram (ECG) sensor, or impedance sensor) in order to determine a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. Such respiratory detection may be received from either a single sensor or any multiple of sensors, or combination of various physiologic

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sensors which may provide a more reliable and accurate signal. In one example, sensing module 90 receives signals from sensor portion 40 and/or sensors 47, 48, 49 in Figure 1A.

In one example, a controller 62 of IPG 60 comprises one or more processing units and associated memories configured to generate control signals directing the operation of IPG 60 and system 10 (Fig. 1A). In particular, in response to or based upon commands received via an input and/or machine readable instructions (including software) contained in the memory 64 associated with the controller 62 in response to physiologic data gathered via the sensors, controller 62 generates control signals directing operation of pulse generator 60 to selectively control stimulation of a target nerve, such as the hypoglossal nerve, to restore airway patency and thereby reduce or eliminate apnea events. In one example, controller 62 is embodied in a general purpose computer.

For purposes of this application, in reference to the controller 62, the term "processor" shall mean a presently developed or future developed processor (or processing resources) that executes sequences of machine readable instructions (such as but not limited to software) contained in a memory. Execution of the sequences of machine readable instructions causes the processor to perform actions, such as operating IPG 60 to provide apply stimulation to a nerve in the manner described in the examples of the present disclosure. The machine readable instructions may be loaded in a random access memory (RAM) for execution by the processor from their stored location in a read only memory (ROM), a mass storage device, or some other persistent storage or non-volatile form of memory, as represented by memory 64. In one example, memory 64 comprises a computer readable medium providing non-transitory or non-volatile storage of the machine readable instructions executable by a process of controller 62. In other examples, hard wired circuitry may be used in place of or in combination with machine readable instructions (including software) to implement the functions described. For example, controller 62 may be embodied as part of at least one application-specific integrated circuit (ASIC). In at least some examples, the controller 62 is not limited to any specific combination of hardware circuitry and machine readable instructions (including software), nor limited to any particular source for the machine readable instructions executed by the controller 62.

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With this in mind, in general terms the therapy manager 72 acts to synthesize respiratory information, to determine suitable stimulation parameters based on that respiratory information, and to direct electrical stimulation to the target nerve.

In one example, among other components, therapy manager 72 includes a stimulation protocol determination module 74.

In one example, the stimulation protocol determination module 74 includes an input function 76 and a selector function 78. In general terms, the input function receives an indication of an upper airway flow limitation that is sensed via respiratory effort information. In one example, input function 76 includes a flow limitation parameter 80 and a respiratory effort parameter 82.

In one example, the flow limitation parameter 80 detects and tracks when a flow limitation is present in the upper airway of a patient. In one aspect, the flow limitation parameter 80 tracks the degree and/or duration of flow limitation. Various examples of recognizing a flow limitation are further described below in association with at least Figures 3-13.

In one example, the respiratory effort parameter 82 detects and tracks respiratory effort information obtained via sensing respiratory information such as, but not limited to, the respiratory sensing methods previously described above in association with Figures 1A-1B. This respiratory effort information corresponds to air flow and enables constructing or determining a degree and/or duration of a flow limitation in the upper airway of a patient.

As noted above, the therapy manager 72 also includes a selector function 78, which in general terms, enables the IPG 60 to select an appropriate stimulation protocol that is responsive to a particular type of upper airway flow limitation. In one example, the selector function 78 includes a respiratory phase parameter 84 and a protocol array parameter 86. The respiratory phase parameter 84 determines which respiratory phase or phases, or portions of the respective phases, in which stimulation should be applied. In one aspect, these determinations are made based on the ongoing sensing of respiratory effort, with the sensed information being received by input function 76.

The protocol array parameter 86 provides an array of stimulation protocols suitable for delivering to a nerve of a patient, depending upon the type, degree, and/or duration of a

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flow limitation. The protocol array parameter 86 does so in cooperation with respiratory phase parameter 84 and input function 76.

Specific examples of treating disordered breathing via the therapy manager 72, and in particular, treating upper airway flow limitations (i.e. obstructions) via the functions, components, parameters, and/or features of protocol determination module 74 of therapy manager 72 are further described and illustrated below in association with Figures 3-13.

In general terms, the stimulation module 68 of IPG 60 is configured to generate and apply a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) 45 in Fig. 1A) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager 72, such as via protocol determination module 74.

In general terms, the patient management module 70 is configured to facilitate communication to and from the IPG 60 in a manner familiar to those skilled in the art. Accordingly, the patient management module 70 is configured to report activities of the IPG 70 (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG 60 from an external source, such as a patient programmer, clinician programmer, etc.

In one example, as shown in Figure 1C, prior to applying stimulation to maintain and/or restore patency in the upper airway, at 102 the method 100 includes identifying a pattern of flow limitation during the respiratory cycle. In one aspect, method 100 identifies the circumstances in which a flow limitation primarily occurs. In particular, with further reference to Figure 1, method 100 distinguishes between a flow limitation occurring: (1) predominantly during inspiration (at 104); (2) predominantly during expiration (at 106); or (3) during both a portion of inspiration and a portion of expiration which acts as a mixed flow limitation (at 108). In one aspect, in the context of the present disclosure, a flow limitation corresponds to a narrowing of the upper airway of the type typically associated with obstructive sleep apnea or other disordered breathing patterns, as familiar to those skilled in the art.

As shown in Figure 1C, in one example, in the event that the flow limitation occurs predominantly during inspiration (at 104), then stimulation is applied during and/or synchronized with inspiration (at 110). On the other hand, in another example, in the event

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that the flow limitation occurs predominantly during (i.e. coincides with) expiration (at 106), and then stimulation is applied during and/or synchronized with expiration (at 112).

However, in some examples, when the flow limitation occurs predominantly during (i.e. coincides with) a portion of inspiration and a portion of expiration (at 108), the stimulation is applied during some portion of inspiration and some portion of expiration (at 114).

In one example, when the flow limitation overlaps the transition between the end of inspiration and the beginning of expiration, the stimulation will be applied to overlap the transition between the end of inspiration and the beginning of expiration.

In another example, when the flow limitation occurs during a portion of inspiration and a portion of expiration (at 108), the stimulation is applied to cover an entire respiratory cycle, including an entire inspiratory phase and an entire expiratory phase.

In order to recognize a flow limitation, the method 100 uses as a reference point a normal breathing pattern 150, as shown in Figure 2. Of course, variances may exist from patient-to-patient so it will be understood that the normal breathing pattern 150 is a representative example provided for illustrative purposes and is not intended to strictly define a breathing pattern that is universally normal for all patients. With this in mind, in some embodiments, the method 100 uses the particular breathing pattern of a specific patient (to which the method is applied) as the reference point to evaluate the presence or absence of a flow limitation in breathing.

In the example of normal breathing pattern 150 shown in Figure 2, a respiratory cycle 160 includes an inspiratory phase 162 and an expiratory phase 170. The inspiratory phase 162 includes an initial portion 164, intermediate portion 165, and end portion 166 while expiratory phase 170 includes an initial portion 174, intermediate portion 175, end portion 176, and an expiratory peak 177. A first transition 180 occurs at a junction between the end inspiratory portion 166 and the initial expiratory portion 174 while a second transition 182 occurs at a junction between the end expiratory portion 176 and the initial inspiratory portion 164.

In one example, the various stimulation protocols described and illustrated in association with Figures 3-13 are implemented via system 10 (Fig. 1A) and/or IPG 60 (Fig. 1B) including at least therapy manager 72 and/or protocol determination module 74.

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However, in another example, the various stimulation protocols described and illustrated in association with Figures 3-13 are implemented via other component, modules, and systems.

Figure 3 is a diagram 200 illustrating a disordered breathing pattern 203A and treated breathing pattern 203B (separated by dashed line 203C), according to one embodiment of the present disclosure. As shown in Figure 3, disordered breathing pattern 203A reflects the presence of a flow limitation in the upper airway that occurs predominantly during the inspiratory phase of a respiratory cycle. The inspiratory phase 202A includes an initial portion 204A, an intermediate portion 205A, and an end portion 206A while the expiratory phase 210A includes an initial portion 214A, intermediate portion 215A, peak 217A, and end portion 216A. In one aspect, intermediate portion 205A of inspiratory phase 202A forms a generally flat or horizontal shape corresponding to a substantially truncated amplitude (as compared to a normal breathing pattern, such as Figure 2) and that reflects the occurrence of a flow limitation (symbolically represented by arrow 201) in the upper airway during inspiration. However, via application of stimulation (symbolically represented by bar 221), breathing is restored as represented by treated breathing pattern 202B in which intermediate portion 205B of inspiratory phase 202B resumes a generally parabolic shape corresponding to a generally normal amplitude and that represents amelioration of the flow limitation. In one embodiment, the stimulation is represented by bar 221, which extends from a first end 222 to a second end 224, with the stimulation substantially coinciding with the entire duration of the inspiratory phase 202B. As shown in Figure 3, the stimulation 221 terminates prior to the expiratory phase 210B. However, as will be explained in more detail below, in other embodiments, the applied stimulation does not extend the entire duration of inspiratory phase 202B but is applied to select portions of the inspiratory phase 202B.

It will be understood that, in one example, the detection of flow limitations and/or associated apneas), as well as the detection of the beginning and end of the respective inspiratory and expiratory phases of the respiratory cycle to enable determining when to stop or start stimulation, is performed according to, or in cooperation with, known methods and devices for doing so. Some non-limiting examples of such devices and methods to recognize and detect the various features and patterns associated with respiratory effort and flow limitations include, but are not limited to: PCT Publication WO/2010/059839, titled A

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METHOD OF TREATING SLEEP APNEA, published on May 27, 2010; Christopherson U.S. Patent 5,944,680, titled RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS; and Testerman U.S. Patent 5,522,862, titled METHOD AND APPARATUS FOR TREATING OBSTRUCTIVE SLEEP APNEA.

Figure 4 is a diagram 250 illustrating a disordered breathing pattern 253A and treated breathing pattern 253B, according to one embodiment of the present disclosure. As shown in Figure 4, disordered breathing pattern 253A reflects the presence of a flow limitation in the upper airway that occurs predominantly during the expiratory phase of a respiratory cycle. In the disordered breathing pattern 253A, the inspiratory phase 252A includes an initial portion 254A, an intermediate portion 255A, and an end portion 256A, with the inspiratory phase 252A exhibiting a generally normal breathing pattern 150 (Figure 2). Referring again to Figure 4, the expiratory phase 262A includes an initial portion 264A, intermediate portion 265A, peak 267A, and end portion 266A. In one aspect, expiratory phase 262A has a relatively shallow peak 267A corresponding to an amplitude or peak pressure that is substantially smaller than a peak 177 of an expiratory phase 170 in a normal breathing pattern 150 (Figure 2). The pattern of expiratory phase 262A, which corresponds to a generally shallow expiration, reflects the occurrence of a flow limitation (symbolically represented by arrow 251) in the upper airway during expiration. Moreover, because the peak 267A is so shallow, the intermediate portion 265A in the expiratory phase 262A has a relatively gradual upward slope instead of the generally steep upward slope present in the intermediate portion 175 in the normal expiratory phase 170 (of a normal breathing pattern 150 in Figure 2).

However, as shown in Figure 4, via application of stimulation (symbolically represented by bar 270), the expiratory phase 262B becomes corrected such that peak 267B resumes its full amplitude and intermediate portion 265B of expiratory phase 262B is restored to a generally steep upward slope, both of which represents amelioration of the flow limitation. In one embodiment, the stimulation (270) is represented by bar 271 (which extends from a first end 272 to a second end 274) and substantially coincides with the entire duration of the expiratory phase 262B. However, as will be explained in more detail below, in other embodiments, the applied stimulation extends only part of the duration of expiratory phase 262B.

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In one embodiment, application of the stimulus occurs at an inspiratory phase (Figure 3) or at an expiratory phase (Figure 4), respectively, of every respiratory cycle. However, in other embodiments, application of the stimulus is applied selectively to just some respiratory cycles, as needed, in association with an auto-titration method. One example of such auto-titration methods include A METHOD OF TREATING SLEEP APNEA as described and illustrated in PCT Publication WO/2010/059839, published on May 27, 2010.

Figure 5A is a diagram 280 illustrating a disordered breathing pattern 283A and treated breathing pattern 283B, according to one embodiment of the present disclosure. As shown in Figure 5A, disordered breathing pattern 283A represents a flow limitation in the upper airway that occurs during both a portion of an inspiratory phase 282 and a portion of the expiratory phase 292 of a respiratory cycle. As shown in Figure 5A, the inspiratory phase 282A includes an initial portion 284A, an intermediate portion 285A, and an end portion 286A while the expiratory phase 292A includes an initial portion 294A, intermediate portion 295A, peak 297A, and end portion 296A.

In one aspect, Figure 5A illustrates that in disordered breathing pattern 283A, intermediate portion 285A of inspiratory phase 282A forms a generally flat or horizontal shape corresponding to a substantially truncated amplitude (as compared to the inspiratory phase 162 of a normal breathing pattern 150, such as Figure 2), with this generally flat shape reflecting the occurrence of a flow limitation (symbolically represented by arrow 281A) in the upper airway during inspiration.

In another aspect, disordered breathing pattern 283A also includes an expiratory phase 292A having a peak 297A corresponding to an amplitude or peak pressure that is substantially smaller than a peak 177 of an expiratory phase 170 in a normal breathing pattern 150 (Figure 2). This pattern 283A, which corresponds to generally shallow expiration, results from a flow limitation (symbolically represented by arrow 281B) in the upper airway during expiration. Moreover, because the peak 297A is so shallow, the intermediate portion 295A has a relatively gradual upward slope instead of the generally steep upward slope present in the intermediate portion 175 in the normal expiratory phase 170 (of a normal breathing pattern 150 in Figure 2).

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In one example, the indicated upper airway flow limitation predominantly coincides with both of a first portion of the inspiratory phase and a first portion of the expiratory phase. In another aspect, this indicated flow limitation does not predominantly coincide with a second portion of inspiratory phase and with a second portion of the expiratory phase.

However, via application of blended stimulation (symbolically represented by bar 300) directed to at least a portion of the inspiratory phase and a portion of the expiratory phase, the flow limitations are mitigated. As shown in treated breathing pattern 283B, a latter segment 285C of intermediate portion 285B (and end portion 286B) resumes a more parabolic shape better resembling a baseline inspiratory phase prior to the flow limitation and that corresponds to amelioration of the "inspiratory" flow limitation.

Likewise, because this stimulation overlaps from the inspiratory phase 282B into the expiratory phase 292B, the treated breathing pattern 283B exhibits a peak 297B approaching a baseline amplitude prior to the flow limitation (like amplitude 177 in the expiratory phase 170 of normal breathing pattern 150 of Figure 2). This treated breathing pattern 283B also exhibits an intermediate portion 295B that is restored to steeper upward slope amplitude, both of which represents amelioration of the "expiratory" flow limitation.

In one embodiment, the stimulation is represented by bar 300, which extends from a first end 301 (in the inspiratory phase 282B) to a second end 303 (in the expiratory phase 292B). The stimulation is applied as a generally continuous stimulation period that is initiated (at a start point located away from a beginning portion 284B of the inspiratory phase 252B) from partway through the intermediate portion 285B and through the end portion 285C of the inspiratory phase 282B, through the transition from inspiration to expiration, through the initial portion 294B and peak 297A of the expiratory phase 292B, and at least partway through the intermediate portion 295B of the expiratory phase 292B (to a termination point prior to end portion 296B of expiratory phase 292B).

In one example, the embodiment of Figure 5A addresses the situation for some patients in which the greatest risk for airway collapse appears to occur near the end of inspiration and the beginning of expiration. In these instances, besides harmfully limiting a duration and volume of inspiration, a partially restricted upper airway throughout the inspiratory phase predisposes the upper airway to be more susceptible to further collapse at

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the end of the inspiratory phase and/or to the beginning of the expiratory phase. Accordingly, in the embodiment of Figure 5A, the blended stimulation (represented by bar 300) begins at start point approximately midway through the inspiratory phase 282B and extends substantially continuously through a transition between the end of inspiration and the beginning of expiration until reaching a termination point approximately midway through the expiratory phase 292B. In one aspect, this blended stimulation is terminated after a bulk of the expiration would have been expected to occur. In this way, continuous stimulation of the hypoglossal nerve through complete respiratory cycles is avoided, which in turn, minimizes unnecessary stimulation of the hypoglossal nerve. Instead, in these embodiments, stimulation is applied strategically in targeted portions of one or more respiratory cycles to prevent upper airway collapse so that stimulation is applied more judiciously while still achieving efficacious results.

Further, it will be understood that diagram 280 in Figure 5A provides just one example schematically illustrating the application of a blended stimulation that overlaps the end of the inspiratory phase and the beginning of the expiratory phase.

Accordingly, applying this blended stimulation overcomes expiratory narrowing, which otherwise might render the upper airway vulnerable to complete collapse during a subsequent inspiratory effort.

Without being bound to any particular theory, it is believed that the blended stimulation that overlaps the end of inspiratory phase and the expiratory phase acts to maintain a minimum level of pressurization within the lungs, which in turn helps maintain airway patency because the minimum level of pressurization helps to prevent a high intensity vacuum from the lungs on the airway, which would otherwise potentially cause collapse of the upper airway.

In this way, for some patients, the stimulation is applied during a period having a higher risk for collapse without having to continuously apply stimulation through the entire respiratory cycle, which in turn, saves energy and minimizes potentially unnecessary stimulation of the nerves.

In one example of a stimulation protocol, such as the one described and illustrated in association with Figure 5A, the generally continuous stimulation period (as represented by bar 300 in Fig. 5A and spanning over a portion of the inspiratory phase and a portion of the

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expiratory phase) is applied to a set of consecutive respiratory cycles over a first time period. Moreover, an input module (such as input module 76 of protocol determination module 74 of therapy manager 72 in Fig. 1B) is configured to evaluate whether flow limitations are persisting despite the stimulation protocol or whether the stimulation protocol has mitigated or eliminated the previously occurring flow limitations. Accordingly, in one aspect, the input module of the therapy manager determines if at least some indications of upper airway flow limitations are received within the first time period. In another aspect, the input module of the therapy manager increases a duration of the generally continuous stimulation period if the input module receives the at least some indications during the first time period when such indications exceed a threshold. In another aspect, the input module of the therapy manager reduces the duration of the generally continuous stimulation period if the input module receives no indications of upper airway flow limitations (or a number of indications less than a threshold) during the first time period.

In one example, the first time period (over which the set of respiratory cycles take place) is a duration, based on an apnea-hypopnea index of a patient, in which an apnea would be expected to occur in the absence of stimulation.

Figure 5B is a diagram schematically illustrating portions of a generally continuous stimulation period relative to portions of an inspiratory phase and an expiratory phase, according to one example of the present disclosure.

As a reference point for illustrating the generally continuous stimulation period, Figure 5B provides substantially the same depiction of a respiratory cycle 160 that was previously shown in Figure 1. Accordingly, the illustrated respiratory cycle 160 includes an inspiratory phase 162 and an expiratory phase 170. The inspiratory phase 162 includes an initial portion 164, intermediate portion 165, and end portion 166 while expiratory phase 170 includes an initial portion 174, intermediate portion 175, end portion 176, and an expiratory peak 177. A first transition 180 occurs at a junction between the end inspiratory portion 166 and the initial expiratory portion 174 while a second transition 182 occurs at a junction between the end expiratory portion 176 and the initial inspiratory portion 164.

According to one example of the present disclosure, Figure 5B further illustrates a first bar 361 that represents a first portion 360 of a generally continuous stimulation period

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358 and a bar 381 that represents a second portion 380 of a generally continuous stimulation period 358. As shown in Figure 5B, the bar 361 includes first end 362 that generally coincides with junction 180 (the end of inspiratory phase 162 and beginning of expiratory phase 170) and a second end 364 located in an intermediate portion of the inspiratory phase 162. As shown in Figure 5B, bar 381 includes first end 382 that generally coincides with junction 180 (the end of inspiratory phase 162 and beginning of expiratory phase 170) and a second end 384 located in an intermediate portion of the expiratory phase 170.

As further demonstrated by Figure 5B, while the generally continuous stimulation period overlaps the inspiratory and expiratory phases 162, 170, the duration of each of the first and second portions of the generally continuous stimulation period can vary among different nerve stimulation protocols as determined by the protocol determination module 74 of therapy manager 72 (Fig. 1B).

In one example, the first portion 360 of the generally continuous stimulation period 358 has a duration of at least one-third (identified by marker 372) of an entirety (E1) of the inspiratory phase 162. In one aspect, the relative proportion of one-third is measured starting at end 362 of bar 361, per directional reference arrow 357. In another example, the first portion 360 of the generally continuous stimulation period 358 has a duration of at least one-half (identified by marker 370) of the entirety (E1) of the inspiratory phase 162. In another example, the first portion 360 of the generally continuous stimulation period 358 has a duration of at least two-thirds (identified by marker 374) of the entirety (E1) of the inspiratory phase 162

In another example, the second portion 380 of the generally continuous stimulation period 358 has a duration of at least one-third (identified by marker 392) of an entirety (E2) of the expiratory phase 170. In one aspect, the relative proportion of one-third is measured starting at end 382 of bar 381, per directional reference arrow 377. In another example, the first portion 380 of the generally continuous stimulation period 358 has a duration of at least one-half (identified by marker 390) of the entirety (E2) of the expiratory phase 170. In another example, the first portion 380 of the generally continuous stimulation period 358 has a duration of at least two-thirds (identified by marker 393) of the entirety (E2) of the expiratory phase 170.

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In one example, the first portion (during which stimulation is applied) of the inspiratory phase 162 corresponds to at least a majority of an entirety (E1) of the inspiratory phase 162 and the first portion (during which stimulation is applied) of the expiratory phase 170 corresponds to at least a majority of an entirety (E2) of the expiratory phase 170. In one example, a majority is defined as at least fifty-one percent (i.e. 51%). In another example, the majority of the inspiratory phase 162 is defined as an at least two-thirds majority of the entirety (E1) of the inspiratory phase 162 and the majority of the expiratory phase is defined as an at least two-thirds majority of the entirety (E2) of the expiratory phase 170.

In one example, variations on the stimulation protocol associated with Figures 5A and 5B are further described later in association with at least Figures 6 and 11.

In another embodiment, as shown in Figure 6, diagram 310 schematically illustrates a disordered breathing pattern 333A resulting from a mixed flow limitation that is substantially similar to the mixed flow limitation in Figure 5A. However, unlike the substantially continuous segment of stimulation 300 applied in Figure 5A, in the embodiment shown in Figure 6, stimulation is applied in two separate relatively short bursts 340, 342. One burst 340 is applied at the beginning of the inspiratory phase 322B while the other burst 342 is applied at the beginning of the expiratory phase 332B. In this embodiment, the stimulation is targeted to anticipate an obstruction, and in turn, apply stimulation at the beginning of one or both of the respective inspiratory and expiratory phases. By stimulating (for a short duration) at the beginning of a respective inspiratory and expiratory phases, the upper airway is held open prior to the maximum flow of air in that phase so that once the flow of air commences, with the upper airway already open to a generally full degree, the inspired or expelled air (respectively) completes the job of maintaining the upper airway in the open state during the remainder of the respective inspiratory or expiratory phase. In another aspect, one potential benefit from applying a stimulation burst at the beginning of an inspiratory phase is the resulting counteraction of the negative pressure (generated by the inspiratory effort) applied to the upper airway.

Without being bound to any particular theory, it is believed that by applying a stimulation burst (e.g., an additional stimulation burst on top of a baseline level of stimulation or an isolated burst of stimulation without a baseline level of stimulation) at the

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beginning of the inspiratory phase, the stimulation causes or ensures radial expansion of the airway at the very time that a high intensity vacuum would be applied (via the lungs) to the upper airway such that the radial expansion of the upper airway (caused by the stimulation burst) directs action or response of tissues in a direction opposite the action of tissue that would might otherwise occur when the vacuum from lungs acts on the upper airway tissues. Accordingly, the stimulation is timed to produce momentum in the tissues of the upper airway toward radial expansion prior to the high intensity vacuum pull (which might otherwise contribute to collapse of the upper airway) from the lungs during the onset of inspiration. Because there is a delay associated with, or caused by, a time constant in the response of the upper airway tissues, by first stimulating the tissue in advance of the vacuum pull from the lungs, enough momentum is established toward radial expansion of the upper airway via the stimulation burst that this momentum counteracts or prophylactically negates the otherwise potentially collapsing effects of the vacuum pull on the upper airway tissues.

In one aspect, by applying stimulation in this manner, it is believed that airway patency is maintained with less overall stimulation being applied because stimulation is applied strategically within one or more respiratory cycles rather than indiscriminately through entire respiratory cycles. With this in mind, in one embodiment the total combined duration of burst 340 and burst 342 (shown in Figure 6) is substantially less than the duration of the stimulation pulse 300 in Figure 5A. Accordingly, adequate airway patency is achieved while significantly reducing the total volume of stimulation applied to the nerve.

In some embodiments in which separate bursts of stimulation are applied to the inspiratory and expiratory phases, respectively, the duration of the bursts in the inspiratory phase differ from the duration of the burst applied in the expiratory phase. For example, as shown in the diagram 400 of Figure 7A, a representative or normal breathing pattern 401 is maintained by applied stimulation. A stimulation burst (represented by bar 420A) of a first duration is applied at the beginning of the inspiratory phase 402A while a second stimulation burst (represented by bar 422A) is applied during substantially the entire expiratory phase 412A. This pattern of stimulation bursts is repeated throughout successive respiratory cycles 402B, 402C, etc.

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In one aspect, the determination regarding the duration of each "inspiratory phase" burst (420A, 420B, 420C) and the duration of each "expiratory phase" burst (422A, 422B, 422C) can vary from patient-to-patient depending upon whether the particular patient tends to exhibit a greater flow limitation in the inspiratory phase 403A or in the expiratory phase 413A. In the example, shown in Figure 7A, the "expiratory phase" bursts (422A, 422B, 422C) have a longer duration than the "inspiratory phase" bursts (420A, 420B, 420C) to treat a patient that generally exhibits a mixed flow limitation (both inspiratory and expiratory) but having greater flow limitations during the expiratory phase.

In one embodiment, anyone of or all of an amplitude, a pulse width, a frequency of applied stimulation during the inspiratory phase is different than anyone of (or all of) an amplitude, a pulse width, a frequency of applied stimulation during the expiratory phase. In addition, a ramped stimulation pattern in which stimulation ramps upward (increases) at the beginning of a stimulation period or ramps downward at the end of a stimulation period, can be applied in one or both of the inspiratory and expiratory phases.

In some embodiments, as shown in Figure 7B, instead of applying a stimulation burst with each respiratory cycle, the stimulation bursts (e.g. 420A, 420C, 422A, 422C) are applied every other respiratory cycle, such that an intermediate "inspiratory phase" burst 422A and an intermediate "expiratory phase" burst 422B are omitted. In this embodiment, the patient need not receive a stimulation burst each respiratory cycle because with this stimulation pattern the patient receives enough oxygen to keep the respiratory drive in equilibrium. In another embodiment, the pattern of stimulation bursts in the inspiratory phase (applied every respiratory cycle, such as 420A, 420B, 420C) need not be matched by the pattern of stimulation bursts in the expiratory phase (applied every other respiratory cycle, such as 422A and 422C), or vice versa. In this way, the upper airway remains patent and the patient receives sufficient oxygen without receiving stimulation in each inspiratory phase or in each expiratory phase.

In yet other embodiments, other forms of alternating stimulation bursts are applied. For example, in one pattern of stimulation, a low amplitude continuous pulsed stimulation is applied and one or more relatively shorter duration stimulation bursts are applied in a targeted and additive manner to the low amplitude continuous stimulation. Figure 8 is a diagram 450 schematically illustrating a method of treating sleep disordered breathing via a

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stimulation pattern, according to one embodiment of the present disclosure. As shown in Figure 8, a respiratory cycle 453 includes an inspiratory phase 451 and an expiratory phase 461. The inspiratory phase 451 includes an initial portion 454, an intermediate portion 455, and an end portion 456 while the expiratory phase 461 includes an initial portion 464, intermediate portion 465, peak 467, and end portion 466.

As further shown in the diagram 450 of Figure 8, a low amplitude continuous pulsed stimulation (represented by bar 470) is applied in the inspiratory phase 451 and a low amplitude pulsed continuous stimulation (represented by bar 480) in the expiratory phase 461. While bars 470, 480 are shown as separate elements for illustrative purposes, it will be understood that the generally continuous stimulation is substantially uninterrupted through the transition from the inspiratory phase 451 to the expiratory phase 461. In addition, as shown in Figure 8, a shorter duration stimulation burst 475 is applied only in the inspiratory phase 451 (for patients having predominantly inspiratory-based flow limitations) in addition to the generally continuous pulsed lower amplitude tone stimulation 470. While the additional stimulation burst 475 could be applied anywhere within the inspiratory phase 451, in the example shown in Figure 8, the burst is applied at the initial portion 454 of the inspiratory phase 451. In one aspect, applying the burst at the initial portion 454 helps to ensure full patency of the upper airway as inspiration begins because the stimulation causes a response like the action of a virtual stent in the upper airway to pre-establish patency prior to the vacuum pull from the lungs. As previously noted, the initial portion of stimulation (during a peak pressure period) effectively establishes momentum of the upper airway to be moving in direction of expansion (radially outward) such that upon a vacuum applied via the lungs during inspiration, the upper airway tends to stay expanded because response of tissue is slow enough such that the vacuum (generated by the lungs) cannot fully overcome the already established momentum of radial expansion of the upper airway and therefore the initial portion of stimulation prevents collapse of the upper airway.

Without being bound by any particular theory, it is believed that using a burst of stimulation (for example, burst 475 in Figure 8) helps to keep blood oxygenation levels and carbon dioxide levels within an acceptable range, which in turn moderates the respiratory drive, which in turn minimizes peak respiratory pressures. Together, these factors minimizes the risk of an upper airway collapse because the lungs are not forced (via the

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respiratory drive) to exert extra vacuum pressure on an upper airway in an attempt to acquire more oxygen.

In one embodiment, the stimulation pattern in Figure 8 is modified, such that the modified pattern omits the base level of generally continuous stimulation 470 in the inspiratory phase 451, leaving just one or more stimulation bursts 475 in the inspiratory phase 451. Meanwhile, the modified pattern retains the base level stimulation 480 during the expiratory phase 461, which effectively acts to maintain tone and patency of the upper airway during the expiratory phase 461.

Figure 9 is a diagram 500 schematically illustrating a method of treating sleep disordered breathing via a stimulation pattern that is modified relative to the stimulation pattern of Figure 8, according to one embodiment of the present disclosure. As shown in Figure 9, a respiratory cycle 503 includes an inspiratory phase 501 and an expiratory phase 511. The inspiratory phase 501 includes an initial portion 504, an intermediate portion 505, and an end portion 506 while the expiratory phase 511 includes an initial portion 514, intermediate portion 515, peak 517, and end portion 516. As further shown in diagram 450 of Figure 9, a shorter duration stimulation burst 535 is applied only in the expiratory phase 511 (for patients having predominantly expiratory-based flow limitations) in addition to the generally continuous pulsed lower amplitude tone stimulation 530. In particular, as shown in Figure 8, a low amplitude pulsed continuous stimulation (represented by bar 520) is applied in the inspiratory phase 501 and a low amplitude continuous stimulation (represented by bar 530) in the expiratory phase 511. While the additional stimulation burst 535 could be applied anywhere within the expiratory phase 511, in the example shown in Figure 9, the burst is applied at the initial portion 514 and peak portion 517 of the expiratory phase 511 to ensure full patency during peak expiration. In another aspect, in this arrangement the low level generally continuous stimulation 530 and burst 535 are applied at the point at which the patient has exhibited the most significant flow limitations in the upper airway.

Figure 10 is a diagram 550 schematically illustrating a method of treating sleep disordered breathing via a stimulation pattern that is modified relative to the stimulation pattern of Figure 8, according to one embodiment of the present disclosure. As shown in Figure 10, a respiratory cycle 503 includes an inspiratory phase 501 and an expiratory phase

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511. The inspiratory phase 501 includes an initial portion 504, an intermediate portion 505, and an end portion 506 while the expiratory phase 511 includes an initial portion 514, intermediate portion 515, peak 517, and end portion 516.

As further shown in Figure 10, the stimulation pattern of Figure 8 is modified so that one additional stimulation burst 560 (in addition to the lower amplitude continuous stimulation 520) is applied at the latter portion of the inspiratory phase 501 and one additional stimulation burst 535 is applied at the initial portion 514 and peak portion 517 of the expiratory phase 511 (in substantially the same manner as in diagram 500 of Figure 8). In this embodiment, the two bursts 560, 535 of stimulation mimic the stimulation pattern in Figure 5 with the overall stimulation pattern also including the low level generally continuous stimulation 520, 530 throughout both the inspiratory and expiratory phases 501, 511.

In some embodiments, the moment at which stimulation burst is initiated (within a given inspiratory phase or give expiratory phase) is optimized so that no surplus stimulation is applied. For example, in an example in which a patient has a mixed flow limitation, and a single longer stimulation burst is applied that overlaps both the inspiratory phase and the expiratory phase (such as shown in Figure 5), an auto-titrating method is applied in which a start point is selected for initiating stimulation during the inspiratory phase and a termination point is selected for terminating stimulation during the expiratory phase.

With further reference to Figures 8-10 and 13, it will be understood that adjusting the stimulation amplitude is just one way of modulating the intensity of stimulation, and that in other embodiments, the stimulation intensity is modulated via adjusting the frequency, pulse width, duration, polarity, etc. of pulsed stimulation. For example, instead of applying a stimulation burst of increase amplitude (such as burst 475 in Figure 8 or burst 535 in Figure 9), the stimulation burst can include an increased pulse width, increased frequency, or change in polarity.

Figure 11 shows a diagram 600 schematically illustrating a method of treating disordered breathing, according to one embodiment of the present disclosure. As shown in Figure 11, a respiratory cycle 603 includes an inspiratory phase 601 and an expiratory phase 611. The inspiratory phase 601 includes an initial portion 604, an intermediate portion 605, and an end portion 606 while the expiratory phase 611 includes an initial portion 614,

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intermediate portion 615, peak 617, and end portion 616. As shown in diagram 600 of Figure 11, an initial start point for stimulation 630 is identified (point A) and an initial termination point of stimulation 640 is identified (point F). It will be understood that in at least one example, stimulation segments 630,640 are shown as separate elements for illustrative clarity, and that in fact segments 630, 640 represent a single substantially continuous period of stimulation.

Using these parameters, therapy is applied through a period of time to observe whether the applied stimulation is efficacious. In the event that the stimulation period (segments 630 and 640) within the respiratory cycle is sufficient to ameliorate the sleep disordered breathing, the method begins to scale back the total duration of the stimulation period (segments 630, 640). Accordingly, the start point of stimulation segment 630 is moved to point B, corresponding to a shorter period of stimulation (in the inspiratory phase 601), and therapy is applied for a period of many respiratory cycles while observing whether the shortened duration of stimulation is efficacious. This adjustment process is continued in which the duration of stimulation segment 630 in the inspiratory phase 601 is reduced one step at a time (as represented by directional arrow R), until a start point (e.g. A, B, C, D, E, etc.) is identified at which the inspiratory-phase stimulation segment 630 becomes too short as evidenced by the stimulation starting to lose its effectiveness in maintaining and/or restoring airway patency. In other words, the start point is moved in decrements closer to the end portion of the inspiratory phase until a loss of efficacious stimulation therapy is identified.

In one example, once the start point has been adjusted by a decrement (one step), the new duration is maintained for a set of consecutive respiratory cycles to provide a sufficient period of time over which to evaluate the new settings.

With this information, one can identify the last initiation point at which the desired effectiveness was achieved, and this point is adopted as the optimal start point for stimulation segment 630 in the inspiratory phase 610 for this patient. For example, if the start point D resulted in a stimulation segment 630 that proved ineffective in maintaining or restoring airway patency, while start point C was the last successful start point, then the optimal stimulation segment 630 would have a start point C. Once the optimal start point is

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adopted, each stimulation segment 630 within a give respiratory cycle 603 would begin at start point C.

In one example, the size of the decrements or steps between the respective start points (A, B, C, etc.) correspond to a fraction (such as 1/10, 1/5, or 1/8, etc. of the entire duration of the first portion 360 of the stimulation period 358.

In another example, the initial starting point (e.g. A) is selected to correspond to one of the example durations (two-thirds, one-half, or one-third) of the first portion 360 of the generally continuous stimulation period 358 shown in Figure 5B.

A similar method is applied to the expiratory phase 611 such that the optimal termination point of the stimulation period (segments 630 and 640) is determined for a given respiratory cycle. In doing so, an initial termination point (e.g. point F) for stimulation segment 640 is identified, and therapy is applied. Provided that efficacy was achieved, the method continues by adopting an earlier termination point (e.g. point G), corresponding to a shorter period of stimulation (in the expiratory phase 611), and therapy is applied for a period of time covering many respiratory cycles. The response of the patient is observed to determine if any loss of efficacy has occurred due to shortening the stimulation segment 640. This process is continued in which the duration of stimulation 640 in the expiratory phase 611 is reduced one step at a time (as represented by directional arrow T), until a termination point (anyone of points F, G, H, I, J, K, etc.) is identified at which the expiratory-phase stimulation 640 becomes too short as evidenced by the stimulation starting to lose its effectiveness in maintaining and/or restoring airway patency. In other words, the termination point is moved in decrements closer to the beginning portion of the expiratory phase until a loss of efficacious stimulation therapy is identified.

With this information, one can identify the last termination point at which the desired effectiveness was achieved, and this point is adopted as the optimal termination point of stimulation segment 640 for this patient to overcome the mixed flow limitation (i.e. a flow limitation that overlaps both the inspiratory and the expiratory phases 601, 611).

In one example, once the termination point has been adjusted by a decrement (one step), the new duration is maintained for a set of consecutive respiratory cycles to provide a sufficient period of time over which to evaluate the new settings.

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In one example, the size of the decrements or steps between the respective termination points (F, G, H, etc.) corresponds to a fraction (such as 1/10, 1/5, or 1/8, etc. of the entire duration of the second portion 380 of the stimulation period 358.

In another example, the initial starting point (e.g. F) is selected to correspond to one of the example durations (two-thirds, one-half, or one-third) of the second portion 380 of the generally continuous stimulation period 358 shown in Figure 5B.

It will be understood, that in addition to optimizing the duration of the stimulation segments 630, 640 shown in association with Figure 11, one also can optimize for other parameters of the stimulation, such as amplitude, polarity, frequency, pulse width, etc., where an increase or decrease in amplitude, frequency, pulse width, duration, etc. (or change in polarity) can allow a concomitant decrease or increase in the duration of the stimulation.

In some embodiments, an implantable stimulator also can be operated in a first mode which attempts to maintain airway patency (and is therefore prophylactic) or a second mode, which recovers airway patency that has been lost. In the first mode, a stimulation pattern is applied that uses the minimum amount of stimulation required to maintain airway patency, and may include (but is not limited to) one of the stimulation patterns previously described and illustrated in association with Figures 1-11. However, in the event that an apnea occurred despite the attempt by the first mode to prevent conditions leading to apnea, the implantable stimulator would switch to a second, "acute" mode of operation, in which the stimulation pattern would become more aggressive in amplitude, frequency, pulse width, and duration of each stimulation burst. The selected duration, amplitude, and frequency would be based on a pre-obstruction respiratory rate. In one embodiment, managing the switch between the first mode and the second mode, as well as managing the stimulation parameters in the second mode, is performed using substantially the same systems and methods, as described in as described and illustrated in PCT Publication WO/2010/059839, entitled A METHOD OF TREATING SLEEP APNEA, published on May 27, 2010, and which is hereby incorporated by reference.

In some embodiments, a flow limitation in the upper airway is detected via respiratory sensors and/or pressure sensors to determine a relative degree of obstruction. These sensors also can be used to determine whether the obstruction is occurring during

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inspiration, during expiration, or during both. Moreover, because each type of obstruction yields a pressure/impedance pattern that is characteristic of the particular type of obstruction, one can use this sensing information to determine an efficacious stimulation pattern.

In some embodiments, a stimulation pattern mimics the pattern of the particular breathing phase. As shown in Figure 12, a respiratory cycle 653 includes an inspiratory phase 651 and an expiratory phase 661. The inspiratory phase 651 includes an initial portion 654, an intermediate portion 655, and an end portion 656 while the expiratory phase 661 includes an initial portion 664, intermediate portion 665, peak 667, and end portion 676. As further shown in the diagram 650 of Figure 12, stimulation patterns 680 and 690 are applied, in which the greatest volume of stimulation corresponds to ensuring airway patency during the greatest volume of air flow during inspiration and expiration. Accordingly, in one stimulation pattern 680 applied during the inspiratory phase 651, the amplitude of stimulation ramps up through the progression of the inspiratory phase 651. In particular, stimulation pattern 680 includes a start point 681, ramp portion 683, plateau portion 684, descent 685, and end portion 682. In general terms, this ramped stimulation pattern increases the stimulation amplitude (via ramp portion 683) as inspiration commences and then maintains heightened stimulation amplitude (via plateau portion 684) throughout most of the second half of the inspiratory phase 651. While the plateau portion 684 ends prior to completion of the inspiratory phase 651 in the example shown in Figure 12, it will be understood that the plateau portion 684 could be extended to last through the completion of the inspiratory phase 651.

Meanwhile, in some embodiments, a ramped stimulation pattern 690 is applied to the expiratory phase 661 as further shown in Figure 12. The stimulation pattern 690 includes a start point 691, plateau portion 693, ramp portion 694, and end portion 692. In general terms, this ramped stimulation pattern begins with a heightened stimulation amplitude (via plateau portion 693) as inspiration commences and then decreases the stimulation amplitude (via ramp portion 694) throughout most of the second half of the expiratory phase 651. In this stimulation pattern 690, a greater stimulation is applied and maintained via plateau portion 693 at (and immediately following) peak expiration 667 in order to ensure airway patency at the beginning of the expiratory phase 661, thereby

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proactively preventing airway collapse. Once expiration has commenced, then the stimulation is decreased via ramp portion 694, as the volume of air from expiration acts to help maintain airway patency, with the stimulation pattern 690 terminating before the end portion 676 of the expiratory phase 661.

Figure 13 includes a diagram 700 schematically illustrating a stimulation pattern 730, 740, according to one embodiment of the present disclosure. As shown in Figure 13, a respiratory cycle 703 includes an inspiratory phase 701 and an expiratory phase 711. The inspiratory phase 701 includes an initial portion 704, an intermediate portion 705, and an end portion 706 while the expiratory phase 711 includes an initial portion 716, intermediate portion 715, peak 717, and end portion 716. As further shown in Figure 13, the stimulation pattern 730 in the inspiratory phase 701 includes a first portion 733 of bursts 734 of stimulation in the first half of the inspiratory phase 701 and then a generally continuous stimulation segment 735 throughout the second half of the inspiratory phase 701. Meanwhile, the stimulation pattern 740 in the expiratory phase 711 includes a first generally continuous stimulation segment 743 through the first half of the expiratory phase 711 and then a second portion 744 of bursts 745 of stimulation in the second half of the expiratory phase 711. It will be understood that in some embodiments, the stimulation segment 735 and the stimulation segment 743 form a substantially continuous single stimulation segment, but are shown separately in Figure 13 for illustrative purposes.

In this embodiment, stimulation is applied in bursts 734 in the early portion of the inspiratory phase 701 to maintain tone of the upper airway and then continuous stimulation 735 is applied during the latter half of the inspiratory phase 701 when maximum air flow would occur and just prior to expiration when the airway could be at greater risk for collapse. On the other hand, in the expiratory phase 711, continuous stimulation 743 is applied during the first half of the expiratory phase when there is a greater risk of airway collapse (and maximum air flow needs to take place) while bursts 745 of stimulation are applied during the second half of the expiratory phase 711 to maintain tone and nominal airway patency.

Although specific embodiments have been illustrated and described herein, it will be appreciated by those of ordinary skill in the art that a variety of alternate and/or equivalent implementations may be substituted for the specific embodiments shown and described

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without departing from the scope of the present disclosure. This application is intended to cover any adaptations or variations of the specific embodiments discussed herein. Therefore, it is intended that this present disclosure be limited only by the claims and the equivalents thereof.

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CLAIMS:

1. A stimulation protocol determination system comprising:

an input module to receive an indication of an upper airway flow limitation via sensed respiratory effort information; and

a selection module to automatically select, based on the indicated upper airway flow limitation, a stimulation protocol including at least one of:

a first protocol to apply stimulation generally synchronous with an expiratory phase of a respiratory cycle; and

a second protocol to apply stimulation during both of a portion of an inspiratory phase of the respiratory cycle and a portion of the expiratory phase.

2. The system of claim 1, wherein the indicated upper airway flow limitation corresponds to at least a partial obstruction of the upper airway associated with sleep apneas.

3. The system of claim 1, wherein the first protocol is automatically selected when the indicated upper airway flow limitation predominantly coincides with the expiratory phase.

4. The system of claim 1, wherein the second protocol is automatically selected when the indicated upper airway flow limitation predominantly coincides with both of a first portion of the inspiratory phase and a first portion of the expiratory phase but does not predominantly coincide with a second portion of inspiratory phase and with a second portion of the expiratory phase.

5. The system of claim 4, wherein the first portion of the inspiratory phase includes at least an end portion of the inspiratory phase and the first portion of the expiratory phase includes at least a beginning portion of the expiratory phase.

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6. The system of claim 5, wherein the first portion of the inspiratory phase excludes a beginning portion of the inspiratory phase.

7. The system of claim 5, wherein the second portion of the expiratory phase excludes an end portion of the expiratory phase.

8. The system of claim 5, wherein the second protocol includes a generally continuous stimulation period applied during at least a portion of at least some respiratory cycles, wherein the generally continuous stimulation period predominantly coincides with the first portion of the inspiratory phase and with the first portion of the expiratory phase, and

wherein the generally continuous stimulation period includes an initial start point located after a beginning of the inspiratory phase and an initial termination point located prior to an end of the expiratory phase.

9. The system of claim 8, wherein the second protocol includes the application of the generally continuous stimulation period for a set of consecutive respiratory cycles over a first time period and wherein the input module is configured to:

determine if at least some indications of upper airway flow limitations (exceeding a dysfunction threshold) are received within the first time period;

maintain or increase a duration of the generally continuous stimulation period if the input module receives the at least some indications during the first time period;

reduce the duration of the generally continuous stimulation period if the input module receives no indications during the first time period.

10. The system of claim 9, wherein the first time period, based on an apnea-hypopnea index, for which an apnea would likely occur in the absence of stimulation.

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11. The system of claim 9, wherein reducing the duration includes at least one of:

decrementally moving the initial start point closer to the end portion of the inspiratory phase for the next set of consecutive respiratory cycles;

decrementally moving the initial termination point closer to the beginning portion of the expiratory phase for the next set of consecutive respiratory cycles.

12. The system of claim 8, wherein a first portion of the generally continuous stimulation period coincides with the first portion of the inspiratory phase and has a duration of at least one of:

at least one-third of an entirety of the inspiratory phase;

at least one-half of the entirety of the inspiratory phase; and

at least two-thirds of the entirety of the inspiratory phase.

13. The system of claim 8, wherein a second portion of the generally continuous stimulation period coincides with the first portion of the expiratory phase and has a duration of at least one of:

at least one-third of the entirety of the expiratory phase;

at least one-half of the entirety of the expiratory phase; and

at least two-thirds of the entirety of the expiratory phase.

14. The system of claim 5, wherein the first portion of the inspiratory phase corresponds to at least a majority of the inspiratory phase and the first portion of the expiratory phase corresponds to at least a majority of the expiratory phase.

15. The system of claim 14, wherein the majority of the inspiratory phase comprises at least two-thirds of the inspiratory phase and the majority of the expiratory phase comprises at least two-thirds of the expiratory phase.

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16. The system of claim 1, wherein the selection module is configured to automatically select a third protocol to apply stimulation generally synchronous with the inspiratory phase when the flow limitation generally coincides with the inspiratory phase.

17. The system of claim 1, comprising

an implantable pulse generator; and

a nerve cuff electrode electrical couplable to the pulse generator to apply a respective one of the first and second stimulation protocols.

18. The system of claim 1, wherein the nerve is the hypoglossal nerve.

19. The system of claim 16, comprising:

a respiration sensor to provide the sensed respiratory effort information.

20. A non-transitory computer readable medium for storing machine readable instructions to provide a stimulation protocol determination module comprising:

an input function to receive an indication of an upper airway flow limitation via sensed respiratory effort information; and

a selection function to automatically select, based on the indicated upper airway flow limitation, a stimulation protocol including at least one of:

a first protocol to apply stimulation generally synchronous with an expiratory phase of a respiratory cycle; and

a second protocol to apply stimulation during a portion of both of an inspiratory phase of the respiratory cycle and the expiratory phase.

21. A stimulation protocol determination system comprising:

a non-volatile memory for storing, and a processor for executing, machine readable instructions to provide:

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an input module to receive an indication of an upper airway flow limitation via sensed respiratory effort information; and

a selection module to automatically select, based on the indicated upper airway flow limitation, a stimulation protocol including at least one of:

a first protocol to apply stimulation generally synchronous with an expiratory phase of a respiratory cycle; and

a second protocol to apply stimulation during a portion of both of an inspiratory phase of the respiratory cycle and the expiratory phase.

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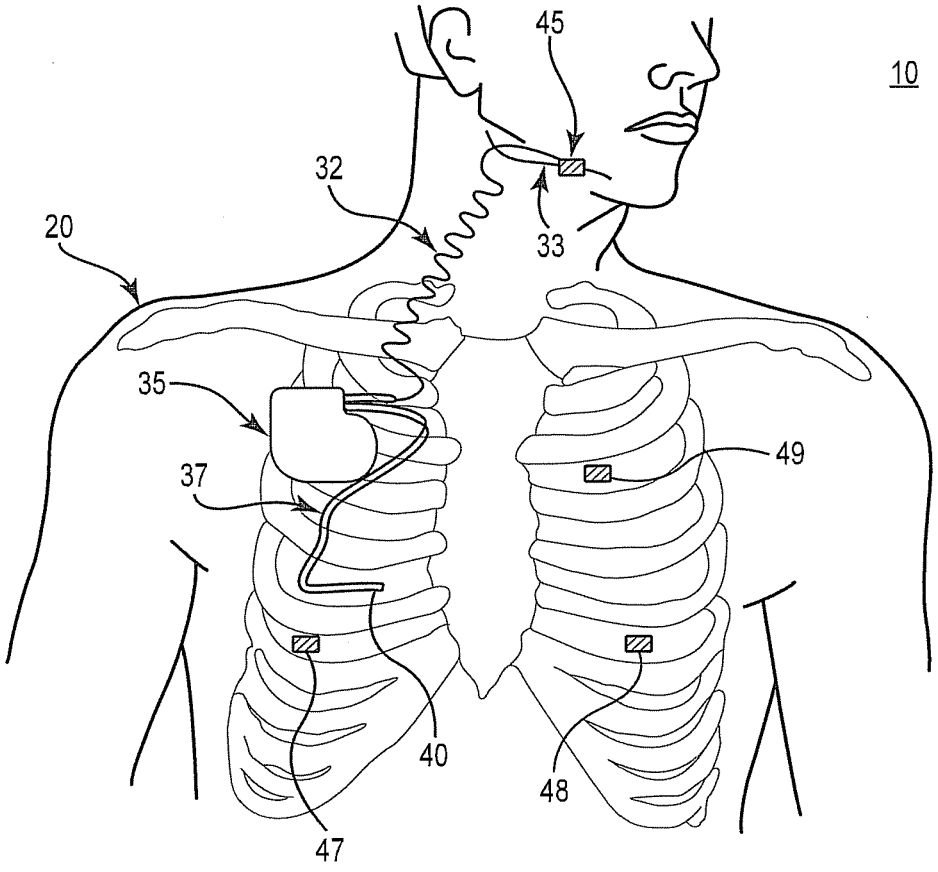


Fig. 1A

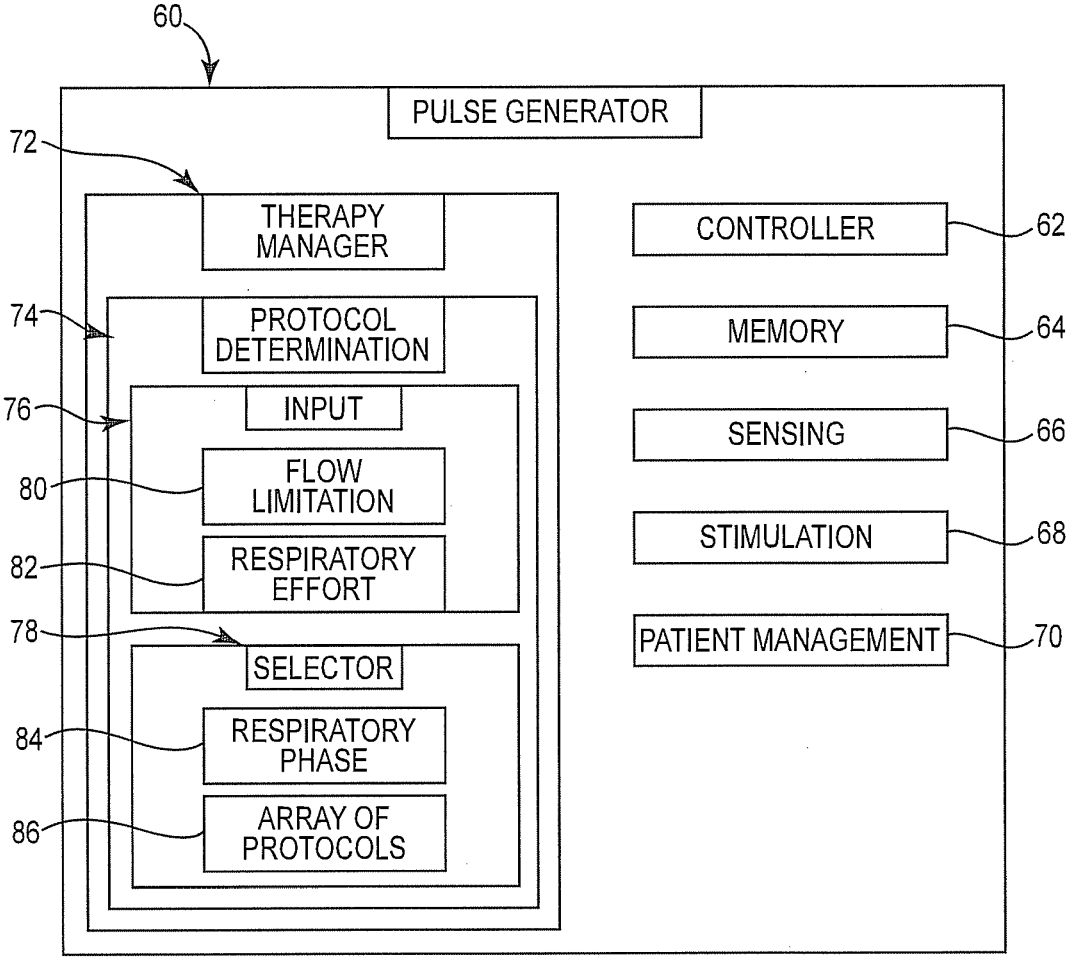

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PULSE GENERATOR
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THERAPY MANAGER
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PROTOCOL DETERMINATION
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INPUT
80
FLOW LIMITATION
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RESPIRATORY EFFORT
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SELECTOR
84
RESPIRATORY PHASE
86
ARRAY OF PROTOCOLS
CONTROLLER
62
MEMORY
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SENSING
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STIMULATION
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PATIENT MANAGEMENT
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Fig. 1B

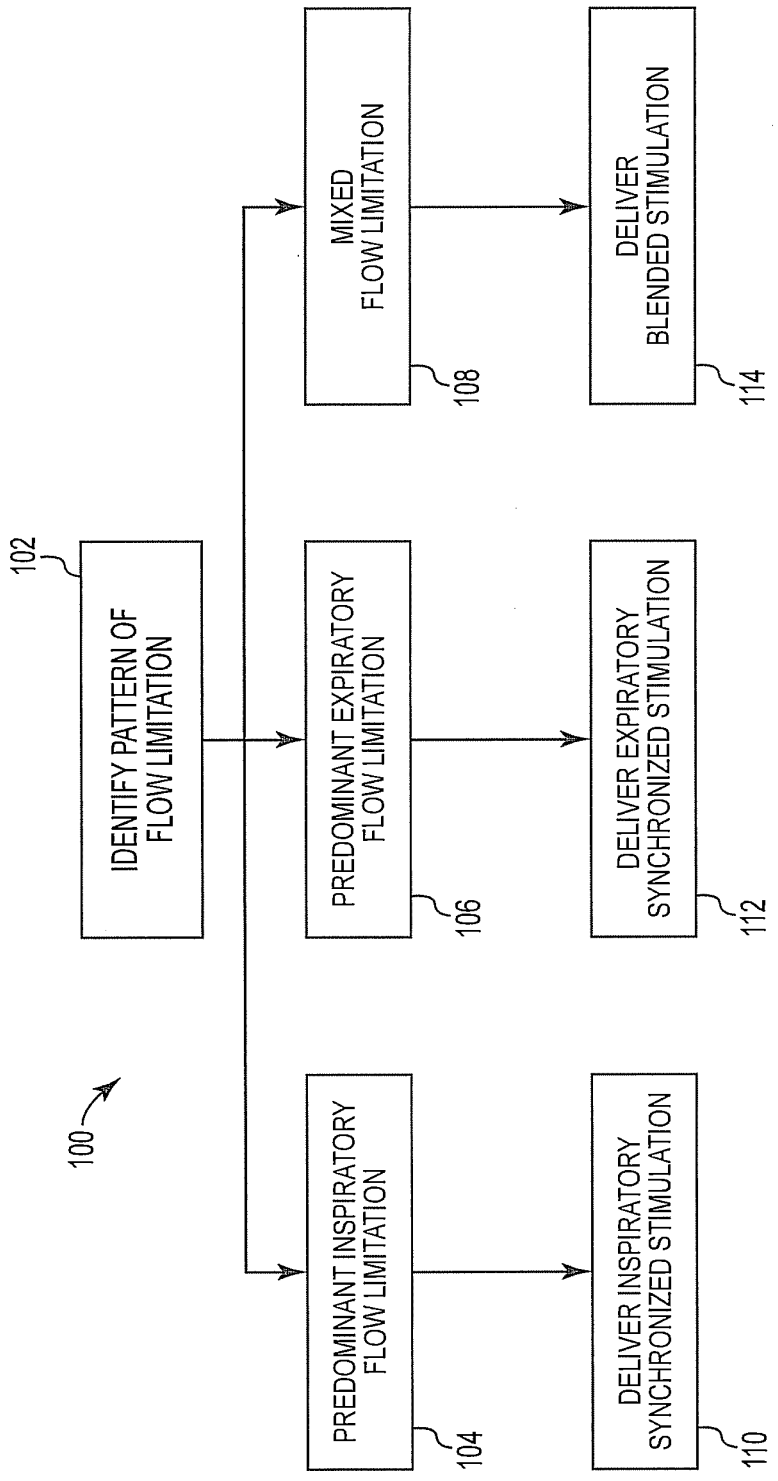

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IDENTIFY PATTERN OF FLOW LIMITATION
PREDOMINANT INSPIRATORY FLOW LIMITATION
104
PREDOMINANT EXPIRATORY FLOW LIMITATION
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MIXED FLOW LIMITATION
108
DELIVER INSPIRATORY SYNCHRONIZED STIMULATION
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DELIVER EXPIRATORY SYNCHRONIZED STIMULATION
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DELIVER BLENDED STIMULATION
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Fig. 1C

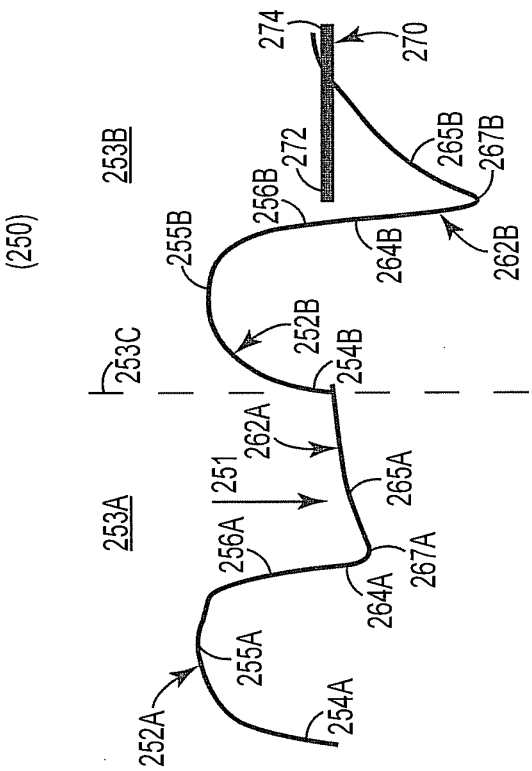


Fig. 4

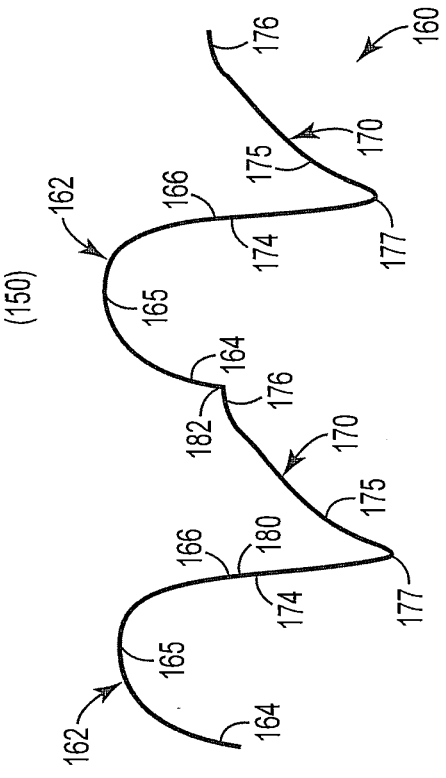


Fig. 2

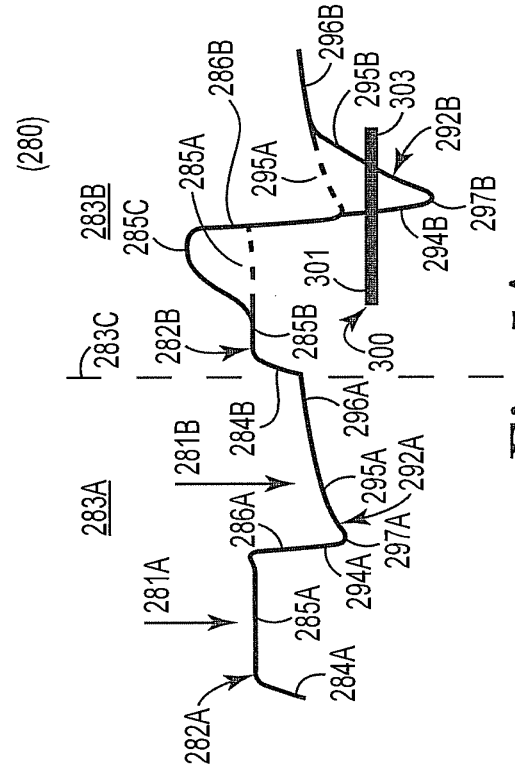


Fig. 5A

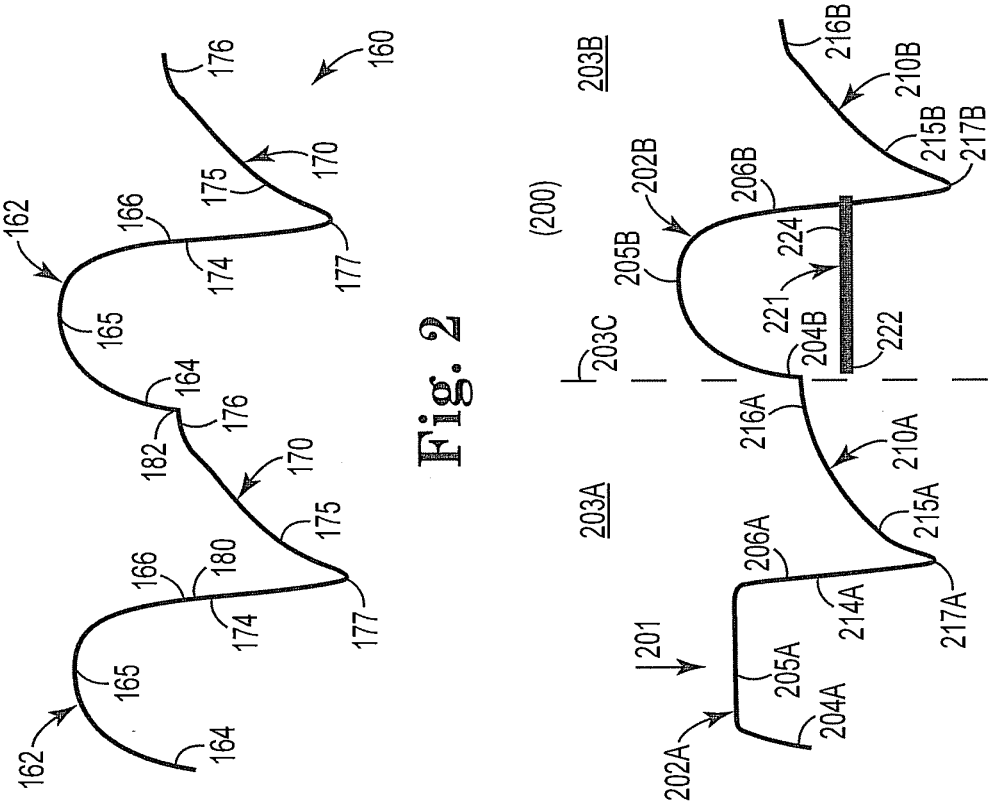


Fig. 3

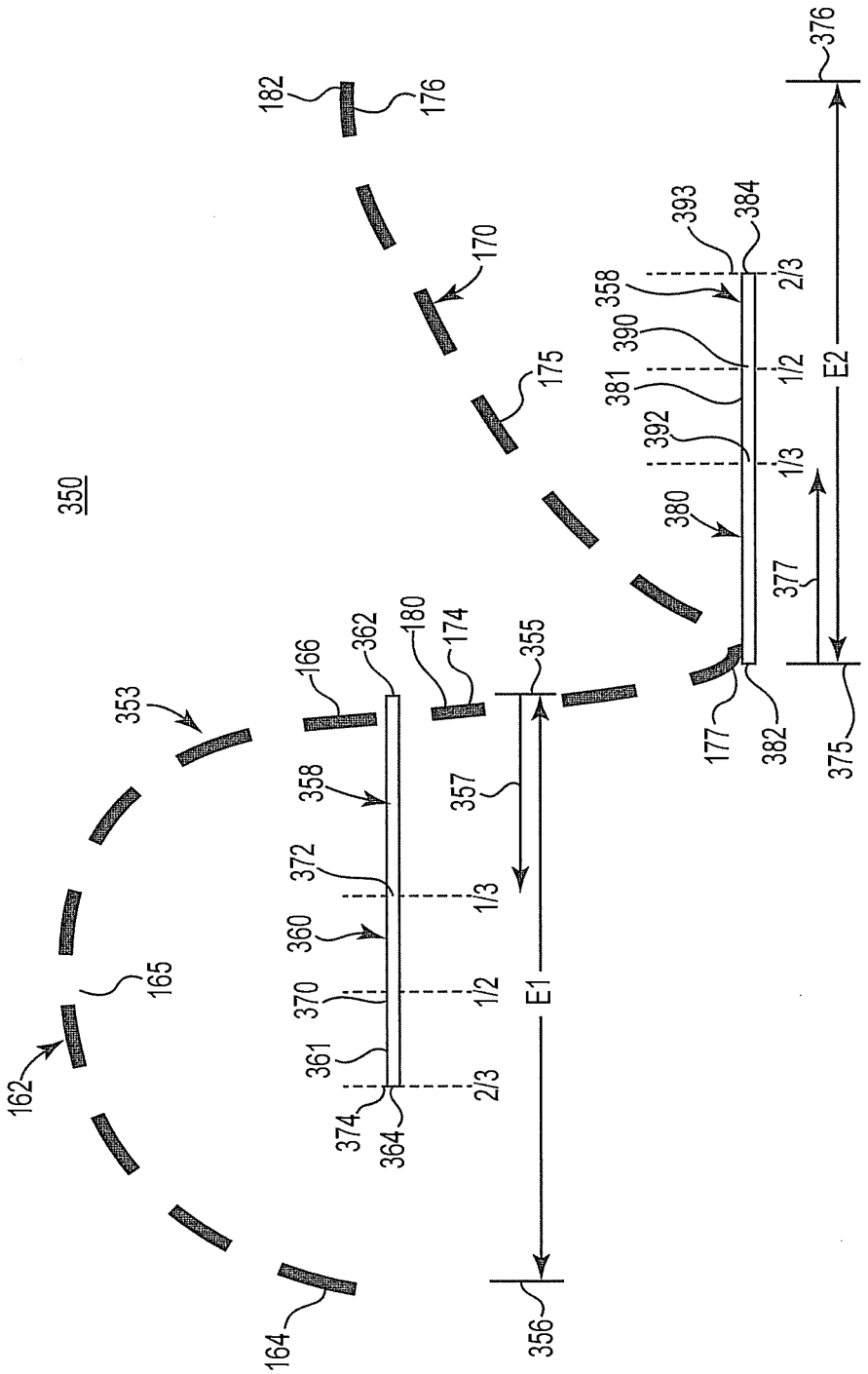

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Fig. 5B

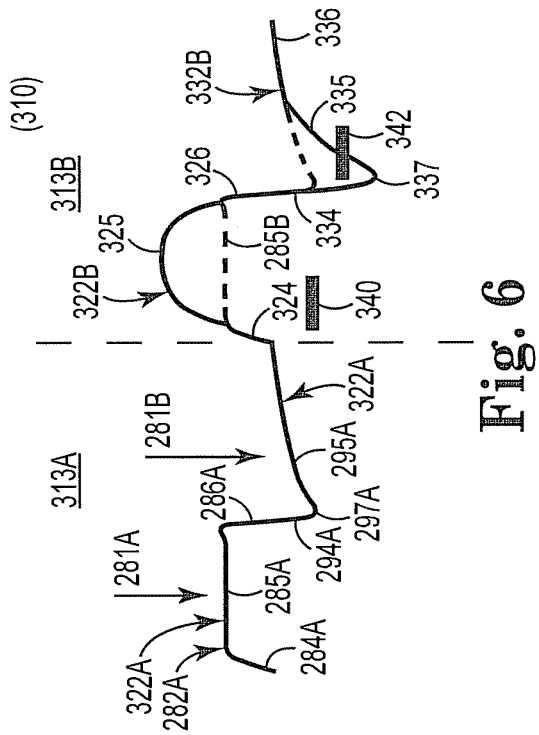

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Fig. 6

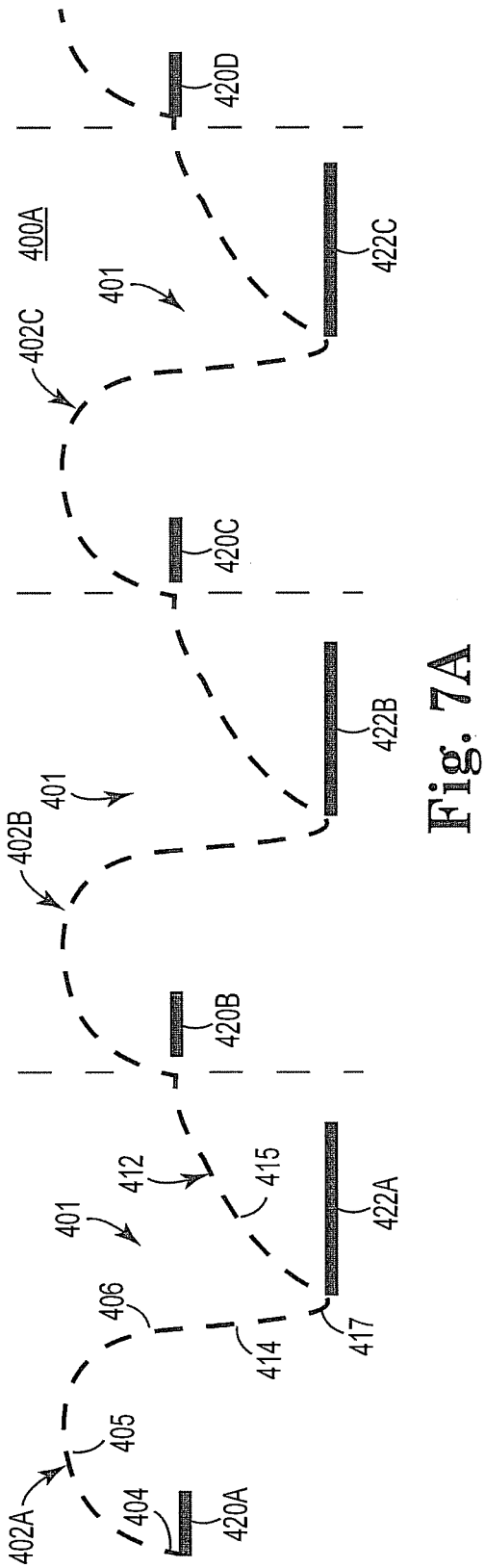

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Fig. 7A

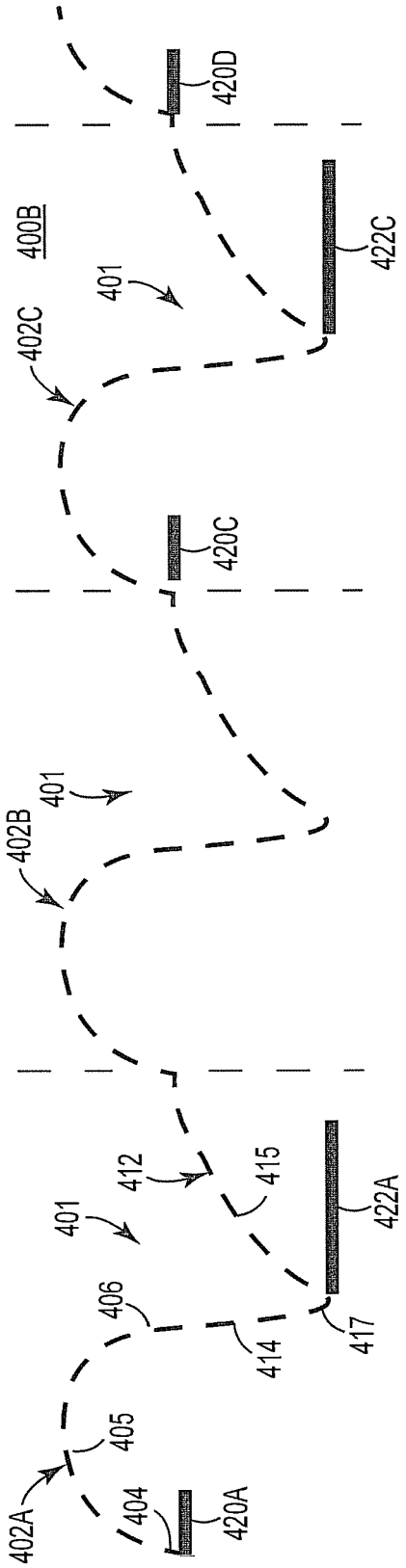

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Fig. 7B

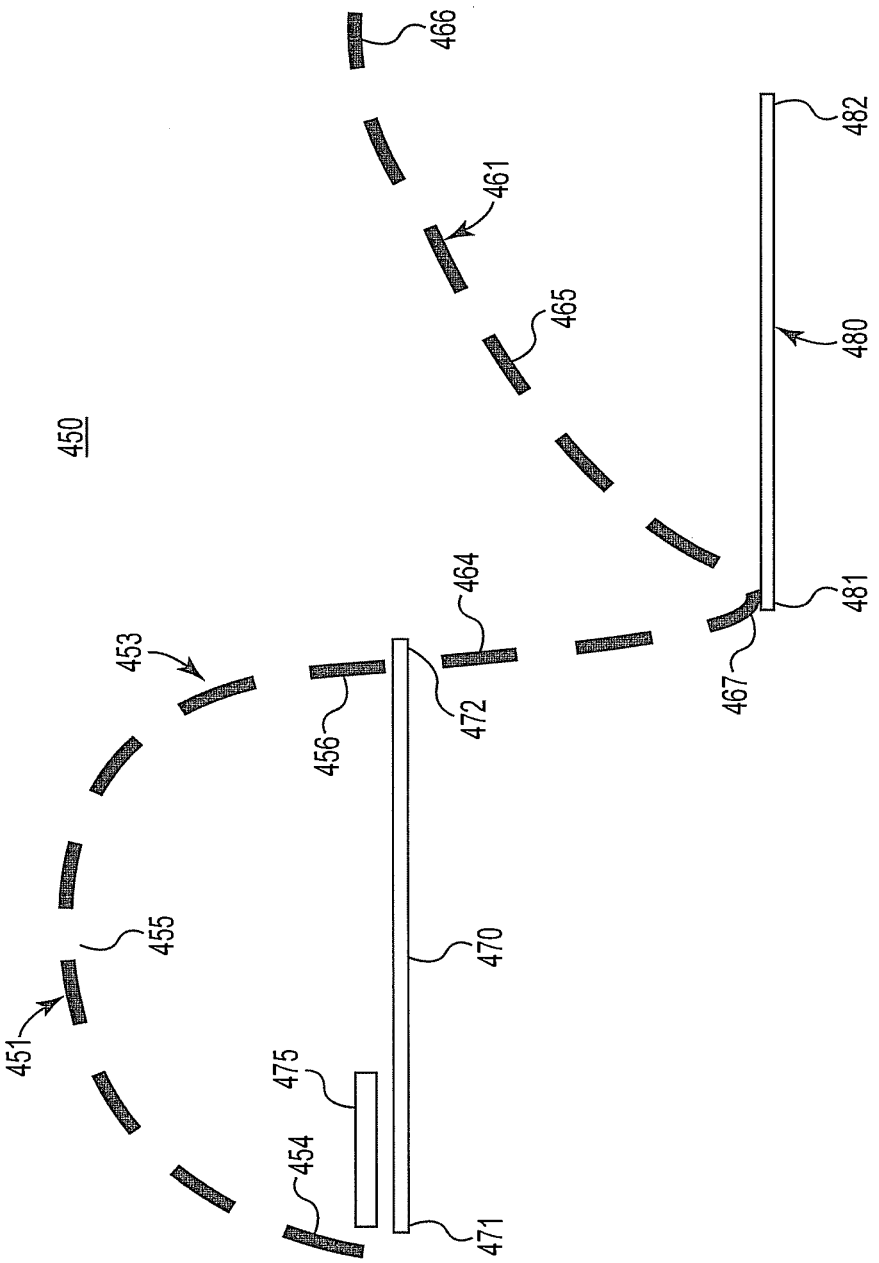

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Fig. 8

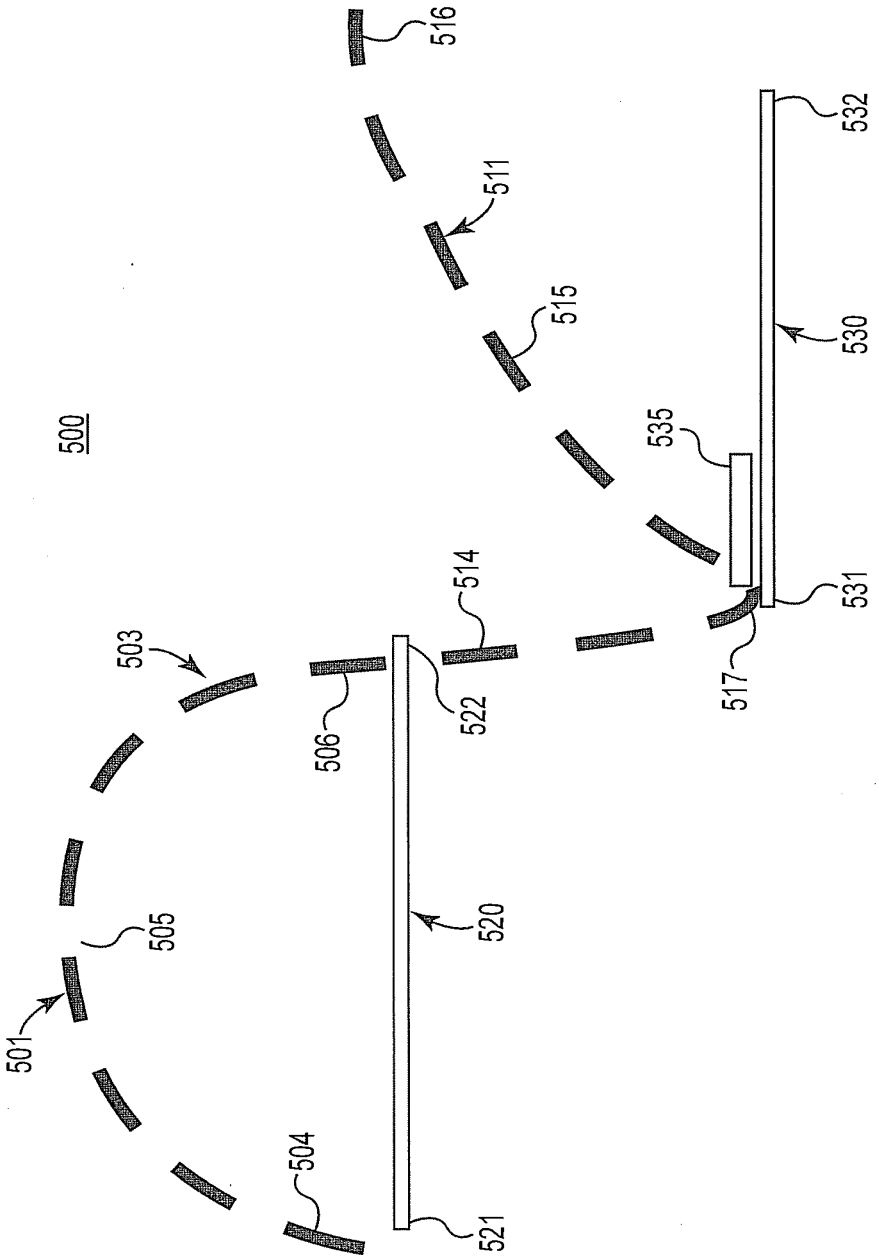

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Fig. 9

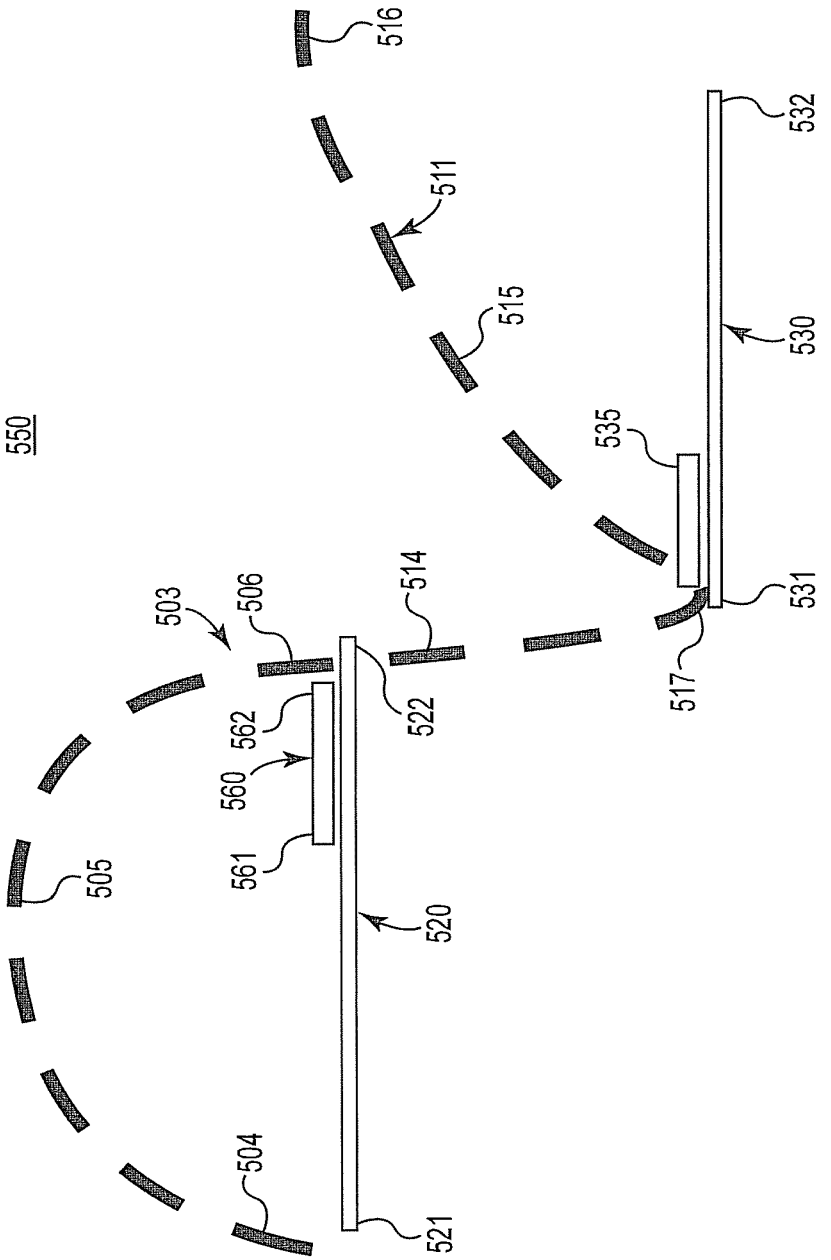

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Fig. 10

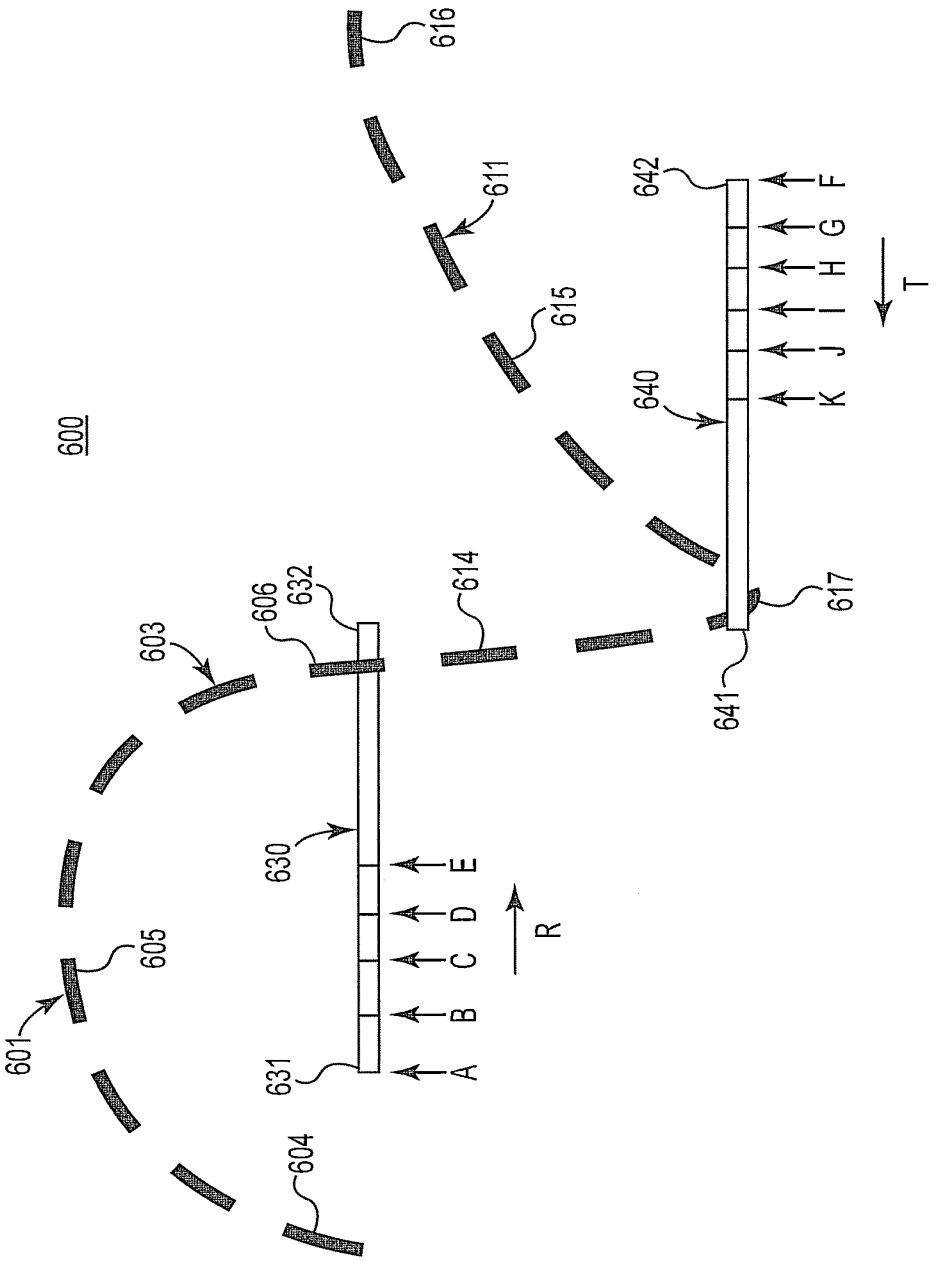

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Fig. 11

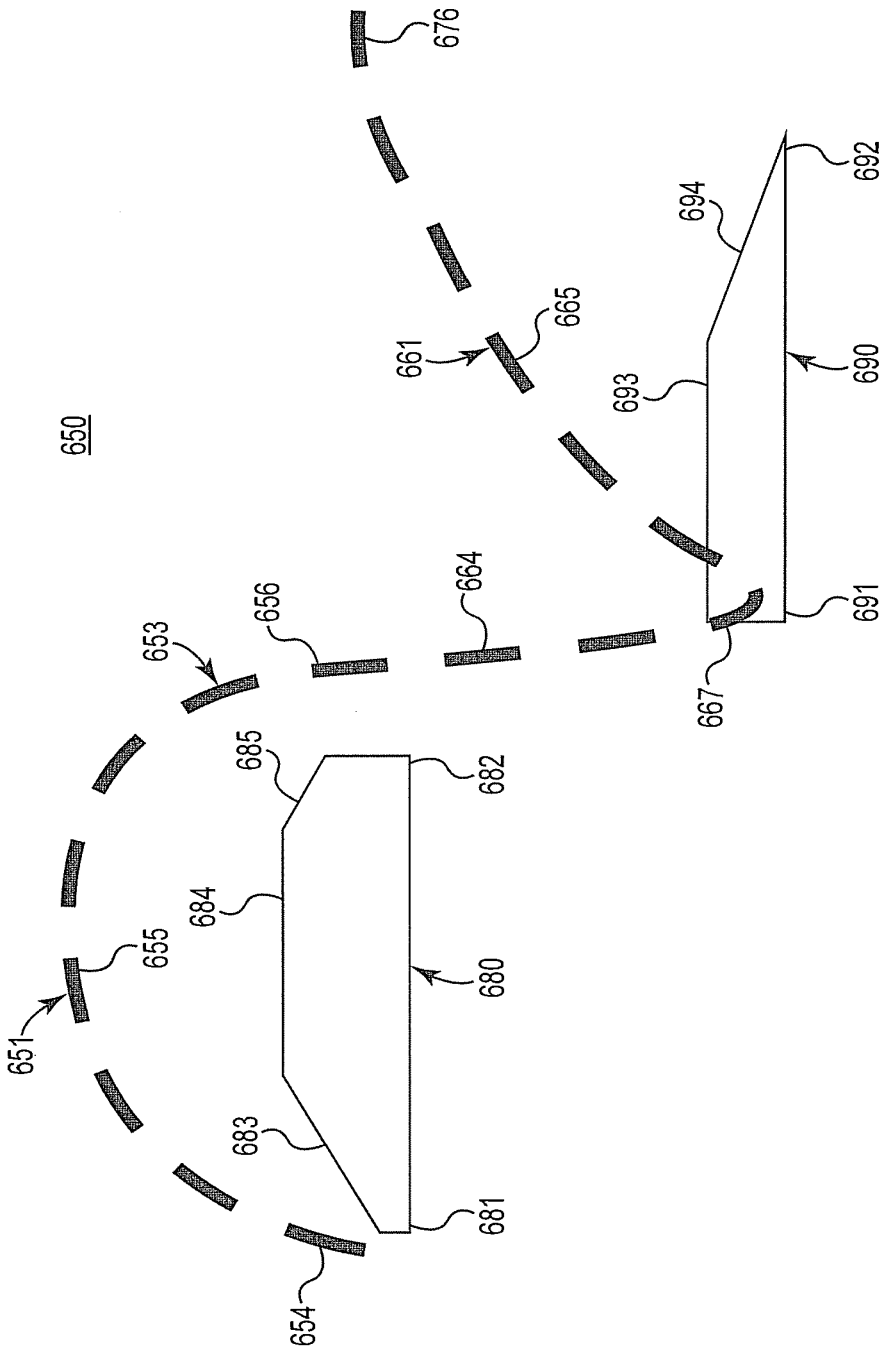

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Fig. 12

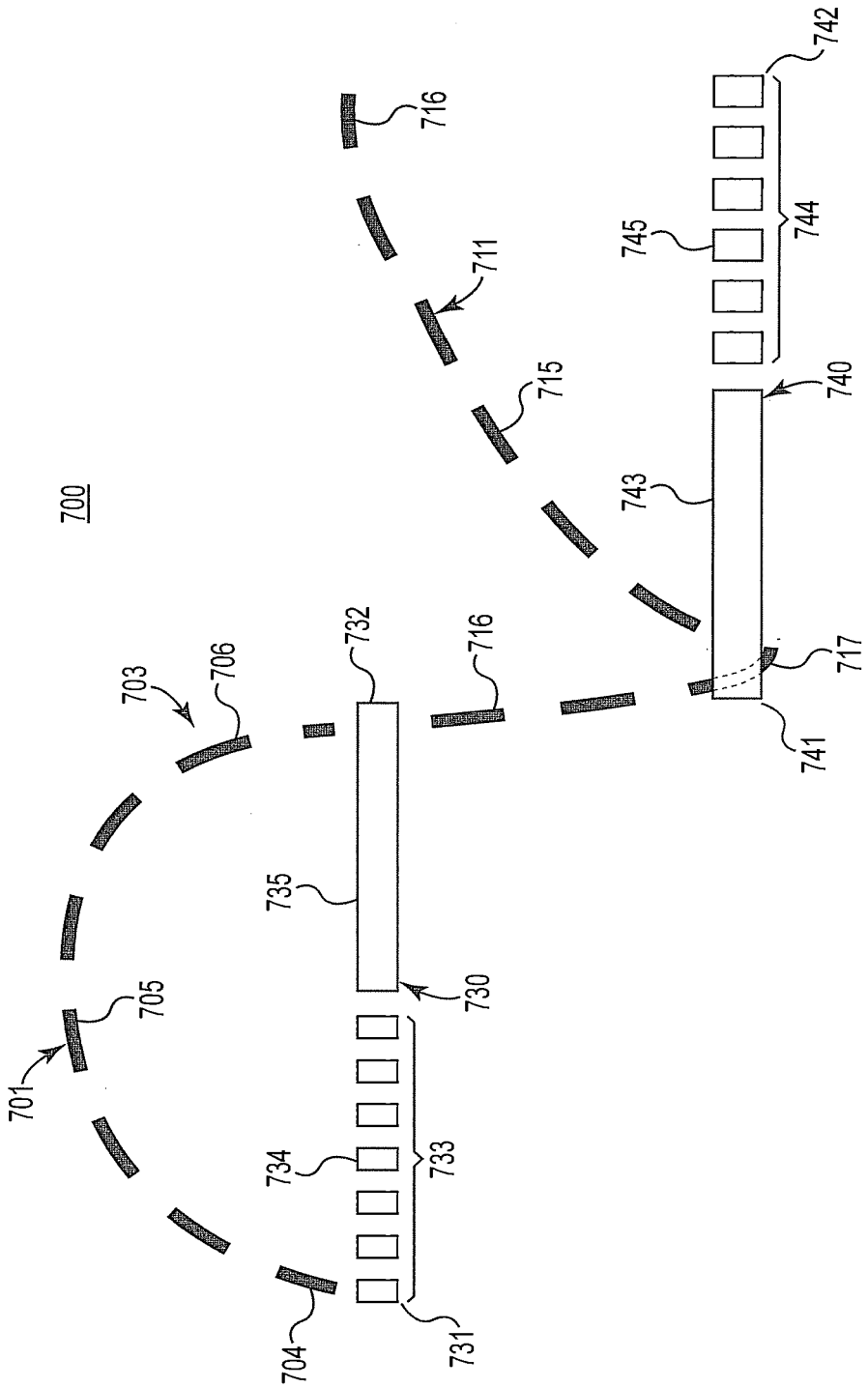

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Fig. 13

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/050615

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/36 A61B5/08
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2011/152706 A1 (CHRISTOPHERSON MARK [US] ET AL) 23 June 2011 (2011-06-23) paragraph [0030] - paragraph [0034] paragraph [0089] - paragraph [0093]; figure 1 -----	1-9, 16-19 11
X Y	WO 2010/059839 A2 (INSPIRE MEDICAL SYSTEMS INC [US]; CHRISTOPHERSON MARK A [US]; NI QUAN) 27 May 2010 (2010-05-27) paragraph [0040] - paragraph [0043] paragraph [0051] - paragraph [0055] paragraph [0084] - paragraph [0086] paragraph [0156]; figure 3A -----	1,2, 4-10, 12-21 11
	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 November 2012	11/12/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Sigurd, Karin

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/050615

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2010/198289 A1 (KAMELI NADER [US] ET AL) 5 August 2010 (2010-08-05) paragraph [0019] paragraph [0052] - paragraph [0055] paragraph [0118] - paragraph [0127]; figures 2, 10 -----	1-3,20, 21
Y	US 2011/160794 A1 (BOLEA STEPHEN L [US] ET AL) 30 June 2011 (2011-06-30) paragraph [0066] - paragraph [0073] paragraph [0118] - paragraph [0120]; figures 14A, 14B -----	11

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2012/050615

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2011152706 A1	23-06-2011	AU 2009246179 A1	19-11-2009
		CA 2724335 A1	19-11-2009
		EP 2323730 A2	25-05-2011
		JP 2011520526 A	21-07-2011
		US 2011152706 A1	23-06-2011
		WO 2009140636 A2	19-11-2009
WO 2010059839 A2	27-05-2010	EP 2389224 A2	30-11-2011
		JP 2012509155 A	19-04-2012
		US 2011264164 A1	27-10-2011
		WO 2010059839 A2	27-05-2010
US 2010198289 A1	05-08-2010	CA 2753356 A1	05-08-2010
		EP 2391264 A1	07-12-2011
		US 2010198289 A1	05-08-2010
		WO 2010087862 A1	05-08-2010
US 2011160794 A1	30-06-2011	US 2010174341 A1	08-07-2010
		US 2011160794 A1	30-06-2011

Exhibit 1002
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01453

Electronic Acknowledgement Receipt

EFS ID:	40981263
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	29-OCT-2020
Filing Date:	04-SEP-2020
Time Stamp:	12:39:50
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Foreign Reference	WO9749455A1.pdf	3726258 e332c4cb12b4c2946aaabd5aa752745c605e33d1	no	97

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4	Foreign Reference	WO2006057734A1.pdf	3896008 8b309b31b673dfe99106e600bc0ad463cd1f264f	no	69
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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.
<u>National Stage of an International Application under 35 U.S.C. 371</u>
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.
<u>New International Application Filed with the USPTO as a Receiving Office</u>
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 November 2009 (19.11.2009)

PCT

(10) International Publication Number
WO 2009/140636 A2

(51) International Patent Classification:
A61N 1/36 (2006.01) *A61B 5/113* (2006.01)

(21) International Application Number:
PCT/US2009/044207

(22) International Filing Date:
15 May 2009 (15.05.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/053,344 15 May 2008 (15.05.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR SENSING RESPIRATORY PRESSURE IN AN IMPLANTABLE STIMULATION SYSTEM

(57) Abstract: A method and system for sensing respiration in the treatment of sleep apnea is disclosed.

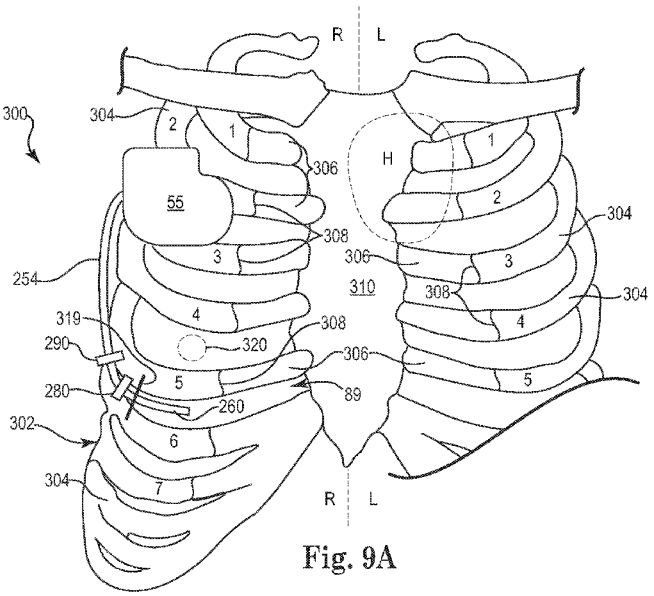


Fig. 9A

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Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

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METHOD AND APPARATUS FOR SENSING RESPIRATORY PRESSURE IN AN IMPLANTABLE STIMULATION SYSTEM

CROSS-REFERENCE TO RELATED APPLICATIONS

[001] This application claims priority under 35 U.S.C. §119(e) to U.S. Provisional Patent Application Serial No. 61/053,344, filed on May 15, 2008, and incorporated herein by reference.

TECHNICAL FIELD

[002] The invention relates generally to an implantable stimulation system for stimulating and monitoring soft tissue in a patient, and more particularly, the invention relates to a method and apparatus for sensing respiratory pressure to control delivery of therapy to nerve tissue.

BACKGROUND

[003] Sleep apnea generally refers to the cessation of breathing during sleep. One type of sleep apnea, referred to as obstructive sleep apnea (OSA), is characterized by repetitive pauses in breathing during sleep due to the obstruction and/or collapse of the upper airway, and is usually accompanied by a reduction in blood oxygenation saturation.

[004] One treatment for obstructive sleep apnea has included the delivery of electrical stimulation to the hypoglossal nerve, located in the neck region under the chin. Such stimulation therapy activates the upper airway muscles to maintain upper airway patency. In treatment of sleep apnea, increased respiratory effort resulting from the difficulty in breathing through an obstructed airway is avoided by synchronized stimulation of an upper airway muscle or muscle group that holds the airway open during the inspiratory phase of breathing. For example, the genioglossus muscle is stimulated during treatment of sleep apnea by a cuff electrode place around the hypoglossal nerve.

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[005] In addition to positioning an electrode to deliver the therapy to the nerve, obstructive sleep apnea treatment may include the use of a sensor that is surgically implanted in a region that has pressure continuity with the intrapleural space, such as the suprasternal notch, the space between the trachea and esophagus, or by being attached to either of the trachea or esophagus. The sensor may also be positioned intercostally, or secured in a position for sensing pressure at the posterior side of the manubrium. The suprasternal notch and manubrium of the sternum are well known structures on the upper chest that are in anatomical continuity with the intrapleural space. Changes in intrapleural pressure provide a characteristic respiratory effort waveform, and therefore the sensor enables respiratory effort waveform information to be utilized to determine increased respiratory effort, which is then used to control delivery of therapy in response to determined increases in respiratory effort.

[006] The location for placement of the sensor is, at least in part, chosen as a function of a delay, i.e. the propagation time associated with a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position. The chosen location is also a function of the amount of filtering necessary to achieve a usable sensed signal at a particular location, i.e. the amount of filtering that is used to remove waveforms other than the waveform associated with the desired sensed characteristic, such as the filtering required to remove cardiac waveform activity, for example.

[007] However, in some conventional locations for sensor placement, the sensed signal tends to be corrupted by an added signal artifacts caused by cardiac vessels because of the close proximity of cardiac vessels to the sensor. In addition, implanting the sensor using the known placement positions tends to be an invasive procedure.

[008] Accordingly, significant challenges remain in providing effective respiratory sensing in the treatment of sleep apnea.

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BRIEF DESCRIPTION OF THE DRAWINGS

[009] The accompanying drawings are included to provide a further understanding of embodiments and are incorporated in and constitute a part of this specification. The drawings illustrate embodiments and together with the description serve to explain principles of embodiments. Other embodiments and many of the intended advantages of embodiments will be readily appreciated as they become better understood by reference to the following detailed description. The elements of the drawings are not necessarily to scale relative to each other. Like reference numerals designate corresponding similar parts. Accordingly, aspects and features of the present disclosure will be appreciated as the same becomes better understood by reference to the following detailed description of the embodiments when considered in connection with the accompanying drawings, wherein:

[010] FIG. 1 is a front view schematically illustrating an implantable stimulation system deployed in a patient, according to one embodiment of the present disclosure;

[011] FIG. 2 is a schematic illustration of a sensor lead deployed intrapleurally, according to one embodiment of the present disclosure;

[012] FIG. 3 is a front view schematically illustrating an implantable stimulation system, with a subcutaneous, extrapleural placement, as deployed in a patient, according to one embodiment of the present disclosure;

[013] FIG. 4 is a front view schematically illustrating an implantable stimulation system, with an intrapleural placement, as deployed in a patient, according to another embodiment of the present disclosure;

[014] FIG. 5 is a top plan view of a sensor lead, according to one embodiment of the present disclosure;

[015] FIG. 6 is a sectional view as taken along lines 6—6 of FIG. 5, according to one embodiment of the present disclosure;

[016] FIG. 7 is a top plan view of a sensor lead, according to one embodiment of the present disclosure;

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[017] FIG. 8 is a partial side view of an anchor of the sensor lead of FIG. 7, according to one embodiment of the present disclosure;

[018] FIG. 9A is a front view schematically illustrating an implantable stimulation system including a respiratory sensor as deployed in a patient, according to one embodiment of the present disclosure;

[019] FIG. 9B is a schematic illustration of a method of implanting the sensor lead of FIG. 9A, according to one embodiment of the present disclosure;

[020] FIG. 10 is a perspective view of a sensor lead, according to one embodiment of the present disclosure;

[021] FIG. 11 is a sectional view as taken along lines 11—11 of FIG. 10, according to one embodiment of the present disclosure;

[022] FIG. 12 is a sectional view as taken along lines 12—12 of FIG. 10, according to one embodiment of the present disclosure;

[023] FIG. 13 is diagram schematically illustrating a respiratory pressure signal, according to one embodiment of the present disclosure;

[024] FIG. 14 is diagram schematically illustrating a respiratory-associated temperature signal, according to one embodiment of the present disclosure;

[025] FIG. 15 is a diagram schematically illustrating a respiratory sensing circuit, according to one embodiment of the present disclosure;

[026] FIG. 16 is a diagram schematically illustrating a respiratory sensing circuit, according to another embodiment of the present disclosure; and

[027] FIG. 17 is a diagram schematically illustrating both pressure and temperature components of a respiratory signal, according to one embodiment of the present disclosure.

DETAILED DESCRIPTION OF EMBODIMENTS

[028] The following detailed description is merely exemplary in nature and is not intended to limit the present disclosure or the application and uses of the

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embodiments of the present disclosure. Furthermore, there is no intention to be bound by any expressed or implied theory presented in the preceding technical field, background, brief summary or the following detailed description.

[029] Accordingly, in the following Detailed Description, reference is made to the accompanying drawings, which form a part hereof, and in which is shown by way of illustration specific embodiments in which the present invention may be practiced. In this regard, directional terminology, such as "top," "bottom," "front," "back," "leading," "trailing," etc., is used with reference to the orientation of the Figure(s) being described. Because components of embodiments can be positioned in a number of different orientations, the directional terminology is used for purposes of illustration and is in no way limiting. It is to be understood that other embodiments may be utilized and structural or logical changes may be made without departing from the scope of the present disclosure. The following detailed description, therefore, is not to be taken in a limiting sense, and the scope of the present invention is defined by the appended claims.

[030] FIG. 1 is a schematic diagram of an implantable stimulation system, according to an embodiment of the present disclosure. As illustrated in FIG.1, an example of an implantable stimulation system 10 according to one embodiment of the present disclosure includes an implantable pulse generator (IPG) 55, capable of being surgically positioned within a pectoral region of a patient 20, and a stimulation lead 52 electrically coupled with the IPG 55 via a connector (not shown) positioned within a connection port of the IPG 55. The lead 52 includes an electrode or electrode system 65 and extends from the IPG 55 so that the electrode system 65 is positioned in proximity to a desired nerve, such as the hypoglossal nerve 53 of the patient 20, to enable stimulation of the nerve 53, as described below in detail. In one embodiment, an implantable stimulation system in which lead 52 may be utilized, for example, is described in U.S. Patent No. 6,572,543 to Christopherson et al., which is incorporated herein by reference in its entirety. In this exemplary system, a sensor lead 57 is electrically coupled to the IPG 55 and extends from the IPG 55 so that a sensor or transducer 60 can be positioned in the patient 20 for sensing of respiratory effort. However, it is understood that respiratory sensing

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embodiments described herein can be used with other implantable stimulation systems for treating sleep apnea.

[031] In some embodiments, system 10 also comprises additional sensors to obtain further physiologic data associated with respiratory functions, such as various sensors distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals.

[032] In some embodiments, the sensing and stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. In other embodiments, one or more components of the system are not implanted in a body of the patient. A few non-limiting examples of such non-implanted components include external sensors (e.g., impedance, heart rate, etc.), an external processing unit, or an external power source. Of course, it is further understood that the implanted portion(s) of the system provides a communication pathway to enable transmission of data and/or controls signals both to and from the implanted portions of the system relative to the external portions of the system. The communication pathway includes a radiofrequency (RF) telemetry link or other wireless communication protocols.

[033] Whether partially implantable or totally implantable, the system is designed to stimulate the hypoglossal nerve during inspiration to thereby prevent obstructions or occlusions in the upper airway during sleep. In one embodiment, the implantable system comprises an implantable pulse generator (IPG), a peripheral nerve cuff stimulation lead, and a respiratory sensing lead.

[034] In one embodiment, the sensor 60 is a respiratory pressure sensor that is surgically implanted in a region that has pressure continuity with the pleura via an intrapleural placement or an extrapleural placement (including but not limited to an intercostal placement), as will be further described in association with Figure 2. The location for placement of the sensor 60 is, at least in part, chosen as a function of a delay, i.e. the propagation time associated with a pressure waveform characteristic of respiratory effort propagating from the respiratory point of origin to the sensor position. The chosen location is also a function of the amount of filtering or signal

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processing necessary to achieve a usable sensed signal at a particular location, i.e. the amount of filtering that is necessary to remove waveforms other than the waveform associated with the desired sensed characteristic, such as the filtering required to remove cardiac waveform activity, for example. The positioning of the sensor 60 enables the IPG 55 to receive respiratory effort waveform information and to use this information to control delivery of the therapy.

[035] As schematically illustrated in Figure 2, in one embodiment of the present disclosure, an implantable stimulation system 10 comprises a sensing system 70 including a lead 75 configured to place a respiratory pressure sensor 71 within an intrapleural space 90 so that sensor 71 is positioned in close proximity to the lung 80. In this arrangement, the sensor 71 becomes directly coupled relative to the respiratory pressures at the pleura. In another aspect, the intrapleural space 90 includes the cavity between the parietal pleura 78 and a pulmonary pleura 79. Finally, it will be understood that FIG. 2 illustrates generous spacing between adjacent anatomical structures for illustrative purposes.

[036] In the one embodiment, lead 75 includes a lead body 72 that supports sensor 71 at its distal end and an anchor 74 (such as a wing-like fixation member) located at a more proximal portion of lead body 72. The anchor 74 ensures that sensor 71 remains positioned to orient the membrane portion of the sensor to face along the lung 80 subsequent to implantation of the sensor 71. The lead body 72 is positioned through an inter-costal space 91 into the pleural space 90 (with a position of sensor 71 and lead body 72 as indicated by reference numeral 88) so that the IPG 55 (Figure 1) receives sensor waveforms from the sensor 71, thereby enabling the IPG 55 (Figure 1) to deliver electrical stimulation synchronously with inspiration, according to a therapeutic treatment regimen in accordance with embodiments of the present disclosure.

[037] As further illustrated by Figure 2, the lead 75 will be inserted so that lead body 72 extends through the intercostal space (e.g. between two ribs 86) to position the sensor 71 for placement intrapleurally, as indicated generally via indicator 90. In one embodiment, the lead 75 incorporates a piezo-electric crystal mounted into a sealed housing and capable of monitoring intra-thoracic pressure associated with respiration. In other embodiments, monitoring the respiratory pressure comprises

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monitoring other physiological data indicative of respiratory pressure (in addition to or instead of monitoring intra-thoracic pressure). The sensor 71 is powered by the IPG 55 (FIG. 1) and the IPG 55 also contains internal circuitry to accept and process the respiration signal from the lead 75.

[038] In one embodiment, the system includes a lead anchor 74 located remotely (by a distance of several centimeters or so) from where the sensor 71 is placed intrapleurally. Tissue movements on the sensor and lead can induce unwanted signal components as well as lead migration/dislodgement; therefore anchoring of the lead body 72, close to where the lead 75 enters the thoracic cavity is warranted. With this in mind, the anchor 74 will be sutured to a subcutaneous connective tissue, such as an intra-costal muscle or fascia during implant, and the anchor 74 is fixed or secured to the lead body 72 and not allowed to slide.

[039] In other embodiments, the respiratory sensor can be any one of an airflow sensor, a pressure sensor, a volume sensor, an accelerometer, an acoustic sensor, a temperature sensor, a mechanical strain sensor, or an effort sensor.

[040] To achieve the placement of the sensor 60 in the positions shown and described in association with FIGS. 1-2, several different approaches can be taken as illustrated in association with at least FIGS. 3-4.

[041] FIG. 3 schematically illustrates an implantable stimulation system 150, with a subcutaneous, extrapleural placement, according to one embodiment of the present disclosure. As shown in FIG. 3, system 150 includes an IPG 155 and a sensor lead 161. In one embodiment, the IPG 155 includes at least substantially the same features and attributes as IPG 55 (FIG. 1).

[042] In general terms, the sensor lead 161 is configured to detect and/or measure respiratory effort in a manner substantially similar to the sensor 60, as previously described in association with FIGS. 1-2, except for having a generally shorter length for sensor lead 161. With this in mind, as shown in FIG. 3, sensor lead 161 includes sensor portion 160, lead body 164, and stability mechanism 162. In one aspect, lead body 164 has a relatively short length such that with the IPG 155 mounted generally over one or more ribs (e.g. such as ribs 86A, 86B, etc.), lead

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body 164 forms a generally straight portion extending directly from the header 156 of IPG 155 to cause lead body 164 to extend generally parallel to ribs 86A, 86B. It will be understood that, in some embodiments, lead body 164 will have a length greater than that shown in FIG. 3.

[043] As illustrated in FIG. 3, sensor lead 161 is implanted in a subcutaneous, extrapleural region 89 (which also includes but is not limited to placement intercostally between a pair of spaced apart ribs 86) that is external to the parietal pleura 78 (FIG. 2). In this subcutaneous, extrapleural position 89 the sensor portion 160 can be against the parietal pleura 78 or within the tissues (which includes several layers of the muscle and related connective tissues) that are external to the parietal pleura 78 and which are accessible between an adjacent pair of ribs. In one aspect, in this arrangement the sensor portion 160 becomes indirectly coupled relative to the respiratory pressures which are present at the pleural space 90.

[044] In this arrangement, sensor lead 161 terminates at sensor portion 160 between that same pair of ribs 86A, 86B. In other words, the sensor lead 161 originates from the IPG 155 between adjacent ribs 86A and 86B, and with sensor lead 161 being generally straight, the entire sensor lead 161 remains within this intercostal space 91A between ribs. Accordingly, in this embodiment, sensor lead 161 does not extend across ribs 86A, 86B in either a superior orientation (toward the head) or an inferior orientation (toward the feet) relative to this intercostal space 91B.

[045] In general terms, the stability mechanism 162 of sensor lead 161 ensures that the sensor portion 160 remains generally fixed in a target location so that a membrane portion of the sensor portion 160 is located to be facing along the lung subsequent to implantation of the sensor 160. Being made from a resilient material, the stability mechanism 162 is flexible enough to facilitate its positioning and not interfere with the surrounding tissues, while still having enough stiffness to hold or maintain its position. In this secured position, the sensor portion 160 is located between ribs 86A, 86B in either of an intrapleural or extrapleural implanted configuration (as previously described in association with FIG. 2).

[046] In one embodiment, the stability mechanism 162 includes a pair of wings that extend laterally outward from both sides of the sensor portion 160, as later

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described in more detail in association with FIGS. 5-6. In some other embodiments, the stability mechanism 162 comprises one or more pairs of anchor elements (e.g. arms) that extend laterally outward from both sides of the sensor lead 161, as later described in more detail in association with at least FIGS. 7-8. In one aspect, these wings or arms of the stability mechanism 162 prevent lateral shifting and/or prevent rotation of the sensor portion 160 to ensure that an active portion of the sensor portion 160 is oriented to face toward the pleura and lungs.

[047] One of the other approaches that achieves an intrapleural placement (consistent with the embodiment of FIG. 2) of a sensor lead is schematically illustrated in association with FIG. 4, according to one embodiment of the present disclosure. As shown in FIG. 4, implantable stimulation system 170 includes an IPG 175 and a sensor lead 181. In one embodiment, the IPG 175 includes at least substantially the same features and attributes as IPG 55 (FIG. 1).

[048] In general terms, the sensor lead 181 is configured to detect and/or measure respiratory effort in a manner substantially similar to the sensor 60, as previously described in association with FIGS. 1-2, except for having a generally shorter length for sensor lead 181. With this in mind, as shown in FIG. 3, sensor lead 181 includes sensor portion 180, lead body 185 (with proximal lead portion 184 and distal lead portion 186), and stability mechanism 188. In one aspect, lead body 185 has a relatively short length such that with the IPG 155 mounted generally over a pair of ribs 86E, 86A, the proximal lead portion 184 forms a generally straight portion extending directly from the header 176 of IPG 155 to cause proximal lead portion 184 to extend between, and generally parallel to, the spaced apart ribs 86A, 86B (which separately connect to manubrium 95 as later described in more detail in association with FIG. 9A).

[049] In one aspect, stability mechanism 188 (e.g., anchor 280 in FIG. 7) is located along the proximal lead portion 184 and secures the proximal lead portion 184 relative to intercostal tissue or adjacent tissues. In another aspect, with proximal lead portion 184 anchored via the stability mechanism 188, distal lead portion 186 forms a generally perpendicular angle relative to the proximal lead portion 184 such that distal lead portion 186 is arranged to extend downward underneath one or more

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ribs 86D, 86E before terminating at sensor portion 180 within the intrapleural space (as shown in FIG. 2).

[050] In this arrangement, the distal lead portion 186 is oriented to be generally perpendicular to a longitudinal axis of the ribs (or relative to a longitudinal axis of a length of the patient's body) to maintain the sensor portion 180 in a generally vertical orientation within the pleura 90 (FIG. 2). This orientation ensures that normal, cyclical movements of the lungs 80 (FIG. 2) during respiration in a generally vertical orientation (toward and away from the head) do not substantially affect the sensing performed by the sensor portion 180 because a longitudinal axis of the sensor portion 180 is aligned along the direction of movement (and not transverse to) of the lungs.

[051] Nevertheless, it will be understood that in some other embodiments, the sensor portion 180 can be implanted intrapleurally with the distal lead portion 186 extending generally parallel to the longitudinal axis of the ribs to orient the sensor portion 180 in a generally horizontal position within the pleura 90. In these embodiments, portions of the distal lead portion 186 proximal to the sensor portion 180 will be positioned between, and extend generally parallel to, an adjacent pairs of ribs in a manner substantially similar to that shown in FIG. 1 or 3.

[052] In some embodiments, the stability mechanism 188 of the embodiment of FIG. 4 can be exchanged for the stability mechanism 162 of the embodiment of FIG. 3 (or the stability mechanism provided by wing-like members 220 of FIG. 5), and vice versa.

[053] Among other features, the embodiments of FIGS. 3-4 allow a relatively simple implantation of an IPG and its sensor lead. While an implantation of the IPG and sensor lead on a right side of the patient's body is preferred, in some other embodiments an implantation of the IPG and sensor lead can be made on a left side of the patient's body.

[054] FIG. 5 is a top plan view schematically illustrating a sensor lead 200, according to one embodiment of the present disclosure. In general terms, sensor lead 200 provides a sensor portion 210 including a pair of wing-like members 220 configured to stabilize the position of sensor portion 210 in its implanted location, in

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manner substantially similar to that previously described in association with at least FIG. 3. As illustrated in FIG. 5, sensor lead 200 comprises a lead body 202 and sensor portion 210. Lead body 202 includes a distal portion 206 supporting sensor portion 210, a mid-portion 205, and a proximal portion 204 configured to extend to (and connect with) IPG 55 of FIG. 1.

[055] In one aspect, sensor portion 210 includes a distal tip 214, which is preferably made of a soft radiopaque material to be visible under fluoroscopy or other radiograph visualization techniques. In another aspect, sensor portion 210 includes the wing-like members 220, which extend outward from opposite sides of the sensor portion 210. While the wing-like members 220 can take a variety of shapes, the members 220 shown in FIG. 6 have a tapered shape in which each member 220 has a generally wide base 221 and the wing-like members 220 become progressively narrower toward curved tip 223. As further shown in the sectional view of FIG. 6, wing-like members 220 have a generally flat cross-sectional shape. However, in some embodiments, the base 221 is thicker than the tip 223 to ensure robust attachment of the members 220 relative to a body of the sensor portion 220.

[056] In one embodiment, the wing-like members 220 do not include any holes or other features configured to facilitate suturing (or other fastening techniques) of the wing-like members 220 relative to the tissues. Instead, the generally large surface area and resiliency of the wing-like members 220 as they extend outward from the sensor portion 210 provide frictional engagement relative to, and physical abutment to, surrounding tissues. In this way, the wing-like members 220 provide a mechanism that maintains the position of sensor portion 210 in a proper orientation relative to the tissue to be sensed. In particular, in some embodiments, the sensor portion 210 includes a directional sensor element 212 (shown in dashed lines) with sensor portion 210 implanted to cause the directional sensor element 212 face the pleura and target lung tissue. In this arrangement, the wing-like members 220 prevent rotation of the directional sensor element away from the target tissue, while also preventing migration of the sensor portion 210 up, down, left, or right relative its implanted position in the body.

[057] In another aspect, sensor element 212 is configured to perform pressure sensing with sensor element 212 comprising an electronic sensor element that

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includes one or more piezo-crystal elements, as later described in more detail in association with FIGS. 10-12.

[058] FIG. 7 is a top plan view schematically illustrating a sensor lead 250, according to one embodiment of the present disclosure. As illustrated in FIG. 7, sensor lead 250 comprises lead body 252 and sensor portion 260. In one embodiment, sensor lead 250 comprises substantially the same features and attributes as sensor 60 as previously described in association with at least FIGS. 1-2. As shown in FIG. 7, sensor portion 260 includes distal tip 264 and sensor element 262. In one aspect, sensor portion 260 has a length (D4) of about 1-3 centimeters.

[059] Lead body 252 includes midportion 255, a proximal portion 254, and a distal portion 256. The distal portion 256 supports sensor portion 260 while the proximal portion 254 configured to extend to, and connect with, IPG 55 (FIG. 1).

[060] In some embodiments, sensor lead 250 includes a first anchor element 280 mounted onto, or formed as part of, lead body 252. In one aspect, first anchor element 280 has a fixed position relative to a length of lead body 252 and includes a pair of arms 284 extending outward from opposite sides of a central portion 282 of anchor element 280. In this position, the arms 284 extend generally perpendicular to a longitudinal axis of the lead body 252. In one embodiment, as illustrated in the side view of FIG. 8, each arm 284 has a thickness substantially less than a diameter of the lead body 252.

[061] In another aspect, each arm 284 includes a hole 285 configured to facilitate suturing (or other fastening techniques) of the arm 284 to surrounding tissues. In some embodiments, the fixed position of first anchor element 280 along lead body 252 is spaced apart a distance (D1) of about 4 to 9 centimeters from the distal tip 264. In other embodiments, the distance (D1) is about 2 to 6 centimeters. In one aspect, this arrangement ensures the sensor lead 250 will extend an adequate distance inside the thoracic cavity or intercostal space to achieve optimal sensing while preventing dislodgements of the sensor lead from its intercostal deployment. Moreover, the resilient arms 284 maintain the orientation of the directional sensor portion 260 to face the lungs or pleura by preventing rotational movement of the sensor portion and/or preventing significant lateral shifting of the sensor portion 260.

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However, the sensor lead is relatively short enough to avoid interference with cardiac functions, as will be further described in association with FIGS. 9A-9B.

[062] In some embodiments, in addition to fixed first anchor element 280, sensor lead 250 includes a second anchor element 290, as illustrated in FIG. 7. In one aspect, this second anchor element 290 is movable along a length of lead body 252 to enable adjusting the position of the second anchor element 290 before securing it relative to surrounding tissues. In this arrangement, the distance (D2) between the respective anchor elements 280, 290 can vary as desired to effect a robust implantation of sensor lead 250. In one non-limiting use, second anchor element 290 is configured to secure proximal portion 254 of sensor lead 250 after tunneling along a lateral side 303 of the body to and/or from the implanted site of the IPG 55 (FIG. 1).

[063] In one aspect, other than its movable position (as represented by directional arrow M in FIG. 7), second anchor element 290 has substantially the same features and attributes as first anchor element 280. Accordingly, second anchor element 290 has a pair of arms 294 extending outward from opposite sides of central portion 292.

[064] However, it is understood that in other embodiments, the second anchor element 290 can have a fixed position along a length of lead body 252 such that the distance (D2) between the respective anchor elements 280, 290 does not vary.

[065] In some embodiments, lead body 252 includes an outer diameter that is no greater than an outside diameter of the sensor portion 260. Further, in some embodiments, it will be understood that the sensor portion 260 and distal portion 256 of lead body 252 are dip coated with thinned medical adhesive to facilitate maintaining the sensor portion 260 in a desired location relative to the target tissue at which sensing is to take place. At the same time, dip coating also softens the sensor surfaces and provides further electrical insulation.

[066] It will be understood that because the sensor portion 260 will be inserted into the pleural cavity (or adjacent to the pleura, but within the thoracic cavity), the outside diameter of the lead body 252 should be minimized (in concert with the lead body conductor 406 shown in FIG. 11) to optimize the flexibility of the device. This

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arrangement acts to minimize any local stresses on the sensor portion 260 in the pleural cavity. Likewise, in the situation in which the sensor lead 250 and sensor portion 260 are deployed in an extra- pleural configuration, then a relatively small outer diameter of the sensor portion 260 will minimize stress on the pleura.

[067] FIG. 9A is front view schematically illustrating a method 300 of implanting a sensor lead 250 of an implantable stimulation system, according to one embodiment of the present disclosure. As illustrated in FIG. 9A, IPG 55 is implanted in a pectoral region of a patient (FIG. 1) in a manner known to the art such that IPG 55 is positioned over a couple of ribs 304 (such as upper ribs 2 and 3) of a ribcage 302. In some embodiments, the IPG 55 is implanted on a right side (R) of the patient, generally opposite the left side (L) at which the heart H (shown in dashed lines) is located. With further reference to FIG. 9A, a sensor lead 250 extends from the IPG 55 while a stimulation lead (not shown) extends from IPG 55 in a direction opposite the sensor lead 250 for coupling to a target nerve.

[068] As illustrated in FIG. 9A, each rib 304 is joined, via a costochondral joint 308, to a costal cartilage 306. Each costal cartilage 306 is joined to manubrium 310. In one embodiment of method 300, sensor lead 250 is implanted to position sensor portion 260, via intercostal placement, in substantially the same as previously described in association with at least FIGS. 2-4. However, in addition, as shown in method 300, proximal portion 254 of lead body 252 extends down a lateral side 303 of the rib cage 302 (and generally parallel to a longitudinal axis of the body) and distal portion 256 of lead body 252 extends generally parallel to the proximal portion 254. In this arrangement, distal portion 256 and sensor portion 260 extend generally parallel to ribs 304. In one aspect, the point 319 of intercostal entry is selected such that sensor portion 260 will become positioned lateral (toward an outer side of the body) to the costochondral joint 308. In some embodiments, sensor portion 260 is positioned directly below or inferior to the nipple 320. While the nipple is not related functionally to the position of the sensor portion 260, the nipple 320 provides a positional marker relative to a desired location between a lateral side of the body and a midline of the body. In particular, method 300 includes implanting the sensor lead 250 and sensor portion 260 away from the lateral side 303 because that location would compromise the accuracy of the readings from sensor portion 260 when the

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patient lies on that side of their body to sleep. At the same time, method 300 includes implanting the sensor portion 260 as far away, both laterally and longitudinally, as possible from heart H in order to minimize the effect of cardiac activity on the readings of sensor portion 260. While FIG. 9A shows placement of the sensor portion 260 between the fifth and sixth ribs 304, it will understood that in other embodiments, placement of the sensor portion 260 could take place between any pair of adjacent ribs within the group of ribs 304 extending from the first uppermost rib 304 through the seventh uppermost rib 304.

[069] Moreover, in some embodiments, method 300 also includes implanting the sensor portion 260 over an adequate volume of lung tissue in order to obtain a representative measurement of respiratory effect and activity. This latter constraint practically limits the distance that sensor portion 260 can be located away from heart H because sensor portion 260, in this embodiment, will have to overlie some portion of lung tissue.

[070] Putting all of these constraints together, the sensor lead 250 is implanted to position sensor portion 260 longitudinally between a fifth rib and a sixth rib (over a corresponding portion of lung tissue). At the same time, the sensor portion 260 is positioned lateral (toward a side of the body) of the costochondral joint 208 of either the fifth or sixth rib with the sensor portion 260 also being located directly below or medial to the nipple. However, it is understood that in some other embodiments, the sensor lead 250 and sensor portion 260 can be deployed between a different set of adjacent ribs, such as within the first through seventh rib space, and more preferably within the second through sixth rib space, etc.

[071] Moreover, with this positioning shown in FIG. 9A, first anchor 280 (which is itself fixed relative to lead body 252) is secured in a fixed position at a lateral side 303 of the body within the subcutaneous, extrapleural tissue region 89 that is external to the parietal pleura 78 (FIG. 2) and lateral to the intercostal entry site 319 for the sensor portion 260. In another aspect, the second anchor 290 is located closer toward the IPG 55, and secured to a lateral side 303 of the body as previously described. Because the second anchor 290 is movable, the position of securing the second anchor 290 can be varied to optimize stability of the proximal portion 254 of lead 250 while also supporting the secured position of first anchor 280. Once the

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desired location of the second anchor 290 is achieved, sutures or other fastening mechanisms are used to fix the second anchor 290 relative to the lead body 252 and relative to subcutaneous connective tissues.

[072] In some embodiments, the deployment location of sensor portion 260 below the nipple 320 (i.e., toward the fee) carries a functional consideration. In particular, by deploying the sensor lead 250 and sensor portion 260 intercostally within the extrapleural region 89 between the fifth and sixth ribs (or between the sixth and seventh ribs), one can avoid penetrating or disturbing the pectoral muscles, and thereby perform the most minimally invasive procedure to place the sensor portion 260 relative to the pleura 90.

[073] FIG. 9B is a diagram that schematically illustrates the position of the sensor lead 250 and sensor portion 260 relative to an incision area 321 and without illustrating the rib cage, as in FIG. 9A. As illustrated in FIG. 9B, the first and second anchors 280, 290 are located on a side portion 303 of the body to cause sensor portion 260 to be positioned lateral (toward outside of body) relative to a costochondral joint (represented by dashed lines 330) of nearby ribs. Moreover, the first anchor 280 is located and secured relative to body tissues external to the intercostal entry site 319 with the distal portion 256 of the lead extending through the intercostal entry site 319 to place the sensor portion 260 within the pleura 90 (see FIG. 2) or in the subcutaneous, extrapleural region 89 between the adjacent ribs (e.g., see FIG. 3 or 9A).

[074] FIG. 10 is a perspective view that schematically illustrates a sensor portion 360 of a lead 350 for an implantable stimulation system, according to one embodiment of the present disclosure. In one embodiment, the sensor portion 360 has at least substantially the same features and attributes as sensor portions 60, 260 as previously described herein. As illustrated in FIG. 10, sensor portion 360 is supported by a distal portion 356 of a lead body and at the other end, includes a distal tip 364. In one aspect, sensor portion 360 comprises a top portion 361 with its recessed portion 370 and a bottom portion 362.

[075] In general terms, via recessed portion 370, sensor portion 360 provides a directional sensor lead with the recessed portion 370 defining the direction or

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orientation of sensing. With reference to the previously described wings 162 in FIG. 3 or wings 220 in FIG. 5, these wings act to keep recessed portion 370 in a desired orientation that faces the target tissue to be sensed.

[076] In one embodiment, this recessed portion 370 defines a membrane portion 372 interposed between a pair of sloped walls 374 on opposite sides of the membrane portion 372. The membrane portion 372 forms part of a sensor element 400 contained within housing 412 of sensor portion 360.

[077] FIG. 11 is a sectional view as taken along lines 11—11 of FIG. 10, and FIG. 12 is side sectional view as taken along lines 12—12 of FIG. 10, both of which schematically illustrate sensor element 400, according to one embodiment of the present disclosure. In one aspect, this sectional view depicts membrane portion 372 in dashed lines. As illustrated in FIGS. 11-12, sensor element 400 comprises a housing 412 that contains a pressure sensing element 402 (e.g., pressure transducer) configured to measure sensed changes through or along membrane portion 372 and a temperature sensing element 404 (e.g., temperature transducer) configured to measure temperature. In one embodiment, the pressure sensing element 402 is electrically coupled to the temperature sensing element 404, which acts as a temperature compensation unit for pressure sensing element 402. In one aspect, the temperature sensing element 404 is positioned away from the membrane portion 372 and the pressure sensing element 402, so that these respective sensing elements 402, 402 are laterally spaced apart to each other, rather than in a stacked configuration.

[078] In some embodiments, the temperature sensing element 404 is electrically coupled to the pressure sensing element 402 in order to cancel temperature effects and thereby produce a sensor element 400 that produces a sensed respiratory signal that primarily indicates changes in pressure and not temperature.

[079] However, it is also understood that when pressure sensing element 402 comprises a piezo-electric element, pressure sensing element 402 is substantially more sensitive to changes in temperature than to changes in pressure. Accordingly, in some other embodiments, instead of attempting to cancel out temperature effects, the change in temperature sensed via the piezo-based pressure sensing element

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402 is used as a factor in determining whether or not an obstructive sleep apnea event has occurred. As later illustrated in more detail in association with FIGS. 12-13 and 17, a temperature signal can be used, independent of or with a pressure signal, to identify an obstructive sleep apnea event.

[080] Sensor element 400 also includes a transistor 408 to process or amplify the signals measured via the pressure sensing element 402 and the temperature sensing element 404. In some embodiments, the pressure sensing element 402 and/or the temperature sensing element 404 are piezo-electric transducers. In one aspect, the respective elements 402, 404 are in electrical communication with a conductive feed element 406 of sensor portion 260 of lead 250 that provides electrical connection out of the hermetically sealed housing 412. This feed element 406, in turn, communicates signals to IPG 55 (FIG. 1) to indicate a respiratory state or effort.

[081] In some embodiments, the respiratory-associated signals produced from the pressure sensing element 402 and the temperature sensing element 404 are mapped independently, as illustrated in FIGS. 13-14. As illustrated in FIG. 13, a diagram 500 illustrates a signal 510 mapped as pressure (512) over time (514). Signal 510 includes cyclical patterns of inspiration (I) and expiration (E), with diagram 500 also illustrating the nature of these patterns during normal respiration (signal portion 520) and during an obstructive apnea (OSA) event (signal portion 540). During normal respiration, signal portion 520 includes inspiration portions 530 and expiration portions 532 which have a nominal amplitude (A) and which correspond to generally uniform cyclical amplitudes of respiratory pressure. However, during an OSA event, signal portion 540 reveals a substantially greater amplitude of respiratory pressure (such as, 3A or three times the nominal amplitude A in a non-limiting example), indicating increased respiratory efforts through the inspiratory and expiratory phases of the respiration cycle during an obstructive event. Accordingly, these dramatic changes in the cyclical amplitudes of the pressure signal are used to detect obstructive sleep apnea and/or to trigger stimulation therapy for treating the sleep apnea.

[082] As illustrated in FIG. 14, a diagram 550 illustrates a signal 560 mapped as temperature (562) over time (564). Signal 560 includes cyclical patterns of

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inspiration (I) and expiration (E), with diagram 550 also illustrating the nature of these patterns during normal respiration (signal portion 570) and during an obstructive apnea (OSA) event (signal portion 590). During normal respiration, signal portion 570 includes inspiration portions 580 and expiration portions 582 which have a nominal amplitude (A), and which correspond to generally uniform cyclical amplitudes of the sensed temperature. However, during an OSA event, signal portion 590 reveals little difference between the peaks of the cyclical amplitudes of temperature between inspiration and expiration phases of the respiratory cycle, indicating a reduction of airflow. Accordingly, this lack of difference in the cyclical amplitudes of the temperature signal is used to detect obstructive sleep apnea and/or to trigger stimulation therapy for treating the sleep apnea.

[083] Because such a temperature signal provides useful information regarding a state of respiration (normal vs. obstructive), one of the embodiments of the sensor element 400 described above used the temperature sensing element 404 independent of the pressure sensing element 404, i.e. not to compensate for temperature effects on the pressure signal. This temperature signal can stand alone or be combined with a pressure signal. Moreover, one of those embodiments, the piezo-electric sensing element 402 is used as a temperature sensor alone apart from pressure.

[084] FIG. 15 is diagram schematically representing an equivalent circuit 600 of the measurement of temperature and pressure via a sensor element, such as sensor element 400 of FIGS. 11-12, to produce a sensed respiratory signal 620. As illustrated in FIG. 15, circuit 600 includes a first piezo-electric element 610, a second piezo-electric element 612, and a transistor 614 (e.g., a transistor amplifier circuit). In one embodiment, a local tissue temperature 630 (where the sensor element 400 is implanted and oriented) is sensed via first piezo-electric element 610 and via second piezo-electric element 612. Likewise, a local tissue pressure 632 (where the sensor element 400 is implanted and oriented) is sensed via second piezo-electric element 612. In this arrangement, the pressure signal (captured via first sensing element 610) and the temperature signal (captured via second sensing element 612) are summed into one signal 620. In one embodiment, the first and second piezoelectric

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elements 610, 612 are electrically coupled together, to permit cancellation of the temperature effects on the sensing of pressure by the second piezoelectric element.

[085] In another embodiment, as illustrated schematically in FIG. 16, an equivalent circuit 650 for producing a sensed respiratory signal 670 includes just one piezo-electric element 660 and a transistor amplifier 614. In this embodiment, both a local tissue temperature 630 and a local pressure 632 (where the sensor element 400 is implanted and oriented) is sensed via the one piezo-electric element 660. It will be further understood that in some embodiments, various combinations of piezoelectric elements with different locations, different sizes, and/or different polarity connections could be created to created to scale the temperature and pressure responses.

[086] In some other embodiments, the circuit 600 of Fig. 15 and the circuit of Fig. 16 are both implemented in a single sensor housing and, in this arrangement, both of the sensed pressure and sensed temperature signals would be sent separately from each other to the IPG 55.

[087] In some embodiments, a temperature signal and a pressure signal could be provided as input to the pulse generator (e.g., IPG 55 in FIG. 1) as two separate signals to preserve maximum signal content.

[088] FIG. 17 is a diagram 700 schematically illustrating a juxtaposition of an independent respiratory temperature signal 702 (through cycles of inspiration 710 and expiration 720) relative to a pressure signal 704 (through cycles of inspiration 710 and expiration 720). As shown in FIG. 17, during inspiration 710 the temperature falls in a cooling segment 730 (due to air temperature) and rises in a warming segment 732 (due to blood flow). Likewise, during inspiration 710, the pressure rises in a negative pressure segment 740 and falls during a positive pressure segment 742. As illustrated by FIG. 17, the lowest value 731 of the temperature signal 702 occurs simultaneously with a peak 741 of the pressure signal 704. In one aspect, in this embodiment, the piezo-electric element is mounted and connected with the appropriate polarities to cause the cooling temperature during inspiration and the negative pressure during inspiration to be additive. In this way, one can create an additive temperature and pressure signal.

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[089] In this way, the signals from both transducers, such as pressure and temperature, can be either utilized in combination, or utilized separately in a stand alone configuration to determine whether therapy should be delivered. For example (of utilizing the signals separately) if the pressure is determined to increase beyond a predetermined pressure threshold while at the same time no changes in temperature are sensed due to restricted or obstructed airflow into the lungs, it is concluded that an obstruction has taken place, and therefore therapy is delivered or increased based on the sensed obstruction.

[090] However, if the pressure is determined to increase beyond the predetermined pressure threshold while at the same time the temperature is also determined to increase beyond a predetermined temperature threshold (which indicates a deep breath rather than an obstruction), then therapy may be withheld. Alternatively, in this situation, further indicators such as input from an activity sensor, for example, may be required before delivery of therapy it is concluded that an obstruction has occurred and therapy is commenced.

[091] In some embodiments, a sensed temperature signal is used to indicate a polarity of the sensed respiratory pressure and thereby differentiate inspiratory phases from expiratory phases of sensed respiratory pressure. In particular, as shown in FIG. 17, an inspiratory and expiratory pattern of the sensed temperature signal can be correlated with an inspiratory and expiratory pattern of the sensed respiratory signal. This arrangement is useful in certain instances in which the sensed respiratory pressure signal becomes inverted. In this situation, using the sensed temperature signal to differentiate the inspiratory and expiratory phases allows the IPG 55 to properly synchronize an application of electrical stimulation relative to the inspiratory phase, the expiratory phase, and/or a transition between the respective inspiratory and expiratory phases.

[092] With reference to the sensed respiratory pressure signal shown in FIG. 17, it is further understood that peak 741 generally corresponds to a transition region (e.g. end of inspiration and/or onset of expiration) between the inspiratory phase (710) and the expiratory phase (720). Likewise, with further reference to the sensed temperature pressure signal shown in FIG. 17, it is understood that valley 731 generally corresponds to a transition region (e.g. end of inspiration and/or onset of

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expiration) between the inspiratory phase (710) and the expiratory phase (720). Moreover, it will be understood by those skilled in the art that such transition regions include information regarding the onset of inspiration, onset of expiration, and other related respiration timing fiducials. In one aspect, this information is used to trigger or synchronize the application of an electrical stimulation signal from IPG 55 to a stimulation lead (FIG. 1).

[093] The pressure and temperature contribution to the sensor are provided above as illustrations of potential sources of input to the sensor signal. Other input is also possible, such as the local mechanical force associated with respiratory movement or other motion.

[094] Embodiments of the present disclosure provide accurate sensing of respiratory effort suitable for detecting, and/or triggering therapy on, an obstructive sleep apnea event. With sensitivity to pressure and/or temperature, a sensing element provides robust capture of respiratory behavior to more accurately indicate the presence or absence of an obstructive sleep apnea event, thereby leading to a more efficacious delivery of therapy.

[095] While at least one exemplary embodiment has been presented in the foregoing description, it should be appreciated that variations exist. It should also be appreciated that the exemplary embodiment or exemplary embodiments are only examples, and are not intended to limit the scope, applicability, or configuration of the present disclosure in any way. Rather, the foregoing description will provide those skilled in the art with a convenient road map for implementing the exemplary embodiment or exemplary embodiments. It should be understood that various changes can be made in the function and arrangement of elements without departing from the scope of the present disclosure.

What Is Claimed Is:

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1. A method of treating a respiratory dysfunction, the method comprising:

positioning a sensor portion of a lead, via an intercostal access point, into an implanted location in which the sensor portion is coupled relative to respiratory pressures of a pleural space;

sensing, via the sensor portion at the implanted location, at least one of a temperature and the respiratory pressure; and

identifying a respiratory event based on a substantial change in the amplitude of at least one of the sensed temperature and the sensed respiratory pressure.

2. The method of claim 1, wherein the respiratory event includes an obstructive sleep apnea event.

3. The method of claim 1, comprising:

triggering the application of an electrical stimulation signal, from an implantable pulse generator coupled to the sensor portion, based on the substantial change in the amplitude of at least one of the sensed temperature and the sensed respiratory pressure.

4. The method of claim 3, comprising:

synchronizing the application of the electrical stimulation signal according to cyclical respiration waveform parameters, including at least one of:

a portion of inspiratory phase;

a portion of an expiratory phase; or

a transition region between the respective inspiratory and expiratory phases.

5. The method of claim 1, wherein identifying the respiratory event comprises:

using the sensed temperature to indicate a polarity of the sensed respiratory pressure to differentiate inspiratory phases from expiratory phases of sensed respiratory pressure.

6. The method of claim 1, wherein sensing at least one of the pressure and the temperature includes:

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providing a first piezo-electric transducer within the sensor portion to sense the pressure and a second piezo-electric transducer within the sensor portion to sense the temperature, independently from sensing the pressure; and

maintaining electrical independence between the first and second piezo-electric transducers.

7. The method of claim 6, wherein identifying the respiratory event includes:

identifying a substantial increase in the cyclical amplitudes of the sensed pressure relative to a pressure threshold and identifying, at generally the same time, a substantial decrease in the cyclical amplitudes of the sensed temperature.

8. The method of claim 6, comprising:

summing a signal of the sensed pressure and a signal of the sensed temperature to produce a measured respiratory signal;

wherein identifying the respiratory event includes:

identifying a substantial change in the amplitude of the measured respiratory signal.

9. The method of claim 1, wherein positioning the sensor portion comprises:

providing the sensor portion as a directional sensing element including a single side of the sensor portion configured to sense the respiratory pressure;

facing the directional sensing element directly toward the lungs from the extrapleural position or the intrapleural position.

10. The method of claim 1, wherein positioning the sensor portion comprises:

arranging the implanted location to correspond to a subcutaneous, extrapleural position in which the sensor portion is indirectly coupled relative to the respiratory pressures of the pleural space.

11. The method of claim 1, wherein positioning the sensor portion further comprises:

locating and forming the intercostal access point between a pair of immediately adjacent ribs on one side of a patient's body; and

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inserting and advancing a distal portion of the sensor lead, including the sensor portion, through the intercostal access point to orient the distal portion to be generally parallel to the adjacent ribs and pointing toward a centerline of the body.

12. The method of claim 11, wherein positioning the sensor portion comprises:

arranging the implanted location of the sensor portion to be lateral to a costochondral joint of the adjacent ribs.

13. The method of claim 12, wherein positioning the sensor portion includes causing the implanted location to be inferior to, and aligned with, a nipple on the one side of patient's body such that the alignment of the sensor portion and the nipple is generally parallel to a longitudinal axis of the patient's body.

14. The method of claim 12, wherein locating and forming the intercostal access point comprises locating the intercostal access point between the adjacent pair of ribs within a group of ribs extending from a second uppermost rib through a seventh uppermost rib.

15. The method of claim 14, wherein the adjacent pair of ribs comprises the fifth uppermost rib and the sixth uppermost rib.

16. The method of claim 11, wherein locating and forming the intercostal access point comprises at least one of:

locating the intercostal access point inferior to a pectoral muscle of the patient's body; or

locating the intercostal access point between a second uppermost rib and a sixth uppermost rib, of the patient's body.

17. The method of claim 11, wherein positioning the sensor portion comprises:

securing, via a fixed first anchor on the sensor lead that is proximal to the sensor portion, the sensor lead relative to a subcutaneous connective tissue that is external to the intercostal access point.

18. The method of claim 17, wherein securing the sensor lead comprises:

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providing the first anchor as a pair of arms that extend generally perpendicular to, and outwardly from, opposite sides of a body of the sensor lead;

providing the sensor portion as a directional sensing element including a single side of the sensor portion configured to sense the respiratory pressure; and

orienting the arms, in their secured position relative to the subcutaneous connective tissue, in a direction generally perpendicular to the ribs to maintain the sensor portion to be generally parallel to the ribs and to maintain the single side of the sensor portion to face toward the lungs of the patient's body.

19. The method of claim 17, comprising:

securing, via a selectively movable second anchor on the sensor lead that is proximal to the fixed first anchor, the sensor lead relative to a tissue at a lateral side portion of the patient's body; and

arranging a proximal portion of the sensor lead, proximal to the fixed first anchor, to extend along the lateral side of the patient's body for connection to an implantable pulse generator.

20. The method of claim 17, wherein the fixed first anchor is spaced apart from the sensor portion about 3 to 9 centimeters along a length of the sensor lead.

21. The method of claim 1, wherein positioning the sensor portion comprises:

arranging the implanted location to correspond to an intrapleural position in which the sensor portion is directly coupled relative to the respiratory pressures of the pleural space.

22. The method of claim 21, wherein positioning the sensor portion comprises:

locating and forming the intercostal access point between a pair of immediately adjacent ribs on a patient's body; and

inserting and advancing a distal portion of the sensor lead, including the sensor portion, through the intercostal access point to insert the sensor portion into the intrapleural position in which the sensor portion is positioned and maintained between the parietal pleura and the pulmonary pleura.

23. The method of claim 22, wherein positioning the sensor portion comprises:

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securing, via a fixed first anchor on the sensor lead that is proximal to the sensor portion, the sensor lead relative to a subcutaneous connective tissue that is external to the intercostal access point.

24. The method of claim 23, wherein positioning the sensor portion comprises:

maintaining in the implanted location, via the first anchor, an active side of the sensor portion in an orientation that faces toward the lungs.

25. The method of claim 24, wherein inserting and advancing the distal portion of the sensor lead comprises:

arranging portions of the sensor lead proximal to the sensor portion to extend generally perpendicular to a longitudinal axis of the ribs.

26. An implantable respiratory sensor system comprising:

a sensor lead including a lead body and a sensor portion, the sensor portion extending from the lead body and including at least a pressure transducer;

a first anchor located at a fixed position on the lead body.

27. The sensor system of claim 26, comprising:

a second anchor located on the lead body proximal to the first anchor and being selectively movable along a length of the lead body.

28. The sensor system of claim 26, wherein the sensor portion defines a directional sensing element configured to sense respiratory pressures on a single side of a sensor portion, and wherein the first anchor is configured to maintain the single side in an orientation facing toward the lungs.

29. The sensor system of claim 28, wherein the first anchor includes a pair of resilient wings that extend outwardly from opposite sides of, and generally perpendicular to, the sensor lead, each wing having an outer tip and a base wider than the outer tip, and each wing omitting a suture hole.

30. The sensor system of claim 29, wherein the first anchor is located at the sensor portion adjacent a distal end of the sensor lead.

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31. The sensor system of claim 26, wherein the first anchor is proximal to and spaced apart from the sensor, the first anchor including a pair of arms that extend outwardly from opposite sides of the lead body and generally parallel to the lead body, wherein each arm includes a suture hole.

32. The sensor system of claim 26, wherein the fixed first anchor is spaced apart from the sensor about 3 to 9 centimeters along a length of the sensor lead.

33. The sensor system of claim 26, wherein the sensor system includes:

an implantable pulse generator electrically coupled to the sensor portion and configured to monitor the sensed pressure and to identify a substantial change in a cyclical amplitude of the sensed pressure.

34. The sensor system of claim 33, wherein the implantable pulse generator is configured to perform, based on the identified substantial change in the cyclical amplitude of the sensed pressure, at least one of:

detection of a respiratory dysfunction; and

synchronizing delivery of an electrical stimulation therapy, applied via the implantable pulse generator and a stimulation lead, to treat the detected respiratory dysfunction.

35. The sensor system of claim 34, wherein the respiratory dysfunction comprises an obstructive sleep apnea event.

36. The sensor system of claim 34, wherein the sensor portion comprises a temperature transducer in addition to the pressure transducer, wherein signals of each of the respective pressure and temperature transducers are electrically independent from one another.

37. The sensor system of claim 36, wherein at least one of the pressure transducer and the temperature transducer comprise a piezo-electric transducer.

38. The sensor system of claim 36, wherein the implantable pulse generator is configured to perform the synchronized delivery of the stimulation therapy based on

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a substantial decrease in a cyclical amplitude of the sensed temperature that occurs generally at the same time as the substantial change in the cyclical amplitude of the sensed pressure when the substantial change comprises a substantial increase.

39. The sensor system of claim 38, wherein the implantable pulse generator is configured to withhold delivery of the stimulation therapy upon a combination of an absence of the substantial decrease of a cyclical amplitude of the sensed temperature and the substantial increase in the cyclical amplitude of the sensed pressure.

40. An implantable respiratory sensor system comprising:

a sensor lead including a lead body and a directional sensor portion, the directional sensor portion extending from the lead body and including a housing that contains at least:

a pressure transducer located on a single side of the housing to define a directionality of the sensor portion; and

a temperature transducer that is electrically independent of the pressure transducer;

a first anchor located at a fixed position on the lead body that is spaced proximally from the sensor portion by a distance of about 3 to 9 centimeters, the first anchor configured with a pair of elements extending generally outward from opposite sides of the lead body to maintain the single side in an orientation facing toward the lungs;

a second anchor located on the lead body proximal to the first anchor and being selectively movable along a length of the lead body.

41. The sensor system of claim 40, wherein the elements of the first anchor include a pair of resilient wings that extend outwardly from opposite sides of, and generally perpendicular to, the sensor lead, each wing having an outer tip and a base wider than the outer tip, and each wing omitting a suture hole.

42. The sensor system of claim 41, wherein the first anchor is located at the sensor portion adjacent a distal end of the sensor lead.

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43. The sensor system of claim 26, wherein the elements of the first anchor include a pair of arms that extend outwardly from opposite sides of the lead body and generally parallel to the lead body, wherein each arm includes a suture hole.

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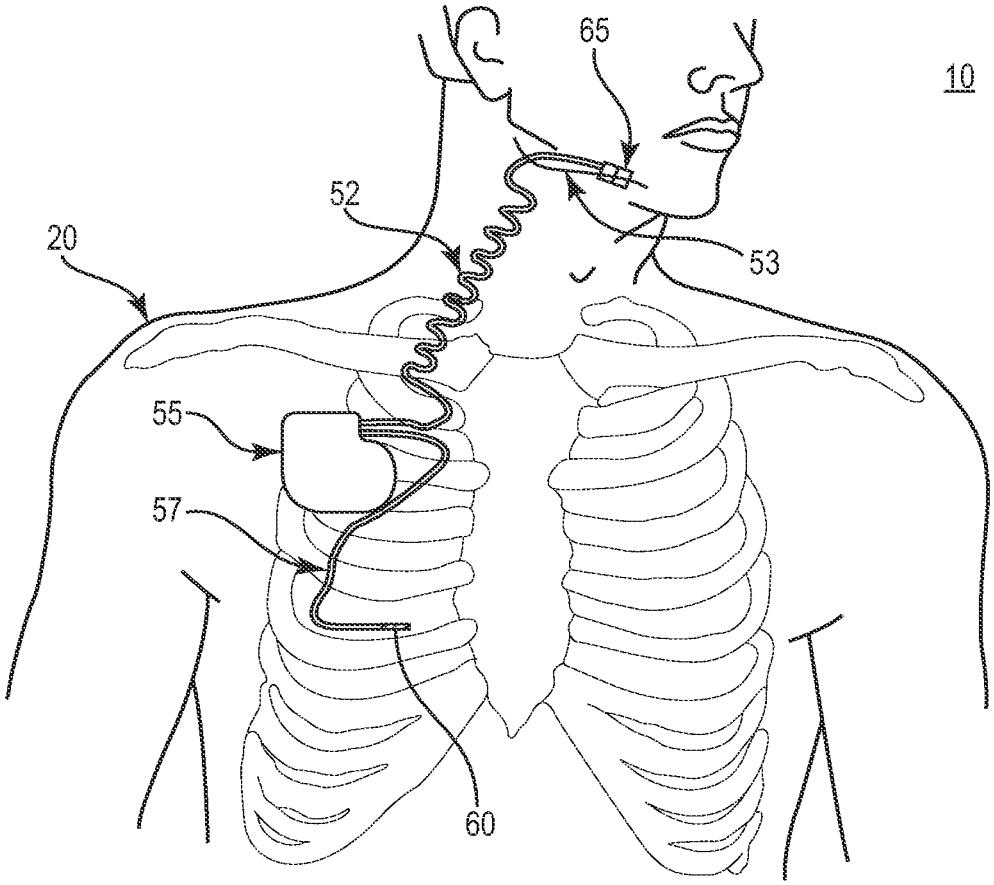


Fig. 1

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Fig. 2

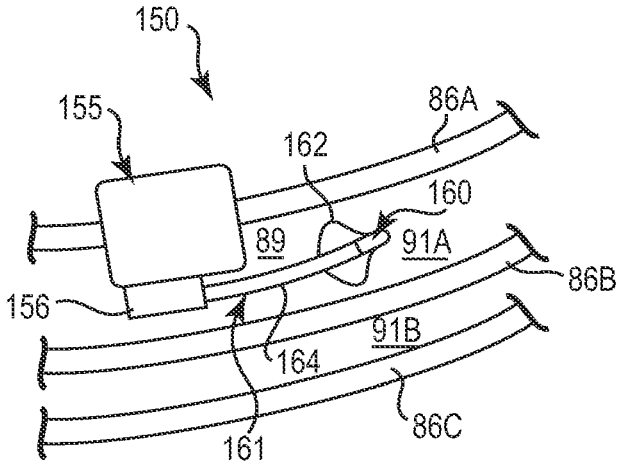


Fig. 3

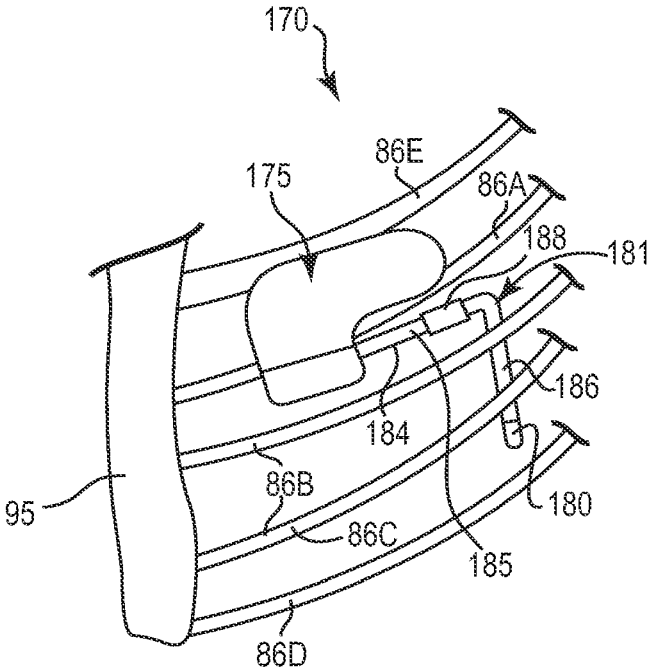


Fig. 4

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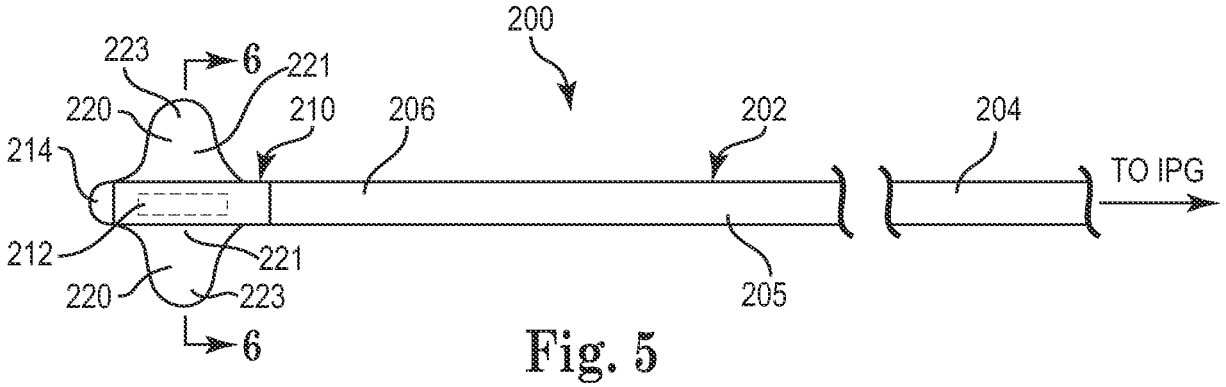


Fig. 5

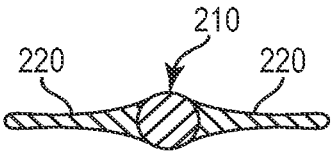


Fig. 6

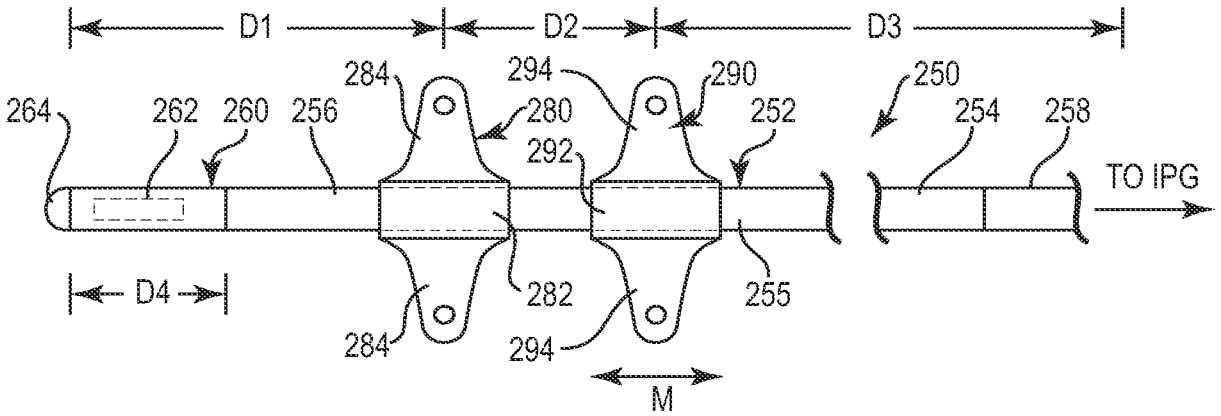


Fig. 7

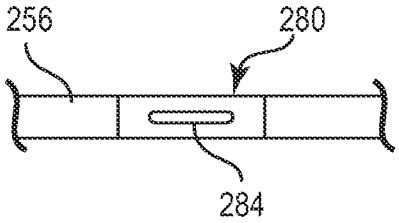


Fig. 8

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01494

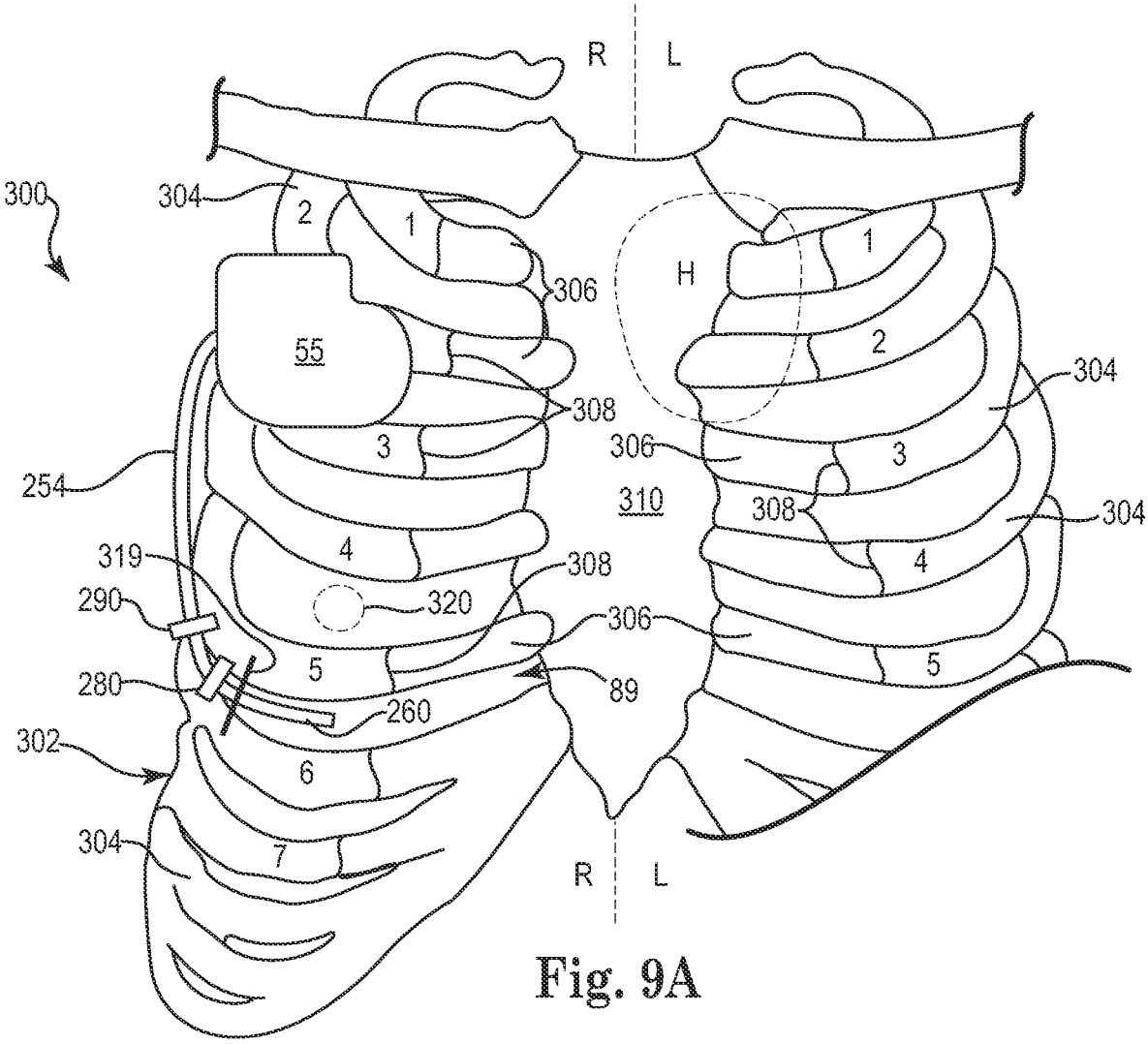


Fig. 9A

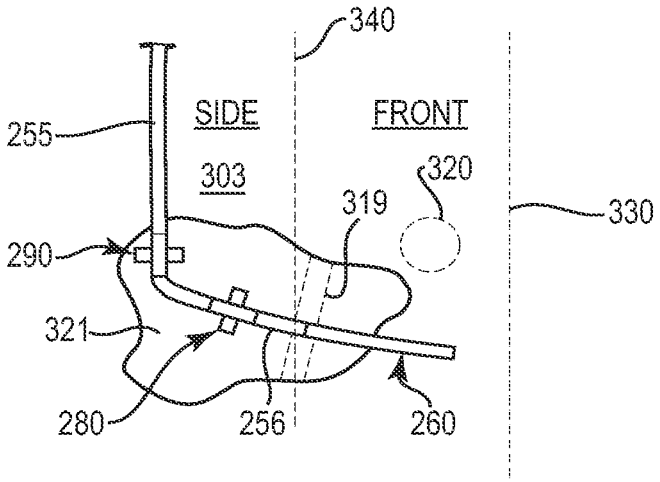


Fig. 9B

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01495

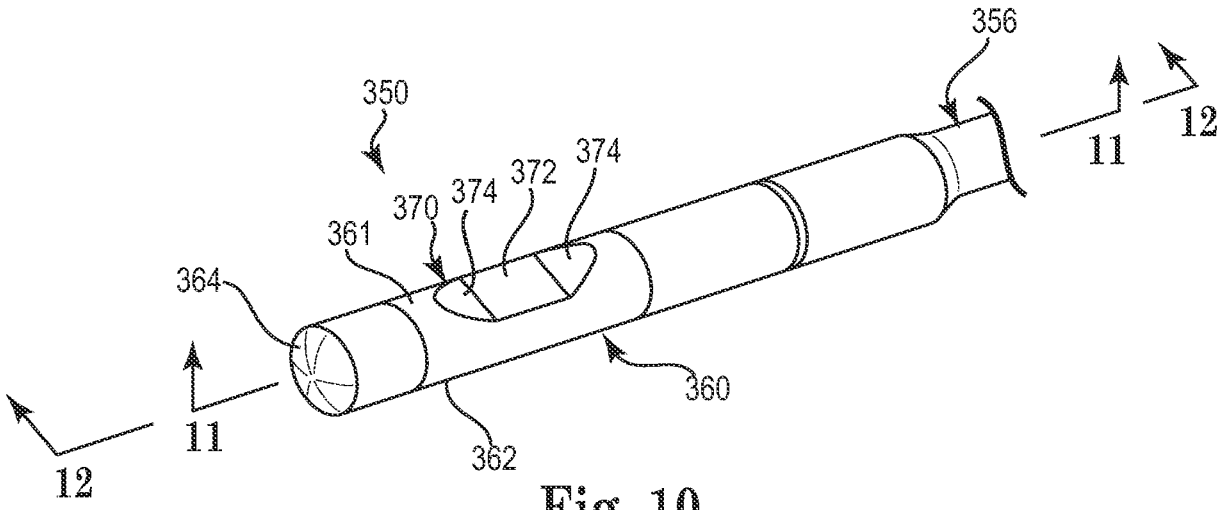


Fig. 10

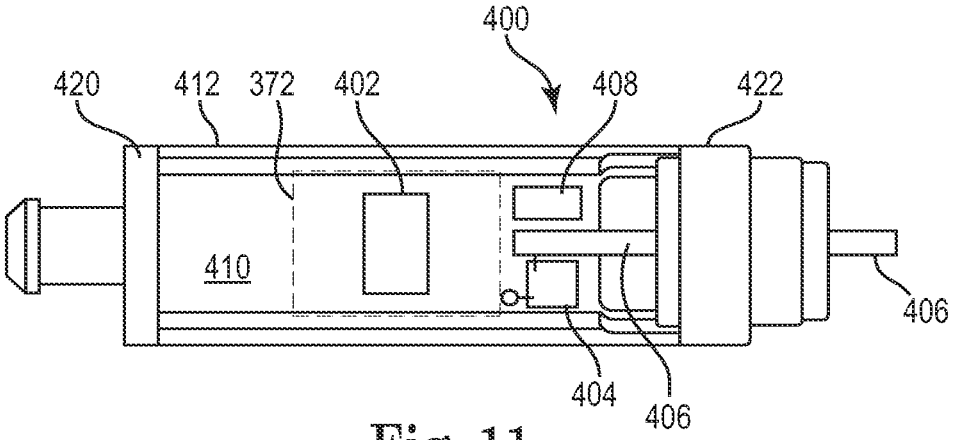


Fig. 11

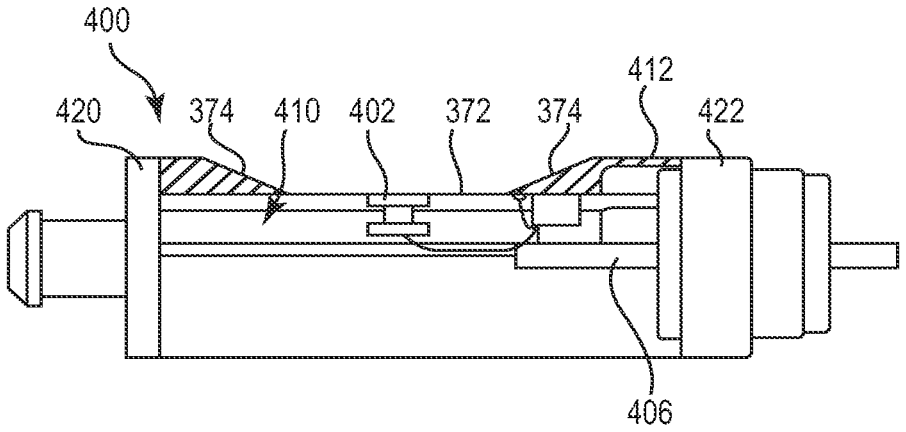


Fig. 12

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01496

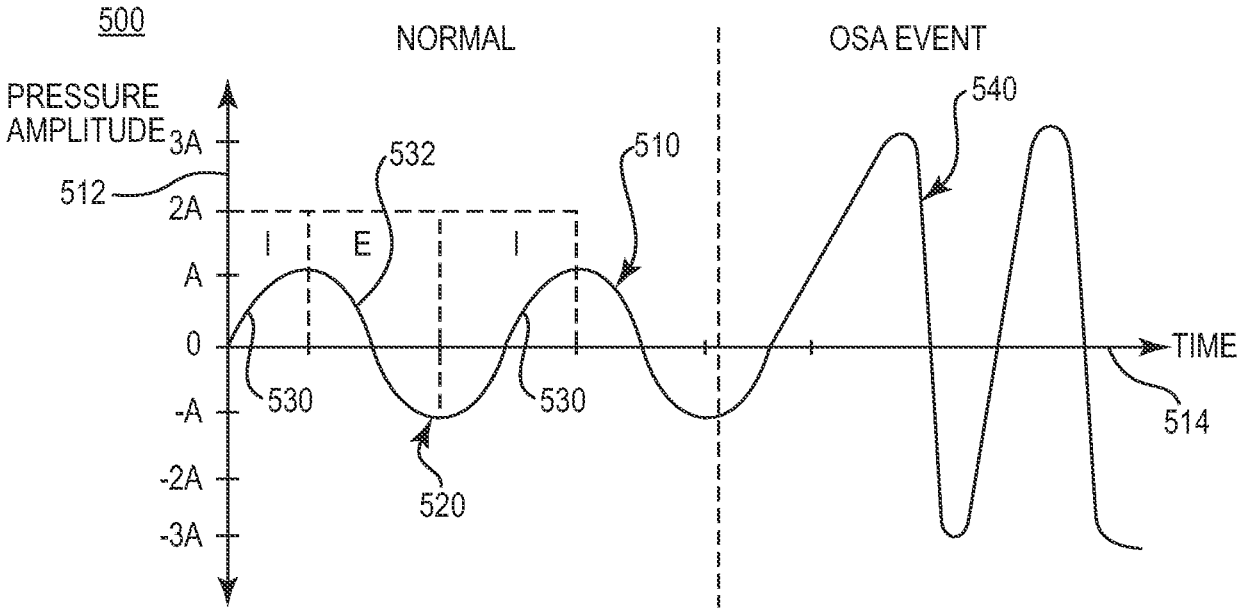


Fig. 13

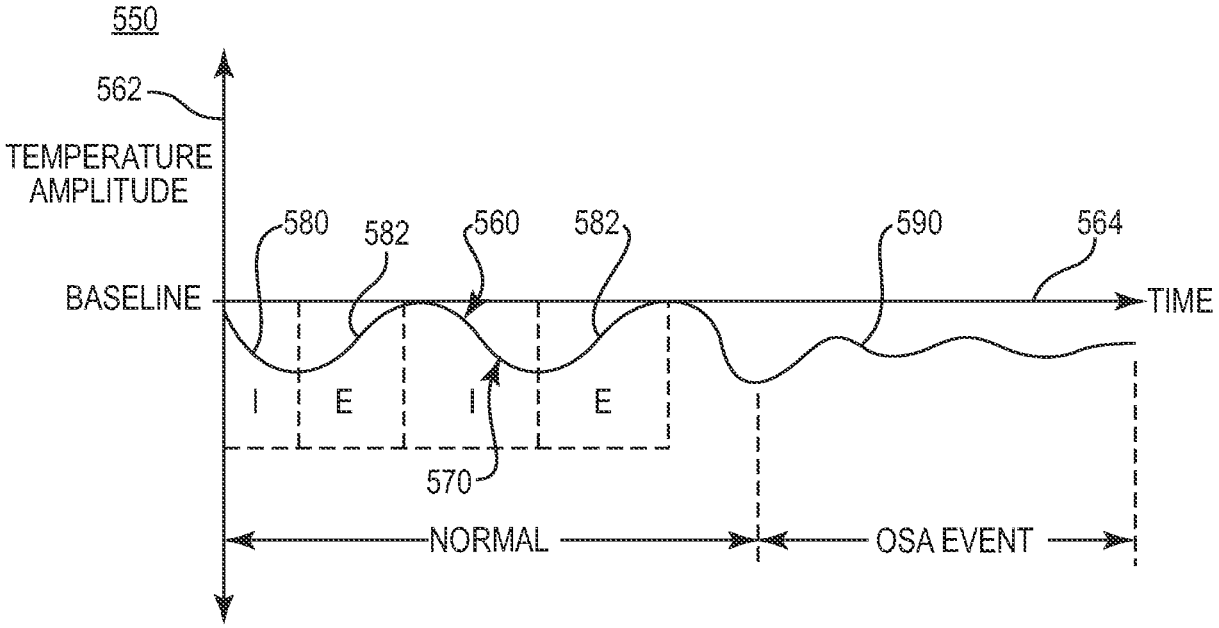


Fig. 14

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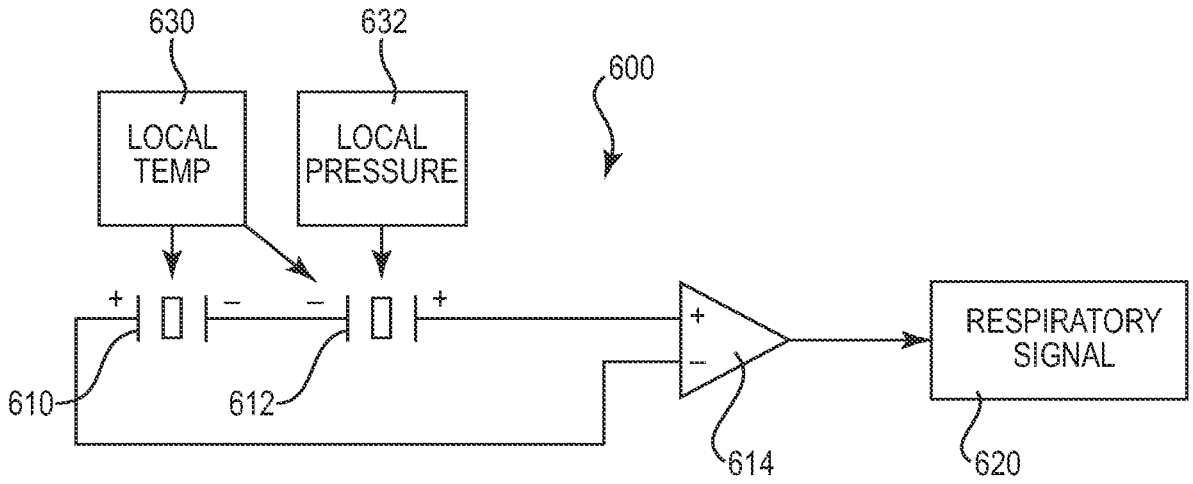


Fig. 15

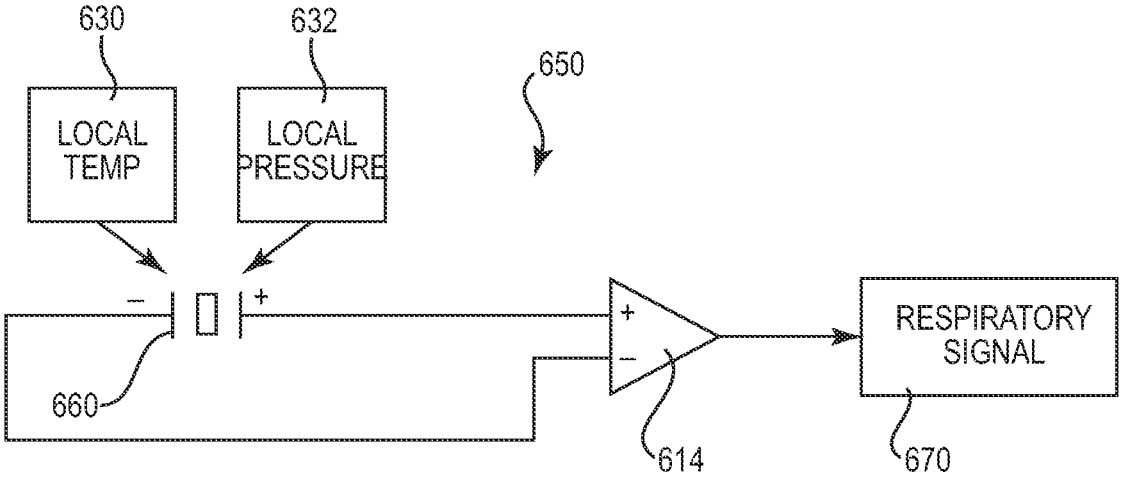


Fig. 16

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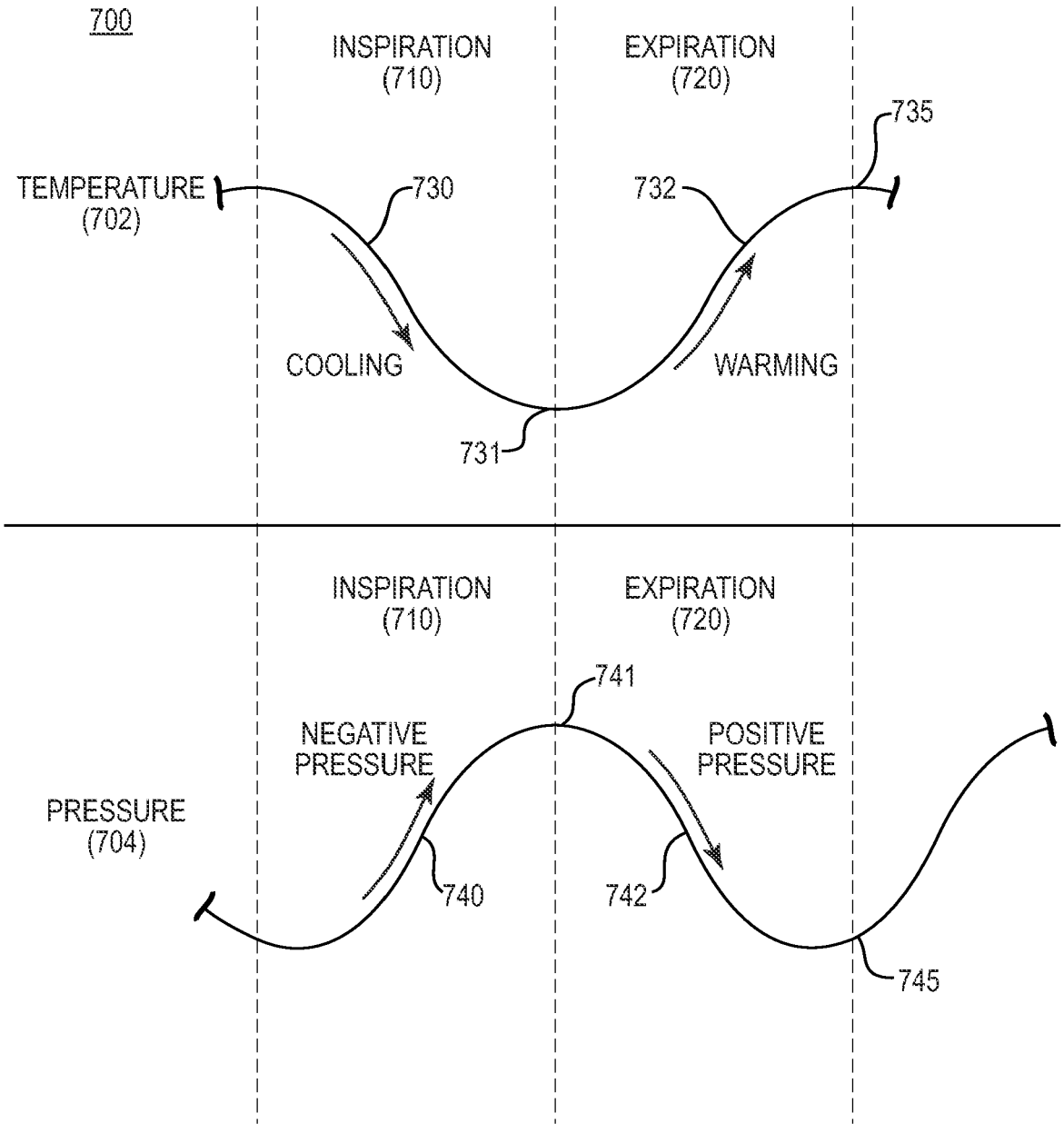


Fig. 17

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01499

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 November 2009 (19.11.2009)

PCT

(10) International Publication Number
WO 2009/140636 A3

(51) International Patent Classification:
A61N 1/36 (2006.01) *A61B 5/113* (2006.01)

(21) International Application Number:
PCT/US2009/044207

(22) International Filing Date:
15 May 2009 (15.05.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/053,344 15 May 2008 (15.05.2008) US

(71) Applicant *(for all designated States except US)*: **INSPIRE MEDICAL SYSTEMS, INC.** [US/US]; 7100 Northland Circle North, Suite 304, Brooklyn Park, MN (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CHRISTOPHERSON, Mark** [—/US]; 4100 Reiland Lane, Shoreview, MN 55126 (US). **HERBERT, Timothy** [US/US]; 14707 62nd Avenue N, Maple Grove, MN 55311 (US). **NI, Quan** [US/US]; 5812 Prairie Ridge Drive, Shoreview, MN 55126 (US).

(74) Agents: **GRUNZWEIG, Paul, S.** et al.; 100 South 5th Street, Suite 2250, Fifth Street Towers, Minneapolis, MN 55402 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: METHOD AND APPARATUS FOR SENSING RESPIRATORY PRESSURE IN AN IMPLANTABLE STIMULATION SYSTEM

(57) Abstract: A method and system for sensing respiration in the treatment of sleep apnea is disclosed.

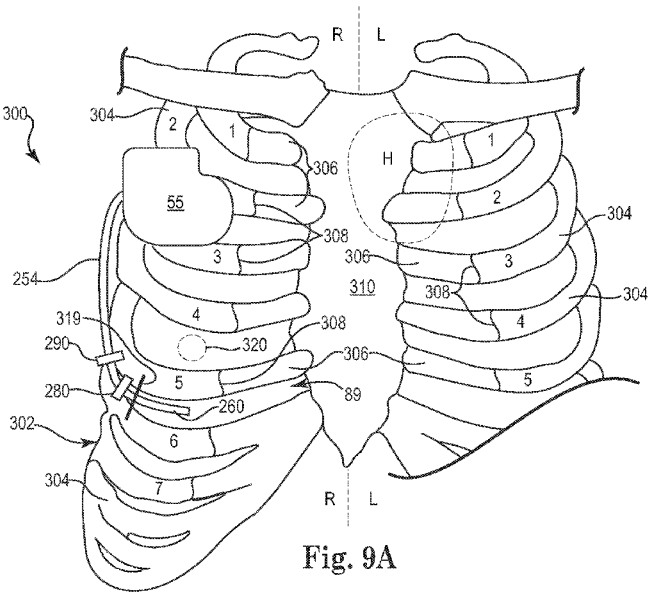


Fig. 9A

WO 2009/140636 A3

WO 2009/140636 A3

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:
11 March 2010

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01501

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/044207

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/36 A61B5/113

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 572 543 B1 (CHRISTOPHERSON MARK A [US] ET AL) 3 June 2003 (2003-06-03) column 9, line 8 - column 14, line 5; figures 10a-11d	26-35, 41-43
A	US 2008/103545 A1 (BOLEA STEPHEN L [US] ET AL) 1 May 2008 (2008-05-01) paragraph [0157] - paragraph [0163]; figures 28,29	26, 28-30, 33-35, 41-43
A	WO 2006/102591 A (UNIV VANDERBILT [US]; ZEALEAR DAVID L [US]) 28 September 2006 (2006-09-28) page 11, line 1; figures 2,4c	26,28-32

☐ Further documents are listed in the continuation of Box C.

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"P" document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search	Date of mailing of the international search report
25 September 2009	22/01/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Strubel, Christine

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/044207

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

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because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery/therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

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4. [X] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01503

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 26,28-32,40(part),41-43

First anchor for a sensor lead

1.1. claims: 27,40(part)

A movable second anchor means

1.2. claims: 33-35

Sensor lead with implantable pulse generator

---

2. claims: 36-39,40(part)

Sensor lead with temperature transducer

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/044207

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6572543 B1	03-06-2003	AT 276793 T	15-10-2004
		AU 3580097 A	14-01-1998
		CA 2258289 A1	31-12-1997
		DE 69730842 D1	28-10-2004
		DE 69730842 T2	29-09-2005
		EP 0917485 A1	26-05-1999
		ES 2229374 T3	16-04-2005
		JP 11514555 T	14-12-1999
		JP 3249826 B2	21-01-2002
		WO 9749454 A1	31-12-1997
		US 6132384 A	17-10-2000
US 2008103545 A1	01-05-2008	AU 2007313319 A1	24-04-2008
		CA 2666529 A1	24-04-2008
		EP 2116274 A2	11-11-2009
		US 2008103407 A1	01-05-2008
		WO 2008048471 A2	24-04-2008
WO 2006102591 A	28-09-2006	NONE	

Form PCT/ISA/210 (patent family annex) (April 2005)

Doc code: IDS
Doc description: Information Disclosure Statement (IDS) Filed

PTO/SB/08a (01-10)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

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	1	8280513		2012-10-02	Tehrani	
	2	8265759		2012-09-11	Tehrani	
	3	8233987		2012-07-31	Gelfand	
	4	8781587		2014-07-15	Alt et al.	
	5	5123425		1992-06-23	Shannon, Jr. et al.	
	6	5190053		1993-03-02	Meer	
	7	8160712		2012-04-17	Freed	
	8	5591216		1997-01-07	Testerman et al.	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	9	8718776		2014-05-06	Mashiach et al.	
	10	9895540		2018-02-20	Mashiach	
	11	8731678		2014-05-20	DeRidder	

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	1	20090308395		2009-12-17	Lee et al.	
	2	20090326408		2009-12-31	Moon	
	3	20100010566		2010-01-14	Thacker et al.	
	4	20100016749		2010-01-21	Atsma et al.	
	5	20100094379		2010-04-15	Meadows	
	6	20100125310		2010-05-20	Wilson et al.	

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	7	20100125314		2010-05-20	Bradley et al.	
	8	20100125315		2010-05-20	Parramon et al.	
	9	20100137931		2010-06-03	Hopper et al.	
	10	20100152553		2010-06-17	Ujhazy et al.	
	11	20100174341		2010-07-08	Bolea et al.	
	12	20100198103		2010-08-05	Meadows et al.	
	13	20100198289		2010-08-05	Kameli et al.	
	14	20100228133		2010-09-09	Averina et al.	
	15	20100228317		2010-09-09	Libbus et al.	
	16	20100241195		2010-09-23	Meadows et al.	
	17	20100262210		2010-10-14	Parramon et al.	

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01508

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	18	20100174341		2010-07-08	Bolea et al.	
	19	20110093036		2011-04-21	Mashiach	
	20	20110112601		2011-05-12	Meadows et al.	
	21	20110152706		2011-06-23	Christopherson et al.	
	22	20110152965		2011-06-23	Mashiach et al.	
	23	20110160794		2011-06-30	Bolea et al.	
	24	20110264164		2011-10-27	Christopherson et al.	
	25	20120290036		2012-11-15	Karamanoglu	
	26	20140364919		2014-12-11	Doan	
	27	20110093032		2011-04-21	Boggs	
	28	20140135868		2014-05-15	Bashyam	

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01509

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	29	20110288609		2011-11-24	Tehrani	
	30	20120192874		2012-08-02	Bolea	
	31	20120253249		2014-10-04	Wilson	
	32	20080161878		2008-07-03	Tehrani	
	33	20080154330		2008-06-26	Tehrani	
	34	20150039045		2015-02-05	Ni et al.	
	35	20160193468		2016-07-07	Rondoni et al.	
	36	20160022204		2016-01-28	Mostov	
	37	20160354602		2016-12-08	Keenan	
	38	20160354603		2016-12-08	Keenan	
	39	20160354608		2016-12-08	Keenan	

Exhibit 1002
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01510

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	40	20060155341		2006-07-13	Tehrani et al.	
	41	20110172733		2011-07-14	Lima et al.	
	42	20100228310		2010-09-09	Shuros et al.	
	43	20050148897		2005-07-07	Cho et al.	
	44	20110060380		2011-03-10	Gelfand et al.	
	45	20170368337		2017-12-28	Steier	
	46	20080154330		2008-06-26	Tehrani et al.	
	47	20090216293		2009-08-27	Sasaki et al.	
	48	20150328451		2015-11-19	Kobayashi	
	49	20140228905		2014-08-14	Bolea	
	50	20130253627		2013-09-26	Meadows et al.	

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NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01511

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	51	20060167523		2006-07-27	Tehrani et al.	

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	1	2010502276	JP		2010-01-28	Cardiac Pacemaker, Inc.	[English Equivalent WO2008027297]	
	2	2011520526	JP		2011-07-21	Inspire Medical Systems, Inc.	[English Equivalent WO2009140636]	
	3	2009140636	WO		2010-03-11	Inspire Medical Systems, Inc.		
	4	2006047264	WO		2006-05-04	Advanced Neuromodulation Systems, Inc.		
	5	2006057734	WO		2006-06-01	Advanced Neuromodulation Systems, Inc.		
	6	2006102591	WO		2006-09-28	Vanderbilt University		
	7	2007068284	WO		2007-06-27	Synergio AG		
	8	2008048471	WO		2008-04-24	Apnex Medical, Inc.		

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	9	2009048580	WO		2009-04-16	Imthera Medical, INc.		
	10	2009048581	WO		2009-04-16	Imthera Medical, Inc.		
	11	2009135138	WO		2009-11-05	Medtronic, Inc.		
	12	2009135140	WO		2009-11-05	Medtronic, Inc.		
	13	2009140636	WO		2009-11-19	Inspire Medical Systems, Inc.		
	14	2010039853	WO		2010-04-08	Inspire medical Systems, Inc.		
	15	2010057286	WO		2010-05-27	Victhom Human Bionics Inc.		
	16	2010059839	WO		2010-05-27	Inspire Medical Systems, Inc.		
	17	2010117810	WO		2010-10-14	Inspire Medical Systems, Inc.		
	18	H11514557	JP		1999-12-14		[English Equivalent WO9749455]	
	19	9749455	WO		1997-12-31	Medtronic, Inc.		

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	20	2013023218	WO		2013-02-14	Inspire Medical Systems, Inc.		
	21	102548610	CN		2012-07-04	CARDIAC CONCEPTS INC	[Equivalent to US20110060380]	
	22	2013509943	JP		2013-03-21	Imthera Medical, Inc.	[Equivalent US20130253627]	
	23	4960704	JP		2008-08-07		[Equivalent US20090216293]	
	24	5636129	JP		2015-12-07	TECHNO LINK CO LTD	[Equivalent US20150328451]	
	25	2008027297	WO		2008-06-05	CARDIAC PACEMAKERS INC		
	26	9750049	WO		1997-12-31	MEDTRONIC INC		

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Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T5
	1	Naples Article – Gregory G. Naples et al., "A Spiral Nerve Cuff Electrode for Peripheral Nerve Stimulation," 8088 IEEE Transactions on Biomedical Engineering, 35. November 1988, No. 11, New York, NY, pages 905-915.	
	2	Eisele Article – David W. Eisele, MD et al., "Tongue neuromuscular and direct hypoglossal nerve stimulation for obstructive sleep apnea," Otolaryngologic Clinics of North America, Otolayngol Clin N Am 36 (2003) 501-510 (10 pages).	

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	3	Goodall Article – Eleanor V. Goodhall et al., "Position-Selective Activation of Peripheral Nerve Fibers with a Cuff Electrode," IEEE Transaction on Biomedical Engineering, Vol. 43, No. 8, August 1996, pages 851-856.	
	4	Oliven Article – Arie Oliven et al., "Upper airway response to electrical stimulation of the genioglossus in obstructive sleep apnea," Journal of Applied Physiology, Volume 95, pages 2023-2029, November 2003, www.jap.physiology.org on September 18, 2006. (8 pages)	
	5	Schwartz Article – Alan R. Schwartz MD et al., "Theraputic Electrical Stimulation of the Hypoglossal Nerve in Obstructive Sleep Apnea, Arch Otolaryngol HeadAnd Neck Surg., Vol. 127, Oct. 2001, pages 1216-1223. Copyright 2001 American Medical Association. (8 pages)	
	6	PARK, "Preoperative Percutaneous Cranial Nerve Mapping in Head and Neck Surgery," ARCH FACIAL PLAST SURG/VOL 5, Jan/Feb 2003, www.archfacial.compages 86-91.	
	7	Stanescu, "Expiratory flow limitation during sleep in heavy snorers" European Respiratory Journal, 1996, 9, 2116-2121.	
	8	J Sleep Res., "Hypoglossal nerve stimulation improves obstructive sleep apnea: 12-month outcomes" Journal, 2014, 23, 77-83.	
	9	The Laryngoscope, "Implanted Upper Airway Stimulation Device for Obstructive Sleep Apnea" Journal, 2012, 122, 1626-1633.	

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through a citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

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A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2020-10-29
Name/Print	Paul S. Grunzweig	Registration Number	37143

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Electronic Acknowledgement Receipt

EFS ID:	40981062
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	29-OCT-2020
Filing Date:	04-SEP-2020
Time Stamp:	12:38:26
Application Type:	Utility under 35 USC 111(a)

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1	Information Disclosure Statement (IDS) Form (SB08)	2020-10-29IDS.pdf	618476 a2a9315e4bc8163d339ea971576c3053b8e4bf8c	no	31
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9	Non Patent Literature	Schwartz.pdf	7553771 dd51793a6763c77056bedb5e34716ffcc06f3689	no	8
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10	Non Patent Literature	Stanescu.pdf	4444517 6608ecfc18862dbe3eec0c170e510367cef50fa2	no	6
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11	Non Patent Literature	Goodall.pdf	1222743 0815355d7516ec68ece6a7c8887daf975366742a	no	6
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (**Not for submission under 37 CFR 1.99)**		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

U.S.PATENTS Remove

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
	1	4379462		1983-04-12	Borkan et al.	
	2	4567892		1986-02-04	Plicchi et al.	
	3	4630614		1986-12-23	Atlas	
	4	4813431		1989-03-21	Brown	
	5	4830008		1989-05-16	Meer	
	6	5133354		1992-07-28	Kallok	
	7	5134995		1992-08-04	Gruenke et al.	
	8	5148802		1992-09-22	Sanders et al.	

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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	9	5158080		1992-10-27	Kallok	
	10	5167229		1992-12-01	Peckham et al.	
	11	5174287		1992-12-29	Kallok et al.	
	12	5178156		1993-01-12	Takishima et al.	
	13	5203343		1993-04-20	Axe et al.	
	14	5211173		1993-05-18	Kallok et al.	
	15	5215082		1993-06-01	Kallok et al.	
	16	5233983		1993-08-10	Markowitz	
	17	5239995		1993-08-31	Estes et al.	
	18	5245995		1993-09-21	Sullivan et al.	
	19	5265624		1993-11-30	Bowman	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	20	5281219		1994-01-25	Kallok	
	21	5300094		1994-04-05	Kallok et al.	
	22	5335657		1994-08-09	Terry, Jr. et al.	
	23	5344438		1994-09-06	Testerman et al.	
	24	5351394		1994-10-04	Weinberg	
	25	5385144		1995-01-31	Yamanishi et al.	
	26	5388578		1995-02-14	Yomtov et al.	
	27	5398682		1995-03-21	Lynn	
	28	5458137		1995-10-17	Axe et al.	
	29	5483969		1996-01-16	Testerman et al.	
	30	5485851		1996-01-26	Erickson	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	17012481
	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	31	5522862		1996-06-04	Testerman et al.	
	32	5524632		1996-06-11	Stein et al.	
	33	5540731		1996-07-30	Testerman	
	34	5540732		1996-07-30	Testerman	
	35	5540733		1996-07-30	Testerman et al.	
	36	5540734		1996-07-30	Zabara	
	37	5546952		1996-08-20	Erickson	
	38	5549655		1996-08-27	Erickson	
	39	5588439		1996-12-31	Hollub	
	40	5591216		1997-01-07	Testerman et al.	
	41	5605151		1997-02-25	Lynn	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	42	5645053		1997-07-08	Remmers et al.	
	43	5671733		1997-09-30	Raviv et al.	
	44	5797852		1998-08-25	Karakasoglu et al.	
	45	5823187		1998-10-20	Estes et al.	
	46	5843135		1998-12-01	Weijand et al.	
	47	5895360		1999-04-20	Christopherson et al.	
	48	5904141		1999-05-18	Estes et al.	
	49	5919221		1999-07-06	Miesel	
	50	5944680		1999-08-31	Christopherson et al.	
	51	5999846		1999-12-07	Pardey et al.	
	52	6015389		2000-01-18	Brown	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	53	6021352		2000-02-01	Christopherson et al.	
	54	6025624		2000-02-15	Figura	
	55	6041780		2000-03-28	Richard et al.	
	56	6099479		2000-08-08	Christopherson et al.	
	57	6120441		2000-09-19	Griebel	
	58	6125290		2000-09-26	Miesel	
	59	6125291		2000-09-26	Miesel et al.	
	60	6126611		2000-10-03	Bourgeouis et al.	
	61	6132384		2000-10-17	Christopherson et al.	
	62	6134459		2000-10-17	Roberts et al.	
	63	6144866		2000-11-07	Miesel et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	64	6175767		2001-01-16	Doyle, Sr.	
	65	6181961		2001-01-30	Prass	
	66	6198952		2001-03-06	Miesel	
	67	6223064		2001-04-24	Lynn et al.	
	68	6240316		2001-05-29	Richmond et al.	
	69	6248080		2001-06-19	Miesel et al.	
	70	6249703		2001-06-19	Stanton et al.	
	71	6251126		2001-06-26	Ottenhoff et al.	
	72	6269269		2001-07-31	Ottenhoff et al.	
	73	6307481		2001-10-23	Lehrman et al.	
	74	6309350		2001-10-30	Van Tassel et al.	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	75	6314324		2001-11-06	Lattner et al.	
	76	6342039		2002-01-29	Lynn et al.	
	77	6345202		2002-02-05	Richmond et al.	
	78	6361494		2002-03-26	Lindenthaler	
	79	6393325		2002-05-21	Mann et al.	
	80	6449507		2002-09-10	Hill et al.	
	81	6450957		2002-09-17	Yoshimi et al.	
	82	6456866		2002-09-24	Tyler et al.	
	83	6522928		2003-02-18	Whitehurst et al.	
	84	6532388		2003-03-11	Hill et al.	
	85	6572543		2003-06-03	Christopherson et al.	

Exhibit 1002
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	86	6574507		2003-06-03	Bonnet	
	87	6587725		2003-07-01	Durand et al.	
	88	6609016		2003-08-19	Lynn	
	89	6609032		2003-08-19	Woods et al.	
	90	6629527		2003-10-07	Estes et al.	
	91	6641542		2003-11-04	Cho et al.	
	92	6645143		2003-11-03	Van Tassel et al.	
	93	6647289		2003-11-11	Prutchi	
	94	6651652		2003-11-25	Ward	
	95	6654634		2003-11-25	Prass	
	96	6665560		2003-12-16	Becker et al.	

Exhibit 1002
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
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	Attorney Docket Number	I618.118.104

	97	6666830		2003-12-23	Lehrman et al.	
	98	6689068		2004-02-10	Hale et al.	
	99	6703939		2004-03-09	Lehrman et al.	
	100	6718208		2004-04-06	Hill et al.	
	101	6719708		2004-04-13	Jansen	
	102	6731976		2004-05-04	Penn et al.	
	103	6731984		2004-05-04	Cho et al.	
	104	6735471		2004-05-11	Hill et al.	
	105	6752765		2004-06-22	Jensen et al.	
	106	6770022		2004-08-03	Mechlenburg et al.	
	107	6773404		2004-08-10	Poezevera et al.	

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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	108	6805667		2004-10-29	Christopherson et al.	
	109	6811538		2004-11-02	Westbrook et al.	
	110	6842647		2005-01-11	Griffith et al.	
	111	6881192		2005-04-19	Park	
	112	6890306		2005-05-10	Poezevera	
	113	6893405		2005-05-17	Kumar et al.	
	114	6904320		2005-06-07	Park et al.	
	115	6907293		2005-06-14	Grill et al.	
	116	6928324		2005-08-09	Park et al.	
	117	6935335		2005-08-30	Lehrman et al.	
	118	6936011		2005-08-30	Sheldon	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	119	6964641		2005-11-15	Cho et al.	
	120	6978171		2005-12-20	Goetz et al.	
	121	6988498		2006-01-24	Berthon-Jones et al.	
	122	7025730		2006-04-11	Cho et al.	
	123	7041049		2006-05-09	Raniere	
	124	7054692		2006-05-30	Whitehurst et al.	
	125	7077810		2006-07-18	Lange et al.	
	126	7081095		2006-07-25	Lynn et al.	
	127	7082331		2006-07-25	Park et al.	
	128	7082336		2006-07-25	Ransbury et al.	
	129	7087053		2006-08-08	Vanney	

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	Filing Date	2020-09-04
	First Named Inventor	Darrell Wagner et al.
	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

	130	7117036		2006-10-03	Florio	
	131	7128717		2006-10-31	Thach et al.	
	132	7145461		2006-12-05	Lehrman et al.	
	133	7149573		2006-12-12	Wang	
	134	7155278		2006-12-26	King et al.	
	135	7160252		2007-01-09	Cho et al.	
	136	7160255		2007-01-09	Saadat	
	137	7167743		2007-01-23	Heruth et al.	
	138	7174215		2007-02-06	Bradley	
	139	7186220		2007-03-06	Stahmann et al.	
	140	7187978		2007-03-06	Malek et al.	

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	Art Unit	3700
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	141	7189204		2007-03-13	Ni et al.	
	142	7195594		2007-03-27	Eigler et al.	
	143	7200440		2007-04-03	Kim et al.	
	144	7206635		2007-04-17	Cho et al.	
	145	7212862		2007-05-01	Park et al.	
	146	7214197		2007-05-08	Prass	
	147	7252640		2007-08-07	Ni et al.	
	148	7269457		2007-09-11	Shafer et al.	
	149	7269459		2007-09-11	Koh	
	150	7277749		2007-10-02	Gordon et al.	
	151	7330760		2008-02-12	Heruth et al.	

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	152	7336996		2008-02-26	Hartley et al.	
	153	7340302		2008-03-04	Falkenberg	
	154	7351208		2008-04-01	Brodnick et al.	
	155	7366572		2008-04-29	Heruth et al.	
	156	7371220		2008-05-13	Koh et al.	
	157	7387608		2008-06-17	Dunlop et al.	
	158	7395113		2008-07-01	Heruth et al.	
	159	7396333		2008-07-08	Stahmann et al.	
	160	7398115		2008-07-08	Lynn	
	161	7422015		2008-09-09	Delisle et al.	
	162	7438686		2008-10-21	Cho et al.	

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	163	7447545		2008-11-04	Heruth et al.	
	164	7454250		2008-11-18	Bjorling et al.	
	165	7453928		2008-12-09	Lee et al.	
	166	7468040		2008-12-23	Hartley et al.	
	167	7469697		2008-12-30	Lee et al.	
	168	7473227		2009-01-06	Hsu et al.	
	169	7491181		2009-02-17	Heruth et al.	
	170	6509164		2009-03-24	Jensen et al.	
	171	7510531		2009-03-31	Lee et al.	
	172	7526341		2009-04-29	Goetz et al.	
	173	7542803		2009-06-02	Heruth et al.	

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	174	7572225		2009-08-11	Stahmann et al.	
	175	7590455		2009-09-15	Heruth et al.	
	176	7591265		2009-09-22	Lee et al.	
	177	7596413		2009-09-29	Libbus et al.	
	178	7603170		2009-10-13	Hatlestad et al.	
	179	7610094		2009-10-27	Stahmann et al.	
	180	7634315		2009-12-15	Cholette	
	181	7644714		2010-01-12	Atkinson et al.	
	182	7662105		2010-02-16	Hatlestad	
	183	7672728		2010-03-02	Libbus et al.	
	184	7678061		2010-03-16	Lee et al.	

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	185	7680538		2010-03-16	Durand et al.	
	186	7702385		2010-04-20	Moffitt et al.	
	187	7717848		2010-05-18	Heruth et al.	
	188	7720541		2010-05-18	Stahmann et al.	
	189	7725195		2010-05-25	Lima et al.	
	190	7734340		2010-06-08	De Ridder	
	191	7734350		2010-06-08	Dubnov et al.	
	192	7742819		2010-06-22	Moffitt	
	193	7747323		2010-06-29	Libbus et al.	
	194	7751880		2010-07-06	Cholette	
	195	7775993		2010-08-17	Heruth et al.	

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	196	7783353		2010-08-24	Libbus et al.	
	197	7792583		2010-09-07	Miesel et al.	
	198	7809442		2010-10-05	Bolea et al.	
	199	7818063		2010-10-19	Wallace et al.	
	200	7853322		2010-12-14	Bourget et al.	
	201	7881798		2011-02-01	Miesel et al.	
	202	7908013		2011-03-15	Miesel et al.	
	203	7917230		2011-03-29	Bly	
	204	7942822		2011-05-17	Koh	
	205	7957809		2011-06-07	Bourget et al.	
	206	7957797		2011-06-07	Bourget et al.	

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	First Named Inventor	Darrell Wagner et al.
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	207	7979128		2011-07-12	Tehrani et al.	
	208	8016776		2011-09-13	Bourget et al.	
	209	8021299		2011-09-20	Miesel et al.	
	210	8150531		2012-04-03	Skelton	
	211	8160711		2012-04-17	Tehrani et al.	
	212	8175720		2012-05-08	Skelton et al.	

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	1	20010010010		2001-07-26	Richmond et al.	
	2	20020010495		2002-01-24	Freed et al.	
	3	20020049479		2002-04-25	Pitts	

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	4	20020156507		2002-10-24	Lindenthaler	
	5	20030093128		2005-05-15	Freed et al.	
	6	20030224895		2003-06-19	Gordon et al.	
	7	20030114905		2003-06-19	Kuzma	
	8	20030163059		2003-08-28	Poezevera et al.	
	9	20030195571		2003-10-16	Burnes et al.	
	10	20030216789		2003-11-20	Deem et al.	
	11	20040015204		2004-01-22	Whitehurst et al.	
	12	20040073272		2004-04-15	Knudson et al.	
	13	20040111139		2004-06-10	McCreery	
	14	20040215288		2004-10-28	Lee et al.	

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	15	20040230278		2004-11-18	Dahl et al.	
	16	20040254612		2004-12-16	Ezra	
	17	20050004628		2005-01-06	Goetz et al.	
	18	20050010265		2005-01-13	Baru Fassio et al.	
	19	20050042589		2005-02-24	Hatlestad et al.	
	20	20050043765		2005-02-24	Williams et al.	
	21	20050043772		2005-02-24	Stahmann et al.	
	22	20050074741		2005-04-07	Lee et al.	
	23	20050076908		2005-04-14	Lee et al.	
	24	20050080348		2005-04-14	Stahmann et al.	
	25	20050080461		2005-04-14	Stahmann et al.	

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	26	20050081847		2005-04-21	Lee et al.	
	27	20050085865		2005-04-21	Tehrani	
	28	20050085866		2005-04-21	Tehrani	
	29	20050085868		2005-04-21	Tehrani et al.	
	30	20050085869		2005-04-21	Tehrani et al.	
	31	20050085874		2005-04-21	Davis et al.	
	32	20050101833		2005-05-12	Hsu et al.	
	33	20050113710		2005-05-26	Stahmann et al.	
	34	20050115561		2005-06-02	Stahmann et al.	
	35	20050145246		2005-07-07	Hartley et al.	
	36	20050165457		2005-07-28	Benser et al.	

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	37	20050182457		2005-08-18	Thrope et al.	
	38	20050209513		2005-09-22	Heruth et al.	
	39	20050209643		2005-09-22	Heruth et al.	
	40	20050222503		2005-10-06	Dunlop et al.	
	41	20050234523		2005-10-20	Levin et al.	
	42	20050251216		2005-11-10	Hill et al.	
	43	20050261747		2005-11-24	Schuler et al.	
	44	20050267380		2005-12-01	Poezevera	
	45	20050277844		2005-12-15	Strother et al.	
	46	20050277999		2005-12-15	Strother et al.	
	47	20050278000		2005-12-15	Strother et al.	

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	48	20060052836		2006-03-09	Kim et al.	
	49	20060058852		2006-03-16	Koh et al.	
	50	20060064029		2006-03-23	Arad (Abboud)	
	51	20060079802		2006-04-13	Jensen et al.	
	52	20060095088		2006-05-04	De Ridder	
	53	20060103407		2006-05-18	Kakizawa et al.	
	54	20060135886		2006-06-22	Lippert et al.	
	55	20060142815		2006-09-29	Tehrani et al.	
	56	20060212096		2006-09-21	Stevenson	
	57	20060224209		2006-10-05	Meyer	
	58	20060241708		2006-10-26	Boute	

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	59	20060247729		2006-11-02	Tehrani et al.	
	60	20060259079		2006-11-16	King	
	61	20060264777		2006-11-23	Drew	
	62	20060266369		2006-11-30	Atkinson et al.	
	63	20060271137		2006-11-30	Stanton-Hicks	
	64	20060276701		2006-12-07	Ray	
	65	20060293720		2006-12-28	DiLorenzo	
	66	20060293723		2006-12-28	Whitehurst et al.	
	67	20070021785		2007-01-25	Inman et al.	
	68	20070027482		2007-02-01	Parnis et al.	
	69	20070038265		2007-02-15	Tcheng et al.	

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	70	20070150022		2007-06-28	Ujhazy et al.	
	71	20070233204		2007-10-04	Lima et al.	
	72	20070255379		2007-11-01	Williams et al.	
	73	20080009685		2008-01-10	Kim et al.	
	74	20080039904		2008-02-14	Bulkes et al.	
	75	20080046055		2008-02-21	Durand et al.	
	76	20080064977		2008-03-13	Kelleher et al.	
	77	20080103545		2008-05-01	Bolea et al.	
	78	20080103570		2008-05-01	Gerber	
	79	20080109046		2008-05-08	Lima et al.	
	80	20080109048		2008-05-08	Moffitt	

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	81	20080132802		2008-06-05	Ni et al.	
	82	20080294060		2008-11-27	Haro et al.	
	83	20090024047		2009-01-22	Shipley et al.	
	84	20090062882		2009-03-05	Zhang et al.	
	85	20090112116		2009-04-30	Lee et al.	
	86	20090118787		2009-05-07	Moffitt et al.	
	87	20090234427		2009-09-17	Chinn et al.	
	88	20090287279		2009-11-19	Parramon et al.	

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	Art Unit	3700
	Examiner Name	Fristoe Jr., John K.
	Attorney Docket Number	I618.118.104

CERTIFICATION STATEMENT

Please see 37 CFR 1.97 and 1.98 to make the appropriate selection(s):

That each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(1).

OR

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the information disclosure statement. See 37 CFR 1.97(e)(2).

See attached certification statement.

The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

☒ A certification statement is not submitted herewith.

SIGNATURE

A signature of the applicant or representative is required in accordance with CFR 1.33, 10.18. Please see CFR 1.4(d) for the form of the signature.

Signature	/Paul S. Grunzweig/	Date (YYYY-MM-DD)	2020-10-29
Name/Print	Paul S. Grunzweig	Registration Number	37143

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 1 hour to complete, including gathering, preparing and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

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2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

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6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01551

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number: 17/012,481

APPLICATION AS FILED - PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY FEE($)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A			N/A	300
SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A			N/A	660
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A			N/A	760
TOTAL CLAIMS (37 CFR 1.16(i))	24 minus 20 =	* 4			OR	x 100 =	400
INDEPENDENT CLAIMS (37 CFR 1.16(h))	3 minus 3 =	*				x 460 =	0.00
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).						0.00
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))							0.00
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL			TOTAL	2120

APPLICATION AS AMENDED - PART II

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	SMALL ENTITY RATE($)	SMALL ENTITY ADDITIONAL FEE($)	OR	OTHER THAN SMALL ENTITY RATE($)	OTHER THAN SMALL ENTITY ADDITIONAL FEE($)
AMENDMENT A	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

		(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE($)	ADDITIONAL FEE($)		RATE($)	ADDITIONAL FEE($)
AMENDMENT B	Total (37 CFR 1.16(i))	*	Minus	**	=	x =		OR	x =	
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x =		OR	x =	
	Application Size Fee (37 CFR 1.16(s))									
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))							OR		
						TOTAL ADD'L FEE		OR	TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest found in the appropriate box in column 1.

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United States Patent and Trademark Office
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
17/012,481	09/04/2020	Darrell Wagner	I618.118.104

CONFIRMATION NO. 3270

25281
DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

INFORMAL NOTICE

OC000000119918284

Date Mailed: 09/16/2020

INFORMATIONAL NOTICE TO APPLICANT

Applicant is notified that the above-identified application contains the deficiencies noted below. No period for reply is set forth in this notice for correction of these deficiencies. However, if a deficiency relates to the inventor's oath or declaration, the applicant must file an oath or declaration in compliance with 37 CFR 1.63, or a substitute statement in compliance with 37 CFR 1.64, executed by or with respect to each actual inventor no later than the expiration of the time period set in the "Notice of Allowability" to avoid abandonment. See 37 CFR 1.53(f).

The item(s) indicated below are also required and should be submitted with any reply to this notice to avoid further processing delays.

- A properly executed inventor's oath or declaration has not been received for the following inventor(s):
  Darrell Wagner
  Quan Ni
  John Rondoni
  Dave Dieken

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at **(571) 272-4000** or **(571) 272-4200** or **1-888-786-0101**.

/hnguyen/

Exhibit 1002
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01553

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY.DOCKET.NO	TOT CLAIMS	IND CLAIMS
17/012,481	09/04/2020		2280	I618.118.104	24	3

CONFIRMATION NO. 3270

FILING RECEIPT

25281
DICKE, BILLIG & CZAJA
FIFTH STREET TOWERS
100 SOUTH FIFTH STREET, SUITE 2250
MINNEAPOLIS, MN 55402

OC000000119918283

Date Mailed: 09/16/2020

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please submit a written request for a corrected Filing Receipt, including a properly marked-up ADS showing the changes with strike-through for deletions and underlining for additions. If you received a "Notice to File Missing Parts" or other Notice requiring a response for this application, please submit any request for correction to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections provided that the request is grantable.

Inventor(s)

Darrell Wagner, Ham Lake, MN;
Quan Ni, Shoreview, MN;
John Rondoni, Plymouth, MN;
Dave Dieken, Minneapolis, MN;

Applicant(s)

INSPIRE MEDICAL SYSTEMS, INC., Golden Valley, MN;

Assignment For Published Patent Application

INSPIRE MEDICAL SYSTEMS, INC., Golden Valley, MN

Power of Attorney: The patent practitioners associated with Customer Number 25281

Domestic Priority data as claimed by applicant

This application is a CON of 15/562,714 09/28/2017
which is a 371 of PCT/US2016/022611 03/16/2016
which claims benefit of 62/135,305 03/19/2015

Foreign Applications for which priority is claimed (You may be eligible to benefit from the **Patent Prosecution Highway** program at the USPTO. Please see http://www.uspto.gov for more information.) - None.
Foreign application information must be provided in an Application Data Sheet in order to constitute a claim to foreign priority. See 37 CFR 1.55 and 1.76.

Permission to Access Application via Priority Document Exchange: Yes

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Permission to Access Search Results: Yes

Applicant may provide or rescind an authorization for access using Form PTO/SB/39 or Form PTO/SB/69 as appropriate.

If Required, Foreign Filing License Granted: 09/15/2020

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 17/012,481**

Projected Publication Date: 12/24/2020

Non-Publication Request: No

Early Publication Request: No

Title

STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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Since the rights granted by a U.S. patent extend only throughout the territory of the United States and have no effect in a foreign country, an inventor who wishes patent protection in another country must apply for a patent in a specific country or in regional patent offices. Applicants may wish to consider the filing of an international application under the Patent Cooperation Treaty (PCT). An international (PCT) application generally has the same effect as a regular national patent application in each PCT-member country. The PCT process **simplifies** the filing of patent applications on the same invention in member countries, but **does not result** in a grant of "an international patent" and does not eliminate the need of applicants to file additional documents and fees in countries where patent protection is desired.

Almost every country has its own patent law, and a person desiring a patent in a particular country must make an application for patent in that country in accordance with its particular laws. Since the laws of many countries differ in various respects from the patent law of the United States, applicants are advised to seek guidance from specific foreign countries to ensure that patent rights are not lost prematurely.

Applicants also are advised that in the case of inventions made in the United States, the Director of the USPTO must issue a license before applicants can apply for a patent in a foreign country. The filing of a U.S. patent application serves as a request for a foreign filing license. The application's filing receipt contains further information and guidance as to the status of applicant's license for foreign filing.

Applicants may wish to consult the USPTO booklet, "General Information Concerning Patents" (specifically, the section entitled "Treaties and Foreign Patents") for more information on timeframes and deadlines for filing foreign patent applications. The guide is available either by contacting the USPTO Contact Center at 800-786-9199, or it can be viewed on the USPTO website at http://www.uspto.gov/web/offices/pac/doc/general/index.html.

For information on preventing theft of your intellectual property (patents, trademarks and copyrights), you may wish to consult the U.S. Government website, http://www.stopfakes.gov. Part of a Department of Commerce initiative, this website includes self-help "toolkits" giving innovators guidance on how to protect intellectual property in specific

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Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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01557

Doc Code: PA..
Document Description: Power of Attorney

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NOTE: This form is to be submitted with the Power of Attorney by Applicant form (PTO/AIA/82B) to identify the application to which the Power of Attorney is directed, in accordance with 37 CFR 1.5, unless the application number and filing date are identified in the Power of Attorney by Applicant form. If neither form PTO/AIA/82A nor form PTO/AIA82B identifies the application to which the Power of Attorney is directed, the Power of Attorney will not be recognized in the application.

Application Number	
Filing Date	Herewith
First Named Inventor	Darrell Wagner
Title	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
Art Unit	
Examiner Name	
Attorney Docket Number	I618.118.04

SIGNATURE of Applicant or Patent Practitioner

Signature	/Paul S. Grunzweig/	Date (Optional)	09/04/2020
Name	Paul S. Grunzweig	Registration Number	37,143
Title (if Applicant is a juristic entity)			
Applicant Name (if Applicant is a juristic entity)			

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. If more than one applicant, use multiple forms.

[X] *Total of 2 forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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Doc Code: PA..
Document Description: Power of Attorney

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POWER OF ATTORNEY BY APPLICANT

I hereby revoke all previous powers of attorney given in the application identified in either the attached transmittal letter or the boxes below.

Application Number	Filing Date

(Note: The boxes above may be left blank if information is provided on form PTO/AIA/82A.)

☑ I hereby appoint the Patent Practitioner(s) associated with the following Customer Number as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above: 25281

OR

☐ I hereby appoint Practitioner(s) named in the attached list (form PTO/AIA/82C) as my/our attorney(s) or agent(s), and to transact all business in the United States Patent and Trademark Office connected therewith for the patent application referenced in the attached transmittal letter (form PTO/AIA/82A) or identified above. (Note: Complete form PTO/AIA/82C.)

Please recognize or change the correspondence address for the application identified in the attached transmittal letter or the boxes above to:

☑ The address associated with the above-mentioned Customer Number

OR

☐ The address associated with Customer Number:

OR

☐ Firm or Individual Name					
Address					
City		State		Zip	
Country					
Telephone		Email			

I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

Inspire Medical Systems, Inc., Golden Valley, MN 55416

☐ Inventor or Joint Inventor (title not required below)

☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)

☑ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)

☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	15 Sep 2020
Name	John Rondoni		
Title	Vice President, Product Development, Inspire Medical Systems, Inc.		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☐ Total of forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

Abstract

A device for treating sleep disordered breathing includes a stimulation element to stimulate an airway-patency-related nerve.

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WHAT IS CLAIMED IS:

1. A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter.

2. The device of claim 1, wherein the asynchronous timing of the stimulation relative to patient breathing comprises the timing being not based on actively-sensed respiration during application of the first stimulation protocol.

3. The device of claim 1, wherein the reference respiration-related parameter comprises a reference respiratory pattern.

4. The device of claim 3, wherein the reference respiratory pattern comprises a reference respiratory cycle and where a duration of each respective stimulation period is greater than a duration of an inspiratory phase of the reference respiratory cycle.

5. The device of claim 1, wherein the reference respiration-related parameter is based on stable respiration.

6. The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is less than a duration of the reference respiratory cycle.

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7. The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is no greater than a duration of a reference respiratory cycle.

8. The device of claim 1, wherein the duration of the respective stimulation periods remain uniform.

9. The device of claim 1, wherein the reference respiratory-related parameter comprises a reference respiratory cycle, and wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 30 percent of duration of a reference respiratory cycle.

10. The device of claim 9, wherein the combined duration of a respective one of the stimulation periods and of a respective one of the non-stimulation periods is less than 20 percent of duration of the reference respiratory cycle.

11. The device of claim 1, wherein a respective one of the stimulation periods and a respective one of the non-stimulation periods are in a proportion of at least 1.5 to 1.

12. The device of claim 11, wherein a duration of a respective one of the stimulation periods exceeds the duration of a respective one of the non-stimulation periods by a factor of 3.

13. The device of claim 1, wherein a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein a duration of the respective one of the stimulation periods comprises at least 80 percent of a duration of the stimulation cycle.

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14. The device of claim 1, wherein each respective stimulation period comprises continuous pulsed stimulation.

15. The device of claim 1, wherein the non-cardiac stimulation element comprises an implantable electrode and the device comprises an implantable pulse generator electrically connectable to the implantable electrode.

16. The device of claim 1, comprising:

a processor; and

a non-volatile computer readable medium storing instructions, executable on the processor, to implement the first stimulation protocol.

17. A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle.

18. The device of claim 17, wherein the duration of each respective non-stimulation period is at least less than half of the duration of each respective stimulation period.

19. The device of claim 17, wherein the reference respiratory cycle comprises at least one of:

a historical patient-specific reference respiratory cycle; and

a multiple patient reference respiratory cycle.

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20. The device of claim 17, wherein the stimulation protocol is to deliver at least some of the multiple stimulation periods within a duration of an inspiratory phase of the reference respiratory cycle.

21. The device of claim 17, wherein the duration of each respective stimulation period is at least less than 30 percent of a duration of the reference respiratory cycle.

22. The device of claim 17, wherein a combination of a respective one of the stimulation periods and a respective one of the non-stimulation periods comprises a stimulation cycle, and wherein the first stimulation protocol is to deliver more than one stimulation cycle within a duration of the reference respiratory cycle.

23. A device for treating obstructive sleep apnea, comprising:

a non-cardiac stimulation element to stimulate an upper airway patency-related nerve, according to a first stimulation protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing, wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle.

24. The device of claim 23, wherein the duration of a respective one of the stimulation periods is greater than the duration of the reference respiratory cycle.

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STIMULATION FOR TREATING SLEEP DISORDERED BREATHING

Cross-Reference to Related Applications

[0001] This application is a continuation of utility application Serial Number 15/562,714, filed September 28, 2017, which is a 371 National Phase Application of PCT Patent Application No. PCT/US2016/022611, filed March 16, 2016, entitled STIMULATION FOR TREATING SLEEP DISORDERED BREATHING, which claims benefit from U.S. Provisional Patent Application 62/135,305, filed March 19, 2015, all of which are herein incorporated by reference.

Background

[0002] Targeted electrical stimulation of a nerve shows great promise in a number of therapies. In one example, such stimulation of a hypoglossal nerve is known to alleviate obstructive sleep apnea by helping to maintain and/or restore upper airway patency.

Brief Description of the Drawings

[0003] Figure 1A is a block diagram schematically illustrating a stimulation element, according to one example of the present disclosure.

[0004] Figure 1B is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

[0005] Figure 2A is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient, according to an example of the present disclosure.

[0006] Figure 2B is a block diagram schematically illustrating an implantable pulse generator, according to one example of the present disclosure.

[0007] Figure 2C is a block diagram schematically illustrating a control portion for the at least partially implantable stimulation system, according to one example of the present disclosure.

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[0008] Figure 2D is block diagram schematically illustrating a stimulation system, according to one example of the present disclosure.

[0009] Figure 2E is top view schematically illustrating a stimulation electrode, according to one example of the present disclosure.

[0010] Figure 3A is a diagram schematically illustrating a respiratory cycle in one example breathing pattern, according to one example of the present disclosure.

[0011] Figure 3B is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

[0012] Figure 3C is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

[0013] Figure 3D is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

[0014] Figure 3E is a diagram schematically illustrating a series of reference respiratory cycles juxtaposed relative to a stimulation protocol, according to one example of the present disclosure.

[0015] Figure 4 is a block diagram schematically illustrating a plurality of stimulation parameters, according to one example of the present disclosure.

[0016] Figure 5 is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

[0017] Figure 6 is a block diagram schematically illustrating power source components of the at least partially implantable stimulation system, according to one example of the present disclosure.

[0018] Figure 7A is a block diagram schematically illustrating a sensing element of the at least partially implantable stimulation system, according to one example of the present disclosure.

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[0019] Figure 7B is a diagram schematically illustrating an at least partially implantable stimulation system relative to a patient and including sensing elements, according to an example of the present disclosure.

[0020] Figure 8 is a block diagram schematically illustrating therapeutic respiratory parameters, according to one example of the present disclosure.

[0021] Figure 9 is a block diagram schematically illustrating a control portion of an at least partially implantable stimulation system, according to one example of the present disclosure.

[0022] Figure 10 is a block diagram schematically illustrating aspects of a control portion, according to one example of the present disclosure.

[0023] Figure 11A is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

[0024] Figure 11B is a block diagram schematically illustrating a user interface, according to one example of the present disclosure.

[0025] Figure 12 is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

[0026] Figure 13 is a block diagram schematically illustrating a respiratory-dependent stimulation element, according to one example of the present disclosure. Figure 14 is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

[0027] Figure 15A is a block diagram schematically illustrating a stimulation protocol element, according to one example of the present disclosure.

[0028] Figure 15B is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

[0029] Figure 15C is a block diagram schematically illustrating a stimulation protocol selector, according to one example of the present disclosure.

[0030] Figure 15D is a diagram schematically illustrating at least some aspects of stimulation protocol selection, according to one example of the present disclosure.

[0031] Figure 16A is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

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[0032] Figure 16B is a diagram schematically illustrating a stimulation protocol, according to one example of the present disclosure.

[0033] Figure 17A is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

[0034] Figure 17B is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

[0035] Figure 17C is a flow diagram schematically illustrating a method of nerve stimulation, according to one example of the present disclosure.

[0036] Figure 18 is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

[0037] Figure 19 is a block diagram schematically illustrating a therapy manager, according to one example of the present disclosure.

Detailed Description

[0038] In the following Detailed Description, reference is made to the accompanying drawings, which form a part hereof, and in which is shown by way of illustration specific examples in which the invention may be practiced. In this regard, directional terminology, such as "top," "bottom," "front," "back," "leading," "trailing," etc., is used with reference to the orientation of the Figure(s) being described. Because components of examples can be positioned in a number of different orientations, the directional terminology is used for purposes of illustration and is in no way limiting. It is to be understood that other examples may be utilized and structural or logical changes may be made without departing from the scope of the present disclosure. The following detailed description, therefore, is not to be taken in a limiting sense.

[0039] At least some examples of the present disclosure are directed to methods of treating obstructive sleep apnea via applying nerve stimulation. By doing so, upper airway patency may be maintained and/or increased while preventing or minimizing collapse of the upper airway. At the same time, by using targeted stimulation, one can limit the overall volume of stimulation applied to a given nerve or set of nerves.

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[0040] In some examples, nerve stimulation is applied during a treatment period. In some examples, a treatment period corresponds to the patient engaging in sleeping behavior, and during which sleep disordered breathing is to be avoided. The treatment period can be manually initiated by the patient or automatically initiated by a device that applies the nerve stimulation.

[0041] In some examples, an at least partially implantable stimulation system for treating sleep disordered breathing includes an independent stimulation element to stimulate an airway-patency-related nerve without synchronization relative to characteristics of respiratory wave form. Accordingly, in some examples, the independent stimulation element forms part of a system that omits any sensing elements. In some examples, the stimulation element comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator. In some examples, the pulse generator is implantable and in some examples, the pulse generator is external to the patient's body. In some examples, the stimulation element is in communication with a therapy manager or is incorporated within a therapy manager. In some examples, the therapy manager is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

[0042] In some examples, the at least partially implantable stimulation system includes sensing element(s) to receive and/or obtain respiratory information but that information is not employed to trigger stimulation by synchronizing the stimulation relative to characteristics of the sensed respiratory waveform. Rather, in these examples, the sensed respiratory information is used to detect and evaluate sleep disordered breathing behavior. When the detected behavior meets or exceeds a severity threshold, the therapy manager generally activates stimulation via the independent stimulation element. In some examples,

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the severity threshold is based on at least a frequency and/or an intensity of apneic events. In some instances, the severity threshold also may be expressed as an obstructive sleep apnea (OSA) burden, i.e. a quantity and/or intensity of apneas which are occurring. In some examples, the severity threshold or OSA burden is expressed as an Apnea-Hypopnea Index (AHI). However, despite the respiratory sensing occurring in these examples, the stimulation is performed via a protocol that remains independent of the particular characteristics of a real-time sensed respiratory waveform. In other words, individual stimulation periods are not triggered and/or synchronized relative to respiratory characteristics, such as the inspiratory phase.

[0043] In some examples, the independent stimulation element is configured to asynchronously stimulate an airway-patency-related nerve, according to a first stimulation protocol independent of sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. In some instances, the first stimulation protocol is referred to as being independent because the first stimulation protocol is not synchronized relative to sensed respiratory information. In some instances, the independence of the first stimulation protocol also may be referred to as being an asynchronous stimulation protocol because the first stimulation protocol is not synchronized relative to the sensed respiratory information.

[0044] In some examples, each stimulation period within a stimulation cycle includes continuous stimulation. In some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. 56 in Figure 2C).

[0045] In some examples, during the above-described continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse

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followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

[0046] In some examples, the stimulation period has a minimum duration equal to or greater than an inspiratory reference. In some examples, the inspiratory reference corresponds to a duration of an inspiratory phase of a reference respiratory cycle. In some examples, each stimulation cycle of the first stimulation protocol includes the stimulation period having a duration greater than a duration of the inspiratory reference followed by the non-stimulation period, which has a duration less than the duration of the stimulation period.

[0047] In some examples, the reference respiratory cycle is defined by a historical patient-specific average respiratory cycle for stable respiration. In some examples, the reference respiratory cycle is defined by a multi-patient average respiratory cycle for stable respiration.

[0048] Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) intentionally does not match the duration (R) of the reference respiratory cycle in at least some examples, the stimulation protocol ensures that each successive stimulation period within the series of stimulation cycles will fall along a different portion of each of the successive reference respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of reference respiratory waveform (which includes the series of reference respiratory cycles), no matter where the stimulation protocol is started relative to the ongoing pattern of reference respiratory cycles, the stimulation period of each stimulation cycle will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period of the initial stimulation cycle at least partially overlaps with the inspiratory phase of a reference respiratory cycle, the stimulation periods of the successive stimulation cycles will at least partially overlap the inspiratory phase of the next reference respiratory cycles. Moreover, at least some of the later successive stimulation periods will significantly overlap (e.g. overlap at least a majority of the inspiratory phase) the inspiratory phase of the at least some of the respective

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successive reference respiratory cycles. In some instances, such significant overlap may include a complete overlap of the inspiratory phase.

[0049] Via this arrangement, it becomes feasible to stimulate an airway-related-nerve to treat sleep disordered breathing either without any sensing elements at all or with minimal use of sensing elements. In this sense, the stimulation is performed asynchronously, i.e. without synchronization relative to sensed respiratory information. Among other benefits, this may reduce the cost of the stimulation system, may simplify its implantation, and may simplify operation of the stimulation system. Moreover, the presence of non-stimulation periods helps to minimize potential muscle fatigue that might otherwise be caused. Finally, providing asynchronous stimulation via the independent stimulation element may help to overcome situations in which sensor-based systems or synchronous systems are unable to achieve synchronization and/or the sensing signal become unstable (or is unavailable).

[0050] However, it will be understood that in some examples, an asynchronous independent stimulation protocol is implemented while still performing sensing respiratory information for non-synchronization purposes, such as evaluating stimulation therapy effectiveness and/or provide information to adjust parameters of the independent stimulation protocol.

[0051] In another aspect, providing stimulation asynchronously via the independent stimulation element may enable leveraging a greater number of different stimulation protocols because of fewer constraints on how the stimulation cycles of the stimulation protocols relate to characteristics of a respiratory waveform. Moreover, in some examples, the stimulation element applies nerve stimulation while rotating application through the plurality of different stimulation protocols, which in some instances provides a more robust therapy than using a single stimulation protocol. In some examples, this rotation also can be used to sort through the relative effectiveness of the different stimulation protocols and select the most effective stimulation protocol for a particular patient.

[0052] In some examples, an independent stimulation protocol is implemented in which the inspiratory phase of a majority of reference respiratory cycles are at least partially overlapped by a stimulation period, with more occurrences of such overlapping being preferred over fewer such occurrences. Similarly, in some examples, it is generally preferred

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to implement such an independent stimulation protocol via providing the sequence of stimulation periods to result in a greater degree of overlap with the inspiratory phase of the reference respiratory cycles rather than a lesser degree of overlap.

[0053] In some examples, the therapy manager includes a stimulation protocol element that provides convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. In this arrangement, the therapy manager causes: operation in the first stimulation mode for at least a first predetermined period of time; conversion of operation into the second stimulation mode upon at least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria; and reversion of operation into the first stimulation mode for at least the first predetermined period of time upon the at least one parameter of the sensed respiratory waveform failing to meet the sensor signal quality criteria. Accordingly, in one aspect, the first stimulation mode comprises the default mode of stimulation.

[0054] In some examples, the conversion between the first stimulation mode and the second stimulation mode is automatic. In some examples, the therapy manager includes a user selection function to enable user selection of either the first mode or the second mode as a default mode.

[0055] In some examples, the therapy manager includes an operator selection function to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented manually during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient.

[0056] In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc. In some examples, the first predetermined period of time does not correspond to a test mode for evaluating the

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operational fitness of the stimulation system. Stated differently, activities occurring during the first predetermined period of time may sometimes be referred to as a non-test mode.

[0057] Via this arrangement, the independent stimulation element first establishes a stable respiratory pattern. This arrangement therapeutically achieves airway patency while simultaneously increasing the likelihood of later successful synchronization of a respiratory-dependent stimulation protocol. In particular, because some examples dictate that stimulation is not implemented until or unless sleep disordered breathing behavior (above a severity threshold) is detected, the available respiratory signal will likely be a poor signal which attempt synchronization of a stimulation signal.

[0058] Accordingly, rather than attempt a likely problematic synchronization, at least some examples of the present disclosure first establish independent nerve stimulation that does not depend on synchronization. This independent stimulation, in turn, helps to establish a stable respiratory pattern or signal, which then in turn, significantly increases the success of later synchronizing a respiratory-dependent stimulation protocol relative to the respiratory signal. Once a robust synchronization is established, then the system is well positioned to maintain a stable respiratory period using less overall stimulation by stimulating on a synchronized basis in which stimulation is limited to generally coinciding with an inspiratory phase (or other characteristic of the sensed respiratory waveform).

[0059] Of course, in the event the sensed respiratory signal changes in a way that hinders synchronization and/or delivery of effective therapeutic stimulation, then in at least some examples, the therapy manager will cause operation to revert to the independent stimulation mode.

[0060] With this arrangement, the independent stimulation mode enables initially applying a higher intensity stimulation to establish and ensure a stable respiratory pattern, which in turn, increases the likelihood of being able to later establish and maintain a lower intensity stimulation via the synchronized, respiratory-dependent stimulation mode. In this way, it is expected that overall muscle fatigue is minimized because of the likelihood of the synchronization mode successfully operating for a longer period of time than if the independent stimulation mode were not applied first.

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[0061] Accordingly, in some examples, an independent stimulation element is implemented alone to treat sleep disordered breathing. However, in some examples, treatment is accomplished via a complementary combination of an independent (i.e. asynchronous) stimulation mode and a synchronous stimulation mode.

[0062] As noted above, in some examples, a stimulation protocol element may provide convertible operation between the above-described independent (i.e. asynchronous) first stimulation mode and a synchronous second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform. However, in one example arrangement, the therapy manager causes: operation in the second stimulation mode and conversion of operation into the first stimulation mode upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria. Later, reversion of operation into the second stimulation mode is made upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria. Accordingly, in one aspect, the second stimulation mode comprises the default mode of stimulation.

[0063] These examples, and other examples, are further described in association with at least Figures 1-19.

[0064] Figure 1A is block diagram schematically illustrating a stimulation element 12, according to one example of the present disclosure. In some examples stimulation element 12 directs and controls nerve stimulation to treat obstructive sleep apnea. In some examples, stimulation element 12 includes an independent stimulation function 14, which in general terms, applies electrical stimulation via a stimulation protocol to an airway-patency-related nerve to treat upper airway obstructions. In some examples, such airway-patency-related nerves include at least the protrusor branches of the hypoglossal nerve.

[0065] In some examples, the independent stimulation function 14 operates to stimulate an airway-patency-related nerve, according to a first stimulation protocol not synchronized relative to sensed respiratory information and in which each stimulation cycle includes a stimulation period and a non-stimulation period. Accordingly, in some examples, via the independent stimulation function 14, nerve stimulation is applied independent of

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characteristics of sensed respiratory information. In other words, once the independent stimulation function 14 has been activated, the initiation and termination of individual nerve stimulation periods is not synchronized relative to a characteristic, such as onset of the inspiratory phase of the patient respiratory cycle and/or other characteristics. In at least this context, operation of independent stimulation function 14 (Fig. 1A) may be referred to as an asynchronous stimulation function or mode.

[0066] In some examples, once a treatment period begins, such as when the patient is engaging in sleeping behavior (and during which sleep disordered breathing is to be avoided), the nerve stimulation function 14 is always in an "on" or active mode, and therefore stimulation cycles are applied to the nerve. In such examples, activation or deactivation of the independent stimulation function 14 is independent of whether or not apneas are occurring. For instance, the general activation and/or deactivation of the independent stimulation function 14 can be controlled according to a selectable time schedule, such as a predetermined start time (e.g. 10 p.m.) and predetermined end time (e.g. 6 a.m.).

[0067] Figure 1B is a block diagram schematically illustrating a therapy manager 16, according to one example of the present disclosure. In general terms, therapy manager 16 directs a therapeutic regimen for controlling sleep disordered breathing such as, but not limited to, obstructive sleep apnea. The therapy manager 16 operates as part of, or in cooperation with, an at least partially implantable nerve stimulation system. In some examples, therapy manager 16 forms at least part of a control portion such as, but not limited to, control portion 360 as later described in association with at least Figures 9-10, and as such, in some examples, therapy manager 16 includes at least some of substantially the same features and attributes as therapy manager 371 described in association with at least Figure 9.

[0068] In some examples, therapy manager 16 is in communication with and/or incorporates at least some aspects of stimulation element 12. In some examples, the therapy manager has access to physiologic sensing information via sensing elements (e.g. at least Figs. 7A-7B). In such examples, general activation and/or general deactivation of the independent

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stimulation function 14 is controlled according to a likelihood of sleep behavior, which is determined according to at least body position, body posture, body motion, and/or body activity parameters, which can be sensed via an accelerometer or other sensing elements. In some examples, determining likelihood of sleep behavior is supplemented via additional sensed physiologic information, including but not limited to sensed respiratory information.

[0069] In some of the examples in which the therapy manager 16 has access to sensed physiologic information (at least Figs. 7A-8), once a treatment period begins, the nerve stimulation function 14 is not generally activated and/or deactivated to stimulate a nerve until prompted to do so based on respiratory behavior criteria (e.g. whether apneas are likely or are occurring, etc.). This determination is separate from, and independent of, timing or synchronizing individual stimulation periods relative to particular characteristics (e.g., inspiration, expiration, etc.) of sensed respiratory information. Accordingly, in these examples, whether or not a patient receives any stimulation at all is governed by whether or not the patient experiences a sufficient quantity, frequency, or intensity of apneas.

[0070] In other words, in some examples, therapy manager 16 operates to apply stimulation when the patient is experiencing apneas or likely to experience apneas. In this way, nerve stimulation is limited to an as needed basis, thereby conserving energy of the stimulation system 20 and reducing potential muscle fatigue. As to the particular strength of the stimulation signal and whether it is applied in view of the relative severity of the sleep disordered respiratory behavior, at least some examples of automatic adjustment of a level of stimulation therapy is described in at least Christopherson, METHOD OF TREATING SLEEP DISORDERED BREATHING, published on October 27, 2011 as US 2011-0264164.

[0071] In some examples, the detection of flow limitations and/or associated apneas, as well as the detection of the beginning and end of the respective inspiratory and expiratory phases of the respiratory cycle, is performed according to, or in cooperation with, known methods and devices for doing so. Some non-limiting examples of such devices and methods to recognize and detect the various features and patterns associated with respiratory effort and flow limitations include, but are not limited to: PCT Publication WO/2010/059839, titled A

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METHOD OF TREATING SLEEP APNEA, published on May 27, 2010; Christopherson U.S. Patent 5,944,680, titled RESPIRATORY EFFORT DETECTION METHOD AND APPARATUS; and Testerman U.S. Patent 5,522,862, titled METHOD AND APPARATUS FOR TREATING OBSTRUCTIVE SLEEP APNEA.

[0072] In some examples, the stimulation element 12 comprises a stimulation engine to determine and administer a stimulation protocol. In some examples, the stimulation element 12 further includes and/or acts in cooperation with a pulse generator and stimulation electrode to deliver the stimulation to a target nerve, such as later described in association with at least Figures 2A-2D and 7B. In such examples, the pulse generator includes the stimulation engine or the stimulation engine is in communication with the pulse generator.

[0073] In some examples, the therapy manager 16 is in communication with the pulse generator and/or incorporated within the pulse generator. In some examples, at least some components, functions, elements, etc. of the therapy manager 16 are incorporated within a physician programmer external to the patient or a patient remote external to the patient.

[0074] Details regarding particular stimulation protocols implemented via the independent stimulation function 14 are later described in association with at least Figures 3B-3E. In particular, at least some details are provided regarding how asynchronous stimulation may increase therapeutic effectiveness in treating sleep disordered breathing.

[0075] Figure 2A is a schematic diagram of an at least partially implantable stimulation system 20, according to an example of the present disclosure. In general terms, the stimulation element 12 of Figure 1A (and/or therapy manager 16 of Figure 1B) is incorporated within and/or operates in association with stimulation system 20 to deliver stimulation.

[0076] As illustrated in Figure 2A, in one example system 20 includes an implantable pulse generator (IPG) 35 and a stimulation lead 32 electrically coupled with the IPG 35 via a connector (not shown) positioned within a connection port of the IPG 35. In some examples, the IPG 35 is surgically positioned within a pectoral region of a patient 22. The lead 32 includes a stimulation electrode portion 45 and extends from the IPG 35 so that the stimulation electrode portion 45 is positioned in contact with a desired nerve, such as an

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airway-patency-related nerve 33 of the patient 10, to enable stimulation of the nerve 33, as described below in detail. In some examples, the stimulation electrode portion 45 comprises a self-sizing cuff such as described in U.S. 8,340,785 to Bonde et al. In some examples, in association with electrode 45, lead 32 includes at least some of the features and attributes described in U.S. Patent Publication 20110160827 to Bonde et al. In some examples, lead 32 includes features and attributes at least consistent for use in an implantable stimulation system as described in U.S. Patent No. 6,572,543 to Christopherson et al.

[0077] As later described more fully in association with at least Figs. 9-10, in some examples the therapy manager 16 controls the IPG 35, and is implemented externally of the IPG 35, entirely within the IPG 35, or partially within the IPG 35.

[0078] In some examples, stimulation electrode portion 45 comprises a cuff electrode including a single operative contact group of at least two electrodes through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. Figure 2E is a top view schematically illustrating one example of such an electrode 50 including a single operative contact group of at least two electrodes 52. In some examples, the stimulation electrode portion 45 comprises a cuff electrode including at least one operative contact group through which the stimulation is deliverable non-selectively to the airway-patency-related nerve. Accordingly, more than one operative contact group of electrodes can be incorporated in a single cuff electrode. In some examples, the stimulation electrode portion 45 can include multiple, separate cuff electrodes with each having at least one operative contact group of electrodes.

[0079] In some examples, the stimulation system for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, in some examples, one or more components of the system are not implanted in a body of the patient, thereby providing an at least partially implantable system. A few non-limiting examples of such non-implanted components include an external processing unit and/or an external power source, as later noted in association with at least Figure 6.

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[0080] In some examples, the at least partially implantable stimulation system 20 does not include any sensing elements. Accordingly, to the extent that the system 20 and its therapy manager 16 apply stimulation protocols to treat respiratory behavior, any patient-specific respiratory information would be received and/or obtained prior to, and/or during, implantation of the system 20. Alternatively, a temporary external sensing system could be employed to periodically calibrate and/or evaluate therapeutic efficacy of the at least partially implantable stimulation system 20 operating according to an independent stimulation function 14 (Fig. 1A).

[0081] At least some examples of the sensor-less stimulation system 20 use significantly less power than some sensor-based systems and are easier to implant. Moreover, in such examples, the system 20 is significantly easier to construct and/or operate because the sensors, certain sensing-related circuitry, and certain operational programming can be omitted.

[0082] However, it will be understood that in some examples, the stimulation system 20 includes sensing elements, at least in the manner later described in association with at least Figures 7A-7B. In at least some of these examples, the sensing elements are used to evaluate therapy and particular stimulation protocols but are not used to synchronize stimulation relative to characteristics of the sensed respiratory waveforms.

[0083] Figure 2B is block diagram of an implantable pulse generator (IPG) 50, according to one example of the present disclosure. In some examples, IPG 50 includes at least some of substantially the same features and attributes as IPG 35 (Fig. 2A). However, in some examples, IPG 50 includes at least some features and attributes different than those in IPG 35 (Fig. 2A). As such, in some examples, IPG 50 can take different forms and be implanted in locations other than those shown in Figure 2A (and also Figure 7B).

[0084] With further reference to Figure 2B, in some examples the implantable pulse generator 50 includes a stimulation element 52 and a communication element 54. The stimulation element 52 generates and applies a neuro-stimulation signal via electrode(s) (such as stimulation electrode(s) 45 in Fig. 2A) according to a treatment regimen programmed by a physician and/or in cooperation with therapy manager 16. In some

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examples, stimulation element 52 comprises at least some of substantially the same features and attributes as stimulation element 12 as previously described in association with Figure 1A.

[0085] The communication element 54 provides a communication pathway to enable transmission of data, power, and/or controls signals both to and from the implanted portions of the system 20 relative to the external portions of the system 20. For instance, in some examples, the communication element 54 is configured to report activities of the IPG 50 (including sensed physiologic data, stimulation history, number of apneas detected, etc.) and is configured to receive initial or further programming of the IPG 50 from an external source, such as a patient programmer, clinician programmer, etc. as later noted in association with at least Figure 10. In some examples, the communication element 54 utilizes a radiofrequency (RF) telemetry link or other wireless communication protocols.

[0086] In some examples, the implantable pulse generator 50 includes a control portion or at least part of a control portion such as control portion 56 shown in Figure 2C. In general terms, control portion 56 directs operation of the pulse generator 50 and the at least partially implantable stimulation system. Further details regarding such a control portion 56 are described later in association with at least Figures 9-10. Moreover, in some examples, control portion 56 is operable in association with a user interface, such as described later in association with at least Figures 11A-11B.

[0087] Figure 2D is a block diagram 70 schematically illustrating an at least partially implantable stimulation system 80, according to an example of the present disclosure. In some examples, system 80 includes at least some of substantially the same features and attributes as system 20 (Fig. 2A), pulse generator 50 (Fig. 2B), and control portion 56 (Fig. 2C), except for system 80 having some portions in a non-pectoral location and located in close proximity to a target nerve to be stimulated, as further illustrated in association with at least Figure 2D.

[0088] In some examples, system 80 is a sensor-less system in a manner substantially similar to the above-described system 20. In other words, as at least partially implanted in the patient's body, system 80 omits a sensor.

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[0089] As shown in Figure 2D, in some examples system 80 includes a nerve-coupling electrode portion 82 and a pulse generator 84. In some examples, the nerve-coupling electrode portion 82 comprises an element which is at least electrically coupled relative to a target nerve 72 suitable to maintain or restore airway patency, such as but not limited to, the hypoglossal nerve.

[0090] In some examples, the electrode portion 82 comprises a cuff, such as one of the stimulation electrode portions 45 described in association with Figure 2A in which the electrode portion is both mechanically and electrically coupled relative to the nerve 72. However, in some examples, the nerve-coupling electrode portion 82 comprises a cuff-less structure that is both mechanically and electrically coupled relative to the nerve 72.

[0091] In some examples, the nerve-coupling electrode portion 82 is not mechanically coupled to the nerve 72, but is mechanically coupled or secured in a location in close proximity to the nerve 72 and that enables electrically coupling of the electrode portion 82 relative to the nerve 72. In one instance, such examples include the electrode portion 82 being delivered to the target nerve 72 via a percutaneous access delivery. In one instance, such examples include the electrode portion 82 being delivered to the target nerve 72 via a transvenous delivery method in which the electrode portion 82 is delivered on a lead maneuvered within and through the vasculature of the patient.

[0092] In some examples, in a manner consistent with the previously described pulse generator 50 (Fig. 2B) pulse generator 84 includes a stimulation element 52 and a communication element 54. In some examples, pulse generator 84 includes solely internal components 90, which are internally within the body below the skin/tissue. However, in some examples, pulse generator 84 includes a combination of some internal components 90 and some external components 92, which are external to the body being above or outside the skin/tissue.

[0093] In some examples, via communication element 54 (Fig. 2B), system 80 includes a wired communication path 94 and/or a wireless communication path 96 between the pulse generator 84 and the nerve-coupling electrode portion 82, as shown in Fig. 2D. In some

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examples, either or both such communication pathways 94, 96 are also employable for communication between internal and external components 90, 92 of a pulse generator 84.

[0094] In some examples, in order to utilize and/or evaluate sensed respiratory information, the therapy manager 16 uses a reference point, such as a normal breathing pattern 150, as shown in Figure 3A. Of course, variances may exist from patient-to-patient so it will be understood that the normal breathing pattern 150 is a representative example provided for illustrative purposes and is not intended to strictly define a breathing pattern that is universally normal for all patients. With this in mind, in some examples, the system 20 uses the particular breathing pattern of a specific patient (to which the method is applied) as the reference point to utilize and/or evaluate sensed respiratory information.

[0095] In the example of normal breathing pattern 150 shown in Figure 3A, a respiratory cycle 160 includes an inspiratory phase 162 and an expiratory phase 170. The inspiratory phase 162 includes an initial portion 164, intermediate portion 165, and end portion 166 while expiratory phase 170 includes an initial portion 174, intermediate portion 175, end portion 176, and an expiratory peak 177. A first transition 180 occurs at a junction between the end inspiratory portion 166 and the initial expiratory portion 174 while a second transition 182 occurs at a junction between the end expiratory portion 176 and the initial inspiratory portion 164. In some instances, end expiratory portion 176 includes and/or is referred to as an expiratory pause that occurs just prior to onset of the initial inspiratory portion 164.

[0096] Figure 3B is a diagram 200 schematically illustrating a stimulation protocol 210 implemented via independent stimulation function 14 (Fig. 1A), according to one example of the present disclosure. In some examples, after initializing the system according to the known/applicable respiratory cycle for that patient and after general activation of the independent stimulation function 14, the initiation, operation, and termination of the stimulation protocol 210 operates without regard to sensed respiratory information. In one aspect, Figure 3B illustrates a respiratory pattern 202 including a series of reference respiratory cycles 204A-204H, with each cycle having substantially the same features and

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attributes as the respiratory cycle 160. Accordingly, each reference respiratory cycle 204A-204H has a duration R.

[0097] In one aspect, the pattern 202 represents a stable respiratory pattern that occurs during normal daytime breathing and/or that results from application of stimulation protocol 210.

[0098] In some examples, because stimulation via the stimulation protocol 210 is not synchronized relative to characteristics of actively-sensed respiratory cycles (such as via real-time measure of respiratory effort), the stimulation protocol 210 operates based on a reference respiratory cycle. In some examples, the reference respiratory cycle includes at least one of a historical patient-specific average respiratory cycle for stable respiration and a multi-patient average respiratory cycle for stable respiration. This historical and/or predictive information is employed in at least some examples in which the therapy manager 16 (Fig. 1B) is not actively sensing respiratory waveforms during operation of the at least partially implantable stimulation system 20.

[0099] As shown in Figure 3B, stimulation protocol 210 includes a series of separate stimulation periods (e.g. pulses) 212A-212J spaced apart by a non-stimulation periods 218A-281I, each of which are interposed between an adjacent pair of stimulation periods. For instance, non-stimulation period 218B is interposed between stimulation periods 212B, 212C. In one aspect, each stimulation period (212A-212I) has a first end 214 and an opposite second end 216.

[00100] In some examples, in order to demonstrate the manner in which the stimulation protocol 210 is juxtaposed relative to the respiratory pattern 202, Figure 3B further illustrates each respiratory cycle being apportioned into a discrete number (e.g. 3, 4, 5, 6, 7, 8, etc.) time units, with each time unit having a duration t. In the example shown in Figure 3B, each respiratory cycle has a duration R and is divided into six time units t.

[00101] In some examples, the duration R is patient specific and is based on a long term average duration of a respiratory cycle. In some examples, the duration R is not patient specific and is based on an average duration of a respiratory cycle for many different patients. In some examples, duration R is about 3 to about 6 seconds. In some examples,

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via therapy manager 16, the duration R can be adjusted to a preferred duration. In some examples, the therapy manager 16 uses the patient-specific information regarding durations.

[00102] However, in some examples, where such information is not available or is problematic, the therapy manager 16 uses multi-patient information. For instance, for at least some patient populations a duration of an entire respiratory period is about 3 to 6 seconds, which corresponds to a general respiratory rate of about 10-18 breaths/minute. Moreover, generally speaking inspiration (e.g. an inspiratory phase) is a minority of the entire respiratory period which includes inspiration, expiration, and expiratory pause.

[00103] In at least some patient populations, an apnea and/or hypopnea has a minimum duration of about 10 seconds, which corresponds to a minimum duration about 2-3 breaths.

[00104] In some examples, an apnea may be avoided via implementation of a stimulation protocol which avoids missing (either completely missing or significantly missing) stimulation for more than one breath (e.g. one inspiratory phase).

[00105] With further reference to Figure 3B, as represented by the legend 209, the stimulation protocol 210 operates according to a stimulation cycle in which the duration of the stimulation cycle is less than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of 3. In some examples, as shown by legend 209, the stimulation period and the non-stimulation period are in a proportion of 4 to 1. In such examples, each stimulation cycle includes a continuous stimulation period of 4 time units followed by a non-stimulation period of 1 time units, with this stimulation cycle being repeated continuously when nerve stimulation is generally activated. The total duration of the stimulation cycle (e.g. 4 time units of stimulation and 1 time unit of non-stimulation) is 5 time units, which is less than the duration R of the respiratory period, which is 6 time units in this example. In one aspect, this example arrangement in which the stimulation period is in much greater proportion to the non-stimulation period may benefit some patients by minimizing tongue rubbing by minimizing the frequency or total volume of tongue motion incident to tongue protrusion intentionally caused by the stimulation therapy to restore airway patency.

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[00106] In Figure 3B, the first end 214 of stimulation period 212A is shown as coinciding with the beginning of an inspiratory phase 162 of the respiratory cycle 204A. However, it will be understood that the beginning 214 of the stimulation period 212A is not synchronized relative to the inspiratory phase 162. Rather, the beginning 214 of stimulation period 212A is shown as coinciding with the beginning of inspiratory phase 162 for illustrative simplicity in juxtaposing the stimulation protocol 210 relative to the respiratory cycles 204A-204H. Accordingly, it will be understood that when stimulation (according to stimulation protocol 210) is initiated during a treatment period, the beginning of the stimulation period 212A may coincide with a different portion of the respiratory cycle (e.g. 204A) than shown in Figure 3B.

[00107] With further reference to the stimulation protocol 210 in Figure 3B, in one aspect, each respective non-stimulation period 218A-218I has a duration less than a duration of each respective stimulation periods 212A-212J. In one aspect, the duration of the stimulation period 212A is less than a duration (R) of the reference respiratory cycle 204A. In one aspect, the relative duration of the respective stimulation periods (e.g. 212A) and non-stimulation periods (e.g. 218A) causes each successive stimulation period (e.g. 212B) to begin at a different place along a successive respiratory cycle, such that the stimulation pattern is independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. For instance, it can be seen from Figure 3B that the first end 214 of stimulation period 212D coincides with a portion of the expiratory phase 170 of respiratory cycle 204C while the first end 214 of stimulation period 212E coincides with a portion of inspiratory phase 162 of the successive respiratory cycle 204D.

[00108] As shown in Figure 3B, each of the respective stimulation periods 212A, 212B, 212C overlaps the entire inspiratory phase 162 of the respective respiratory cycles 204A-204C while stimulation period 212D at least partially overlaps the inspiratory phase 162 of respiratory cycle 204D.

[00109] Because the overall duration of the stimulation cycle (both stimulation period and non-stimulation period) does not match the duration (R) of the reference respiratory cycle, the stimulation protocol 210 ensures that each successive stimulation period within the series

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of stimulation cycles will fall along a different portion of the successive respiratory cycles. Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 210 is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol 210 happens to be initiated at a time that the non-stimulation period (e.g. 218D, 218E) at least partially overlaps with the inspiratory phase 162 of a respiratory cycle (e.g. 204D, 204E), the succeeding stimulation periods 212F, 212G, etc. at least partially overlaps the inspiratory phase 162 of the next respiratory cycle 204F, 204G, etc., with these later successive stimulation periods significantly overlapping (e.g. stimulation period 212F, which overlaps by at least a majority) or even completely overlapping (e.g. stimulation period 212G) the inspiratory phase 162 of the respective successive respiratory cycles (e.g. 204F, 204G).

[00110] In one aspect, in stimulation protocol 210 the duration of each stimulation period (e.g. 212A-212J) is less than a duration (R) of the reference respiratory cycles (204A-204H) but greater than a duration of the inspiratory phase 162 of an individual respiratory cycle (e.g. 204A).

[00111] In one aspect, a duty cycle for the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles 204A, 204B, 204C, 204D, 204F, 204G, 204H the duty cycle is 5 time units of continuous stimulation and 1 time unit of non-stimulation, which equals about 83%. However, during respiratory cycle 204E, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 5 respiratory cycles , the series of stimulation cycles repeats itself, as illustrated at respiratory cycle 204F, at which the first end 214 of the stimulation period 212G once again coincides with the beginning of the inspiratory phase 162 of the respiratory cycle 204F in a manner similar to respiratory cycle 204A. Accordingly, in one aspect, the long term duty cycle over an indefinite number of respiratory cycles (or average duty cycle over a sufficient number of time frames) is about 80%.

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[00112] In some examples, via stimulation protocol 210, no sequence of four respiratory cycles occurs without a stimulation period significantly overlapping the inspiratory phase 162 (e.g. overlapping at least majority of the inspiratory phase 162) of respiratory cycles in Figure 3B. This criteria is based on the longest period of time, in at least some examples, that a patient can go without a breath while avoiding a respiratory-event related arousal and/or to maintain near normal blood oxygenation.

[00113] In some examples, via stimulation element 12 (Fig. 1A) and/or therapy manager 16 (Fig. 1B) a clinician can implement a stimulation protocol in which a quantity (e.g. 2, 3, 4) is selected by the operator regarding how many respiratory cycles can pass without a significantly overlapping stimulation period, according to a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

[00114] It will be understood that each inspiratory phase 162 of each respiratory cycle (204A-204H) is shown in its ideal form in Figure 3B, and that in some instances where the inspiratory phase 162 at least partially coincides with one of the respective non-stimulation periods (e.g. 218D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in Figure 3B.

[00115] Accordingly, via stimulation protocol 210, the independent stimulation function 14 of stimulation element 12 (Fig. 1A) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

[00116] With the example of pattern 202 and stimulation protocol 210 as a foundation, it will be understood that in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 50 percent of the duration of the reference respiratory cycle. In at least some contexts, this arrangement may ensure that the probability of entirely missing inspiration in an asynchronous stimulation protocol is less than 50%, such that a majority of the treatment period, stimulation will be delivered during at least a portion of inspiration, which may be sufficient to minimize or prevent sleep disordered breathing (e.g. apneas).

[00117] In some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is 80 percent of the duration of the reference

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respiratory cycle. For instance, such an arrangement might be employed in some example patients having severe obstructive sleep apnea in which an inspiration can be missed for no more than 1 of 5 breaths. When applied asynchronously, such a duty cycle may likely ensure effective treatment (assuming other stimulation parameters are effective) while still allowing the protrusor muscles to rest sufficiently.

[00118] While not depicted in Figure 3B, in some examples, a stimulation protocol is adopted in which the duration of the stimulation period of each stimulation cycle is at least 25 percent of the duration of the reference respiratory cycle. When employed in an asynchronous arrangement, such an arrangement will likely ensure that at least one stimulation period significantly overlaps with the inspiratory phase at least one breath (e.g. one respiratory cycle) out of every three breaths (i.e. three respiratory cycles). For some patients which exhibit less severe apneas, this arrangement can be sufficient to prevent obstructive events.

[00119] Figure 3C is a diagram 221 schematically illustrating a stimulation protocol 220 implemented via independent stimulation function 14 (Fig. 1A), according to one example of the present disclosure. In one example, diagram 221 includes at least some of substantially the same features and attributes as diagram 201, except for having a different stimulation protocol 220.

[00120] Moreover, as represented by the legend 229, the stimulation protocol 220 operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 1.5. As represented via legend 229, in some examples stimulation protocol 220 includes a stimulation cycle including a stimulation period of 4 ½ time units and a non-stimulation period of 2 ½ time units, with the overall stimulation cycle of 7 time units having a duration greater than the duration R of the respiratory cycle (e.g. 204A) of 6 time units.

[00121] In a manner substantially the same as previously noted for stimulation protocol 210, even though stimulation protocol 220 is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 220

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is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period. For instance, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period 228B generally coincides with the inspiratory phase 162 of a respiratory cycle 204C, the succeeding stimulation period 222C at least partially overlaps the inspiratory phase 162 of the next respiratory cycle 204D, and with later successive stimulation periods significantly overlapping (e.g. stimulation period 222D, exhibiting at least a majority overlap) or completely overlapping (e.g. stimulation period 222E) the inspiratory phase 162 of the respective successive respiratory cycles (e.g. 204E, 204F).

[00122] In some examples, a stimulation protocol is applied in which a total duration of stimulation via the first stimulation protocol during a treatment period is greater than 30 percent of the total duration of the treatment period.

[00123] In one aspect, in stimulation protocol 220 the duration of each stimulation period (e.g. 222A-222G) is less than a duration (R) of the respiratory cycles 204A-204H) but greater than a duration of the inspiratory phase 162 of an individual respiratory cycle (e.g. 204A).

[00124] In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles 204D, 204E, 204F, 204G the stimulation duty cycle is 3 ½ time units of continuous stimulation and 2 ½ time units of non-stimulation, which equals about 58%. However, during respiratory cycles 204A and 204B the stimulation duty cycle is 4 ½ time units of continuous stimulation and 1 ½ time units of non-stimulation, which equals about 75%. Meanwhile, during respiratory cycles 204C, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 67%. Every 8 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle 204H, at which the first end 224 of the stimulation period 222G once again coincides with the beginning of the inspiratory phase 162 of the respiratory cycle 204H in a manner similar to respiratory cycle 204A. Accordingly, in one aspect, the long term or average duty cycle over a long period of time is about 64%.

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[00125] In some examples, via stimulation protocol 220 no more than four respiratory cycles occur without a stimulation period significantly overlapping (e.g. at least a majority of the) inspiratory phase 162 of respiratory cycles in Figure 3C.

[00126] Figure 3D is a diagram 231 schematically illustrating a stimulation protocol 230 implemented via independent stimulation function 14 (Fig. 1A), according to one example of the present disclosure. In one example, diagram 231 includes at least some of substantially the same features and attributes as diagram 201 (Fig. 3B) or diagram 221 (Fig. 3C), except for having a different stimulation protocol 230.

[00127] Moreover, as represented by the legend 239, the stimulation protocol 220 operates according to a stimulation cycle in which the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle. In some examples, the duration of the stimulation period exceeds the duration of the non-stimulation period by a factor of at least 3. As represented via legend 239 in Figure 3D, in some examples stimulation protocol 230 includes a stimulation cycle including a continuous stimulation period of 7 ½ time units and a non-stimulation period of 2 ½ time units, with the overall stimulation cycle of 10 time units having a duration greater than the duration R of the respiratory cycle (e.g. 204A) of 6 time units.

[00128] In a manner substantially the same as previously noted for stimulation protocols 210, 220, even though stimulation protocol 230 is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 230 is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period 238B generally coincides with the inspiratory phase 162 of a respiratory cycle 204D, the succeeding stimulation period 232C at least partially overlaps the inspiratory phase 162 of the next respiratory cycle 204E.

[00129] In one aspect, in stimulation protocol 230 the duration of each stimulation period (e.g. 232A-232D) is greater than a duration (R) of the respiratory cycles 204A-204G) and

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greater than a duration of the inspiratory phase 162 of an individual respiratory cycle (e.g. 204A).

[00130] In one aspect, a duty cycle exhibited by the repeating stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycle 204A, the duty cycle is 6 time units of continuous stimulation, which equals 100%. However, during respiratory cycles 204B and 204E the stimulation duty cycle is 3 ½ time units of continuous stimulation and 2 ½ time units of non-stimulation, which equals about 58%. Meanwhile, during respiratory cycle 204C, the duty cycle is 5 1/2 time units of continuous stimulation and 1/2 time units of non-stimulation, which equals about 92 percent. Meanwhile, during respiratory cycle 204D, the duty cycle is 4 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 66 percent.

[00131] Every 5 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle 204F, at which the first end 234 of the stimulation period 232D once again coincides with the beginning of the inspiratory phase 162 of the respiratory cycle 204F in a manner similar to respiratory cycle 204A.

[00132] In one aspect, the long term (i.e. average) duty cycle over a sufficient number of respiratory cycles is about 75 percent.

[00133] In one aspect, this stimulation protocol provides an occasional 100% duty cycle (e.g. stimulation period 232D) to ensure that an inspiratory phase will be not missed during a stimulation period, while the overall average duty cycle is 75 percent. In some examples, such stimulation protocols are suitable for a patient in which the pattern of the respiratory waveform varies considerably but where effective therapy can be achieved without using continuous stimulation.

[00134] In some examples via stimulation protocol 230 no sequence of four respiratory cycles occurs without a stimulation period at least significantly overlapping the inspiratory phase 162 of respiratory cycles in Figure 3D.

[00135] Figure 3E is a diagram 241 schematically illustrating a stimulation protocol 240 implemented via independent stimulation function 14 (Fig. 1A), according to one example of the present disclosure. In one example, diagram 241 includes at least some of

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substantially the same features and attributes as diagram 201, except for having a different stimulation protocol 240.

[00136] As represented via legend 249 in Figure 3E, stimulation protocol 240 includes a stimulation cycle including a continuous stimulation period of 4 time units and a non-stimulation period of 2 time units, with the overall stimulation cycle of 6 time units having a duration generally matching the duration R of the reference respiratory cycle (e.g. 204A) of 6 time units. As in the prior examples associated with Figures 3A-3E, the stimulation protocol 240 is independent, i.e. not synchronized relative to sensing of respiratory information.

[00137] In some patients the duration (R) of their respiratory cycle may vary slightly over time as the respiratory cycle might shorten or lengthen. Diagram 241 schematically illustrates just one example in which the reference respiratory cycle represents a situation in which the duration of the respiratory cycle lengthens to R1 due to lengthening of the expiratory phase 171 of the respiratory cycles of the patient. It will be understood that other characteristics, parameters, features of the respiratory cycle often change as well, but these changes are not depicted in Figure 3E for illustrative simplicity and clarity.

[00138] It will be further understood that such changes may develop gradually over time and that Figure 3E provides a snapshot of one such change after it has already at least partially developed. Moreover, because this arrangement of independent stimulation operates without synchronization relative to sensed respiratory information, Figure 3E schematically represents at least some aspects regarding how stimulation protocol 240 may provide therapeutic effectiveness in this situation of lengthening respiratory cycles (or shortened respiratory cycles) as represented by the reference respiratory cycles 204A-245M in Figure 3E.

[00139] Accordingly, in this example, the stimulation cycle repeats itself in what otherwise would be exactly matching each reference respiratory cycle, but the elongated duration of the reference respiratory cycle causes the stimulation cycle to no longer coincide with various portions of the respiratory cycle.

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[00140] It will be understood, of course, as previously noted elsewhere that at the time the stimulation protocol is initiated and while not shown in Figure 3E, the first end 244 of the initial stimulation period 242A may not necessarily coincide with the beginning of an inspiratory phase 162 of a respiratory cycle 245A.

[00141] In some examples, even though stimulation protocol 240 is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 240 is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective respiratory cycles for a significant majority of the treatment period. Accordingly, even if the stimulation protocol happens to be initiated at a time that the non-stimulation period 248H 248I, 248J generally coincides with the inspiratory phase 162 of a respiratory cycle 245H, 245I, 245J, at least some subsequent stimulation periods 242L, 242M, 242N significantly overlap (at least a majority overlap) the inspiratory phase 162 of the next respiratory cycles 245K, 245L, 245M. As further seen in Figure 3E, other example stimulation periods also significantly overlap (e.g. stimulation period 242F) the inspiratory phase 162 of the corresponding respective respiratory cycle 245F.

[00142] In some examples, the stimulation periods 242A-242E, 242N completely overlap the inspiratory phase 162 of the respective respiratory cycles (e.g. 245A-245E, 245M). However, it will be understood that in some examples, such complete overlap with the inspiratory phase of some respiratory cycles may not be exhibited, and a significant overlap would suffice to achieve adequate airway patency.

[00143] In one aspect, in stimulation protocol 240, the duration of each stimulation period (e.g. 242A-242M) is less than a duration (R) of the respiratory cycles (245A-245M) but greater than a duration of the inspiratory phase 162 of an individual respiratory cycle (e.g. 245A).

[00144] In one aspect, the duty cycle associated with the stimulation cycle varies on a respiratory cycle-by-respiratory cycle basis. For instance, during respiratory cycles 245A, 245B, 245C, 245D, 245E, 245F, 245G, 245H, 245M the duty cycle is 4 1/2 time units of continuous stimulation and 2 time units of non-stimulation, which equals about 75 percent.

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However, during respiratory cycles 245I, 245J, 245K, 245L the duty cycle is 4 time units of continuous stimulation and 2 ½ time units of non-stimulation, which equals about 62 percent.

[00145] For at least the time that a particular duration (R1) of the elongated respiratory cycle persists (as represented by reference respiratory cycles), every 12 respiratory cycles, the series of stimulation cycles repeats itself, as illustrated at respiratory cycle 245M, at which the first end 244 of the stimulation period 242N once again coincides with the beginning of the inspiratory phase 162 of the respiratory cycle 245M in a manner similar to respiratory cycle 245A.

[00146] In one aspect, the long term, average stimulation duty cycle over a sufficient period of time is about 67 percent.

[00147] Accordingly, in some examples, via stimulation protocol 240 no sequence of four respiratory cycles occurs without a stimulation period at least partially overlapping or even significantly overlapping the inspiratory phase 162 of respiratory cycles in Figure 3E.

[00148] It will be further understood that the various stimulation protocols described and illustrated in association with at least Figures 3B-3E are implemented via the at least partially implantable stimulation system 20 as described in association with at least Figures 1-14. However, in some examples, the various stimulation protocols described and illustrated in association with at least Figures 3B-3E are implemented via at least some components, elements, systems etc. other than those described in association with Figures 1-14.

[00149] While the independent stimulation function 14 (Fig. 1A) does not use sensed respiratory information to trigger each stimulation period or synchronize each stimulation period, in some examples the independent stimulation mode 14 uses sensed respiratory information to track how a stimulation protocol is matching up relative to the characteristics of the sensed respiratory waveform. Accordingly, upon elongation or shortening of the sensed respiratory cycles, the therapy manager 16 (including independent stimulation function 14) can choose to maintain or modify which stimulation protocol is being applied in order to ensure that the desired amount and timing of stimulation is being applied. In addition, or as an alternative, the therapy manager 16 uses the sensed respiratory information

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to adjust or calibrate features of the reference respiratory cycle associated with a particular stimulation protocol.

[00150] In some examples, operation of the therapy manager 16 (as part of an at least partially implantable stimulation system 20) is not limited to the specific stimulation protocols described in association with at least Figures 3B-3E, as other stimulation protocols can be implemented with longer or shorter stimulation periods and with longer or shorter non-stimulation periods.

[00151] In some examples the independent stimulation function 14 (Fig. 1A) includes a complex stimulation cycle in which at least two different length stimulation periods is employed and/or at least two different length non-stimulation periods is employed. As one non-limiting example to illustrate the principle, one stimulation protocol could include a first continuous stimulation period of three time units, a first non-stimulation period of two time units, a second continuous stimulation period of three time units, followed by a second non-stimulation period of one time unit. The example later described in association with Figure 16A illustrate some aspects of these features.

[00152] In some examples, and as illustrated in the diagrams of Figures 3B-3E, the stimulation cycles are not centered relative to a characteristic or feature of a respiratory waveform. In other words, the respective continuous stimulation periods or non-stimulation periods (in the example stimulation protocols) are not fixed or tied to a particular landmark or fiducial of the respiratory waveform. Accordingly, the respective continuous stimulation periods and non-stimulation periods within stimulation cycles (of a particular stimulation protocol) vary regarding which portion of a respiratory cycle (of a series of respiratory cycles) with which they coincide.

[00153] In some examples, the independent stimulation function 14 provides a stimulation protocol having a duty cycle of 80 percent, where a 100 percent duty cycle would correspond to continuous stimulation over a full respiratory cycle. In one example, a first portion of the duty cycle comprises a continuous stimulation period and a second portion of the duty cycle comprises a continuous non-stimulation period immediately following the first portion. In a non-limiting example in which a respiratory cycle has a duration of 5 seconds, the duty

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cycle includes applying continuous stimulation for 4 seconds immediately followed by continuous non-stimulation for 1 second, with the duty cycle being repeated.

[00154] Figure 4 is a block diagram 251 schematically illustrating a plurality of stimulation parameters 250, according to one example of the present disclosure. In general terms, these stimulation parameters may be employed as part of implementing one of the stimulation protocols described in association with Figures 3B-3E and/or as part of general operation of stimulation element 12 (Fig. 1A) and/or therapy manager 16 (Fig. 1B). In one example, a single parameter is implemented, while in some examples, several of these parameters may be implemented. When several parameters are implemented, they are implemented separately but contemporaneously in some examples and in other examples, they are implemented in combination.

[00155] As shown in Figure 4, these stimulation parameters 250 include amplitude parameter 252, a duty cycle parameter 254, a respiratory cycle duration parameter 260, a time unit parameter 262, and a time frame parameter 270. The amplitude parameter 252 controls an amplitude of the stimulation signal, which can be selected for a particular stimulation protocol.

[00156] In some examples, the duty cycle parameter 254 tracks and/or controls a duty cycle of stimulation. In some examples, the stimulation duty cycle is expressed relative to a duration (R) of one respiratory cycle (per parameter 260) in the manner previously described regarding the stimulations protocols previously described in association with at least Figures 3B-3E. The duty cycle parameter 254 comprises a constant function 256 and a variable function 258. The constant function 256 implements a duty cycle in which the stimulation duty cycle is identical relative to each respiratory cycle, while the variable function 258 implements a duty cycle in which the stimulation duty cycle varies relative to at least some respiratory cycles within a series of respiratory cycles.

[00157] As previously described in association with at least Figures 3B-3E, in some examples, the stimulation duty cycle is implemented according to a series of stimulation cycles in which each stimulation cycle includes at least one continuous stimulation period and at least one non-stimulation period. At least some stimulation protocols includes

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stimulation cycles in which the duration of the stimulation period(s) differs relative to the duration of the non-stimulation period(s) through a series of stimulation cycles such that an average duty cycle can be calculated.

[00158] Accordingly, the various stimulation protocols provide some duty cycles that vary from one respiratory cycle to the next, while simultaneously providing an overall or average duty cycle. By selecting a particular stimulation cycle, specific duty cycles are implemented on a respiratory-cycle by respiratory-cycle basis and an overall or average duty cycle is achieved.

[00159] In some examples, a respiratory cycle duration parameter 260 identifies a duration of a patient-specific average respiratory cycle during reasonably stable respiration (e.g. normal breathing) or a duration of a multi-patient average respiratory cycle during reasonably stable respiration. In some examples, the patient-specific average respiratory cycle is determined according to recent sensed respiration information while in some examples, the patient-specific average respiratory cycle is determined according to long term data gathered for that patient during reasonably stable respiration (e.g. normal breathing).

[00160] In some examples, the respiratory cycle duration parameter 260 tracks a duration of the sensed respiratory cycles of a patient and determines an average.

[00161] In some examples, the time unit parameter 262 tracks and controls a number of time units by which a stimulation cycle operates. In some examples, the time unit parameter 262 implements time units as a multiple of some natural time unit associated with a respiratory waveform. For instance, in some examples such as the stimulation protocols described and illustrated in association with Figures 3B-3E, the time unit parameter 262 equates six time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle. However, it will be understood that in some examples, the time units (per parameter 262) are unit-less. For instance, suppose the respiratory period has a duration R of five seconds, and a convention has been adopted that the respiratory cycle is divisible into six time units. Then, the six time units would be distributed across the five second duration of the respiratory cycle.

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[00162] In some examples, the time unit parameter 262 implements time units which are entirely arbitrary relative to one or more natural time units associated with a respiratory waveform. For instance, in some examples such as the stimulation protocol described and illustrated in association with Figure 16A, the time unit parameter 262 equates eight time units with a duration of a respiratory cycle, and in which an inspiratory phase comprises one-third of the entire respiratory cycle.

[00163] In some examples, the time frame parameter 270 in Figure 4 identifies a respiratory cycle series parameter 272 and a stimulation cycle parameter 274. The respiratory cycle series parameter 272 identifies and tracks the number of respiratory cycles that occur before a particular portion of a particular stimulation cycle (274) would coincide again with a particular portion of a respiratory cycle. For example, it was previously noted in association with at least Figure 3C that the stimulation protocol 220 operated based on a time frame of seven respiratory cycles such that a sequence of seven respiratory cycles would occur before a beginning of a stimulation period of a stimulation cycle would coincide with a beginning of an inspiratory phase of the repeating respiratory cycle. While the stimulation protocols associated with independent stimulation function 14 (Fig. 1A) are not synchronized relative to characteristics (e.g. inspiratory phase) of a sensed respiratory waveform, the time frame parameter 270 enables tracking and adjusting how a given stimulation protocol is juxtaposed relative to sensed patient respiratory behavior.

[00164] Figure 5 is a block diagram of a stimulation protocol element 280, according to one example of the present disclosure. As shown in Figure 5, the stimulation protocol element 280 comprises an array parameter 282, a rotation parameter 284, an automatic parameter 286, a manual parameter 288, a static parameter 290, and a custom parameter 291.

[00165] In some examples, stimulation protocol element 280 includes at least some of substantially the same features and attributes as stimulation protocol element 12, as previously described in association with at least Figures 1-4. In particular, as previously noted, in some examples the independent stimulation function 14 (Fig. 1A) provides at least one stimulation protocol suitable for delivering electrical stimulation to a nerve of a patient,

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such as one of the stimulation protocols as previously described and illustrated in association with Figures 3B-3E.

[00166] With this in mind, array parameter 282 of stimulation protocol element 280 provides an array of stimulation protocols that can be applied, such as but not limited to those illustrated in association with Figures 3B-3E.

[00167] In some examples, via a rotation parameter 284, the stimulation protocol 280 enables delivering therapeutic nerve stimulation to a patient while rotating through different stimulation protocols available via array parameter 282. In some examples, such rotation enables identifying a stimulation protocol that works best for a particular patient on a particular day or on a long term basis. However, in some examples, rotation through different stimulation protocols is maintained for a particular day or on a long term basis to provide a large degree of variability in the overall stimulation pattern to thereby provide a robust therapy regimen when a patient's respiratory behavior is consistently erratic and/or when sensing of a patient's respiratory behavior is consistently problematic.

[00168] In some examples, in cooperation with an automatic parameter 286, the rotation parameter 284 automatically rotates through the different stimulation protocols to achieve goals set by therapy manager 16 (Fig. 1B). In some examples, via automatic parameter 286, the therapy manager 16 (Fig. 1B) automatically selects at least one stimulation protocol suitable for a particular patient. In some examples, the automatic selection of which stimulation protocol(s) is best suited for a particular patient is based on a sensed respiratory waveform of the patient.

[00169] In some examples, via a static parameter 290 shown in Figure 5, therapy manager 16 (Fig. 1B) enables selecting and then maintaining a single stimulation protocol indefinitely until and unless a user or operator selects a different stimulation protocol or parameters affecting the selected stimulation protocol. In some examples, if a particularly effective stimulation protocol is identified during operation of the rotation parameter 284, the therapy manager 16 (Fig. 1B) deactivates automatic rotation of the stimulation protocols and operates that single, "particularly effective" stimulation protocol, per the static parameter 290.

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[00170] In some examples, stimulation protocol element 280 includes custom parameter 291, which enables adjusting a selected stimulation protocol or making a custom stimulation protocol by selecting a duration of respiratory cycle, duration of stimulation period(s), duration of non-stimulation periods, duration of stimulation cycle, and/or other parameters identified in the plurality of stimulation parameters 250 (Fig. 4).

[00171] In some examples, the range of stimulation protocols available to a patient via stimulation protocol element 280 are selected and/or bounded according to the discretion of a physician or physician programmer.

[00172] Figure 6 is a block diagram of a power element 320, according to one example of the present disclosure. In one example, power element 320 represents IPG 35, 50 (Figs. 2A-2B) as having an external power source 322 and/or an on-board power source 324.

[00173] In some examples, an at least partially implantable stimulation system (according to examples of the present disclosure) operates in cooperation with and/or incorporates sensing functionality. With this in mind, in some examples, such systems include a sensing element 330, according to one example of the present disclosure, as shown in Figure 7A. The sensing element receives and/or obtains respiratory information.

[00174] In some examples, the sensing element 330 includes an on-board sensing element 332, which is physically incorporated into IPG 35 (Fig. 2A) or IPG 50 (Fig. 2B) in some manner such that communication between the on-board sensing element 332 and other elements of the IPG 35, 50 will occur within the case or housing of the IPG. In some examples, the on-board sensing element 332 includes internal components, such as an accelerometer and in some examples, the on-board sensing element 332 includes surface components, such as the external surface of the case or housing of the IPG 35, 50 acting as a sensing element alone or in combination with other sensing elements.

[00175] In some examples, the sensing element 330 includes an implanted sensing input 334 to receive signals from a sensor implanted within the body physically separate from the IPG 35, 50, with the sensing input 334 in communication with and/or connected to the IPG 35, 50 via wired or wireless communication pathways.

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[00176] In some examples, the sensing element 330 includes an external sensing input 336 to receive signals from a sensor external to the patient's body, with the sensing input 336 in communication with the IPG 35, 50 via wireless communication pathways.

[00177] In some examples, sensing element 330 does not comprise a physically-embodied sensor but rather a sensing input to receive information sensed via sensors separate from, and independent of, sensing element 330 with such sensors in communication with sensing element 330.

[00178] In some examples, sensing element 330 can comprise both a sensing input and a physically-embodied sensor.

[00179] Via these various sensing elements and inputs, the sensing element 330 receives and tracks signals from at least one physiologic sensor in order to gather information pertinent to treating sleep disordered breathing. In some examples, this information includes respiratory information such as, but not limited to, determining a respiratory state of a patient, whether or not the patient is asleep or awake, and other respiratory-associated indicators, etc. In some examples, the type of sensed physiologic information received by, and/or the type of physiologic sensors embodied within, one of the sensing elements/inputs 332, 334, 336 (Fig. 7A) include, but are not limited to, a pressure sensing, blood oxygenation sensing, acoustic sensing, posture sensing, motion/activity sensing, differential pressure sensing, electrocardiogram (ECG) sensing, or impedance sensing. Via such sensing modalities, the system can measure thoracic impedance, respiratory pressure, diaphragm-based parameters, electrocardiac monitoring, airflow monitoring, snoring, etc. Gathering of this respiratory information, including information regarding respiratory-related behaviors, may be implemented via either a single sensor or any combination of various physiologic sensors that can provide a reliable and accurate signal. In some examples, these various measures of respiratory-related behavior can be considered alone or together in combination to indicate respiratory effort, which is at least one type of respiratory information receivable and/or obtainable by the sensing element.

[00180] In some examples, the therapy manager 16 (Fig. 1B) maintains the sensing components of the sensing element 330 in a default, dormant mode (i.e. off or low power)

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and periodically activates one or more of the available sensing element(s) to gather patient data. After gathering the data, the sensing elements are deactivated, thereby resuming their dormant mode. In some examples, the gathered patient data is used to evaluate the effectiveness of the therapy, such as the number, intensity, and/or frequency of apneas occurring. After such data gathering, the therapy manager 16 (Fig. 1B) deactivates the sensing element(s), thereby returning them to a dormant mode.

[00181] In some examples, the gathered patient data is used to measure the respiratory period to verify its duration and to determine or verify the relative durations (or absolute duration) of the inspiratory and expiratory phases. This information is used to assess a current stimulation protocol and potentially determine whether adjustments to the stimulation protocol are warranted or whether a different stimulation protocol should be employed. For instance, in some examples, the gathered patient data from the temporarily activated sensing elements is used to calibrate the reference respiratory cycle associated with implementation of a particular stimulation protocol.

[00182] Figure 7B is a schematic diagram of an at least partially implantable stimulation system 340, according to an example of the present disclosure. In one example, the system 340 includes at least some of substantially the same features and attributes as system 20 (previously described in association with at least Fig. 2A), except further including sensing functionality via at least one sensing element to sense respiratory information. In some examples, this sensing functionality is implemented via sensing element 330 (Fig. 7A).

[00183] In some examples, the system 340 comprises an additional lead 137 including at least one sensor portion 341 (electrically coupled to the IPG 35 and extending from the IPG 35) positioned in the patient 22 for sensing respiratory information, such as respiratory effort, respiratory pressure, etc. In some examples, this information includes identifying and tracking characteristics and parameters of sensed respiratory waveforms.

[00184] In some examples, the sensor portion 341 is a pressure sensor. In one example, the pressure sensor detects pressure in the thorax of the patient. In some examples, the sensed pressure could be a combination of thoracic pressure and cardiac pressure (e.g., blood flow).

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Via sensor portion 341, therapy manager 16 (Fig. 1B) is configured to analyze this pressure sensing information to identify, track, and evaluate the respiratory patterns of the patient.

[00185] In some examples, the respiratory sensor portion 341 comprises a bio-impedance sensor or forms one of a pair of bio-impedance sensors. In some examples, the respiratory sensor portion 341 is located in regions other than the pectoral region. In some examples, the sensor portion 341 is used to sense impedance in cooperation with other electrodes (e.g. a stimulation electrode) or with an electrically conductive exterior housing of the IPG 35, 50 (Figs. 2A-2B, 7B). In some examples, as shown in Figure 7B, additional sensors 347, 348, 349 are distributed about the chest area for measuring a trans-thoracic bio-impedance signal, an electrocardiogram (ECG) signal, or other respiratory-associated signals. In some examples, sensor portion 341 is omitted and sensors 347, 348, 349 are implemented.

[00186] In some examples, the system 340 for treating obstructive sleep apnea is a totally implantable system which provides therapeutic solutions for patients diagnosed with obstructive sleep apnea. However, as identified in various examples, in some examples, the system is partially implantable with some components (e.g. power source, sensing elements, or control circuitry) being at least partially or completely external to the patient's body.

[00187] In some examples, the previously-described at least partially implantable system 80 (Fig. 2D) includes at least some of substantially the same features described and illustrated in association with Figs. 4-7B, except for system 80 having a non-pectoral location and those attributes specific to system 80 as described in association with Figure 2D.

[00188] In some examples, the respiratory information and/or other physiologic information gathered via the sensing element 330 (Fig. 7A) and associated sensor schemes (Fig. 7B) is used to identify, track, evaluate, etc. various therapeutic parameters. Accordingly, in some examples the at least partially implantable stimulation system includes a therapeutic monitoring element 350, which as shown in Figure 8, includes a plurality of therapeutic parameters. In some examples, these parameters include identifying, tracking, and evaluating apnea events per parameter 352 and/or computing and tracking an apnea severity index 354, such as AHI or other index. The index parameter 354 determines a

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frequency, intensity, duration, etc. of detected apneas to indicate the relative severity of sleep disordered breathing for the patient.

[00189] In some examples, one therapeutic parameter of monitoring element 350 includes a minute ventilation parameter 356 to track minute ventilation of the patient before, during, or after a therapy regimen. In some examples, one therapeutic parameter of monitoring element 350 includes a tidal volume parameter 357 to track the tidal volume of a patient before, during, or after a therapy regimen.

[00190] In some examples, one therapeutic parameter of monitoring element 350 includes a body position parameter 358. In some examples, one therapeutic parameter of monitoring element 350 includes a posture parameter 359. Together or separately, the body position parameter 358 and posture parameter 359 determine and track a body position of the patient and posture of the patient. Among other uses, such information can be used to activate or deactivate a therapy, to select a therapeutic regimen (e.g. stimulation protocol), and/or to adjust a therapeutic regimen. It will be understood that these example parameters are not exhaustive and can be employed separately from each other or in various combinations.

[00191] In some examples, this information obtained via any one or several parameters 352, 354, 356, 357, 358, 359 of the therapeutic monitoring element 350 is used to initiate, terminate, select, and/or adjust stimulation applied via the IPG 35, 50 and stimulation electrode 45. For instance, upon determining that the number and/or intensity of apneic events has met or exceeded a severity threshold, the therapy manager 16 (Fig. 1B) can utilize control portion 56 (Fig. 2C) to initiate application of stimulation to the airway-patency related nerves to open the airway and thereby reduce the associated sleep disordered breathing behavior. However, it will be understood that in at least some examples, this arrangement does not include causing (or depend on) the stimulation signal to become synchronized relative to a characteristic (e.g. inspiratory phase, expiratory phase, etc.) of the respiratory waveform. Rather, as noted in association with at least Figure 1A, in the examples described thus far in association with Figures 1-8, such stimulation is applied independent of such synchronization.

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[00192] In some examples, the therapeutic parameters element 350 may be employed to select one of a plurality of stimulation protocols and/or to evaluate the therapeutic effectiveness of a particular stimulation protocol(s) for a particular patient for a given period of time or on a long term basis.

[00193] In at least this context and/or other contexts in at least some examples of the present disclosure, therapeutic effectiveness may correspond to alleviating sleep disordered breathing, which in some instances is measurable via a severity threshold, such as an apnea-hypopnea index (AHI) and/or other scoring mechanisms. In some examples, the therapeutic effectiveness may also be measured or evaluated relative to sensor signal quality, such as via sensor signal quality criteria as described in at least some of the examples of the present disclosure.

[00194] Figure 9 is a block diagram schematically illustrating a control portion 360, according to one example of the present disclosure. In some examples, control portion 360 includes a controller 362 and memory 370. In some examples, therapy manager 371 is stored in memory 370, and in some examples, therapy manager 371 includes at least some of substantially the same features and attributes as therapy manager 16 (Fig. 1B), as previously described in association with at least Figures 1-8.

[00195] In general terms, controller 362 of control portion 360 comprises at least one processor 364 and associated memories that are in communication with memory 370 to generate control signals to direct operation of at least some components of the systems and components described throughout the present disclosure. In some examples, these generated control signals include, but are not limited to, employing therapy manager 371 to manage operation of the stimulation system to control sleep disordered breathing. In some examples, a control portion 360 is present in the IPG 35, 50, 84 (Figs. 2A, 2B, 2D) as control portion 56 (Fig. 2C) and/or is accessible to the IPG 35, 50, 84. In some examples, at least some aspects of stimulation element 12 (Fig. 1A) are at least partially implemented via control portion 360 and/or in communication with control portion 360, with at least some aspects of stimulation element 12 being storable in memory 370 with or as part of therapy manager 371.

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[00196] In particular, in response to or based upon commands received via a user interface 396, 400 (Figs. 11A, 11B) and/or machine readable instructions (including software), controller 362 generates control signals to implement a nerve stimulation protocol to control sleep disordered breathing, in accordance with at least some of the previously described examples and/or later described examples of the present disclosure. In some examples, controller 362 is embodied in a general purpose computer while in other examples, controller 362 is embodied in at least some of the components described throughout the present disclosure, such as IPG 35, 50, 84 or external components operatively coupled to implantable pulse generator 35, 50, 84. For purposes of this application, in reference to the controller 362, the term "processor" shall mean a presently developed or future developed processor (or processing resources) that executes sequences of machine readable instructions contained in a memory. In some examples, execution of the sequences of machine readable instructions, such as those provided via therapy manager 371 stored in memory 370 of control portion 360, cause the processor to perform actions, such as operating controller 362 to implement stimulation protocols as generally described in (or consistent with) at least some examples of the present disclosure. The machine readable instructions may be loaded in a random access memory (RAM) for execution by the processor from their stored location in a read only memory (ROM), a mass storage device, or some other persistent storage (e.g., non-transitory tangible medium or non-volatile tangible medium), as represented by memory 370. In some examples, memory 370 comprises a computer readable tangible medium providing non-volatile storage of the machine readable instructions executable by a process of controller 362. In other examples, hard wired circuitry may be used in place of or in combination with machine readable instructions to implement the functions described. For example, controller 362 may be embodied as part of at least one application-specific integrated circuit (ASIC). In at least some examples, the controller 362 is not limited to any specific combination of hardware circuitry and machine readable instructions , nor limited to any particular source for the machine readable instructions executed by the controller 362.

[00197] In some examples, user interface 396 shown in Figure 11A comprises a user interface or other display that provides for the simultaneous display, activation, and/or

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operation of at least some of the various components, functions, features, and of stimulation element 12 (Fig. 1A), therapy manager 16 (Fig. 1B), control portion 360 (Fig. 9), IPG 35, 50, 84 (Figs. 2A, 2B, 2D), and related elements, as described throughout the present disclosure. In some examples, at least some portions or aspects of the user interface 396 are provided via a graphical user interface (GUI) and may include an input and a display.

[00198] In some examples, user interface 396 includes at least some of the components illustrated in user interface 400 schematically depicted in Figure 11B.

[00199] As shown in Figure 11B, user interface 400 includes at least some of the various components, functions, elements, and features as described and illustrated in association with at least stimulation protocol elements 280 (Fig. 5), 490 (Fig. 15A), therapeutic monitoring element 350 (Fig. 8), stimulation parameters 250 (Fig. 4), stimulation protocol element 450 (including independent function 454, respiratory-dependent function 456 in Fig. 12), automatic protocol selector 470 (Fig. 14), and stimulation protocol selection 500 (Fig. 15B).

[00200] Figure 10 is a diagram 380 schematically illustrating a manner in which the control portion 360 is implemented, according to one example of the present disclosure. In some examples, control portion 360 is entirely implemented within or by an implantable pulse generator 385, which has at least some of substantially the same features and attributes as pulse generator (IPG) 35, 50, 84 as previously described in association with at least Figures 1-9. In some examples, control portion 360 is entirely implemented within or by a remote control 390 (e.g. a programmer) external to the patient's body, such as a patient control 392 and/or a physician control 394. In some examples, the control portion 360 is partially implemented in the pulse generator 385 and partially implemented in the remote control 390 (at least one of patient control 392 and physician control 394).

[00201] In some examples, in association with control portion 360, user interface (396 in Fig. 11A; 400 in Fig. 11B) is implemented in remote control 390.

[00202] Figure 12 is a block diagram of a stimulation protocol element 450, according to one example of the present disclosure. As shown in Figure 12, stimulation protocol element 450 includes an independent stimulation function 454 and a respiratory-dependent function

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456. In some examples, the independent stimulation function 454 includes at least some of substantially the same features as independent stimulation function 14 associated with stimulation element 12 (Fig. 1A) and/or therapy manager 16 (Fig. 1B) as part of an at least partially implantable stimulation system, as previously described in association with Figures 1-11B. Meanwhile, Figure 13 is a block diagram of a respiration-dependent function 456, according to one example of the present disclosure.

[00203] After describing the features and attributes associated with the respiration-dependent stimulation function 456, at least some examples regarding the relationship and relative operation of the independent stimulation function 454 and respiratory-dependent stimulation function 456 will be addressed.

[00204] As shown in Figure 13, in some examples, the respiratory-dependent function 456 includes a synchronous parameter 460, a synchronization characteristic parameter 462, and a stability parameter 464.

[00205] In some examples, via the synchronous parameter 460, respiratory-dependent function 456 implements a stimulation protocol in which each individual nerve stimulation period (within a treatment period) is triggered by and/or synchronized relative to a synchronization characteristic of the patient's respiratory waveform. For instance, in some examples, respiratory-dependent function 456 causes individual stimulation periods to occur substantially simultaneous with the inspiratory phase (e.g. 162 in Fig. 3B) of the patient's respiratory cycle (e.g. 204A in Fig. 3B) such that stimulation is considered to be synchronous with inspiration.

[00206] In some examples, per synchronization characteristic parameter 462, one can select (or a therapy manager can automatically select) the characteristic to which stimulation will be synchronized. In some examples, via parameter 462 respiratory-dependent stimulation function 456 causes nerve stimulation periods to be synchronized relative to a junction or transition between expiratory pause and the onset of inspiration. In some examples, via parameter 462, nerve stimulation periods are synchronized relative to a junction or transition between inspiration and the onset (i.e. beginning) of expiration. In some examples, the

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characteristic to which stimulation will be synchronized can be peak inspiration, peak expiration, or expiratory pause.

[00207] In some examples, stability parameter 464 of respiratory-dependent stimulation function 456 (Fig. 13) tracks and determines at least one parameter of a sensed respiratory waveform to determine the relative stability of the respiratory waveform (e.g. sensor signal quality) to provide a reliable, accurate indication of respiratory behavior to the therapy manager (371 in Figure 9). Without a reasonably stable respiratory waveform, the respiratory-dependent function 456 cannot be implemented. In such a situation, the independent stimulation function 454 is implemented until the control portion 360 determines via stability parameter 464 that a reasonably stable respiratory waveform is available (e.g. the sensor signal has sufficient quality) and by which stimulation can be triggered and/or synchronized relative to a characteristic of the respiratory waveform.

[00208] Via the stability parameter 464, the control portion 56 of Fig. 2C (control portion 360 in Fig. 9) determines whether the respiratory waveform is stable enough (e.g. sensor signal quality is sufficient) to support synchronizing stimulation relative to characteristics (e.g. inspiratory phase) of the respiratory waveform. In some examples, the stability parameter 464 identifies and tracks parameters such as a peak-to-peak amplitude, a respiratory rate, sensor signal frequency content, signal morphology, and a duty cycle associated with at least one of inspiration, expiration, and expiratory pause, or various combinations of these parameters. In some examples, the at least one parameter comprises a statistical stability of these identified parameters. In some examples, a determination of such statistical stability may be performed relative to a known good state for the patient or a moving baseline of known good state for the patient. In some examples, a known good state corresponds to a period of respiration free from obstructive sleep apnea. In some examples, the determination of statistical stability may be performed relative to an independent threshold of statistical goodness.

[00209] In some examples, the inspiratory duty cycle is defined as the ratio of inspiration duration to the duration of respiratory period.

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[00210] In some examples, the above-noted waveform signal stability or quality parameter may be evaluated after sufficient gain is applied to the signal to enable analysis. For instance, if the peak to peak amplitude is low and sensor signal quality is low, then signal gain can be increased to determine if signal quality analysis can be performed. In some examples, a sensed signal can be subject to a process in which a sensor obtains a physiologic signal, to which gain is applied prior to quality analysis, and then potentially used for synchronization of a stimulation protocol relative to the sensed respiratory waveform. In some examples, an automatic gain control mechanism is employed and queried to determine if the gain is stable so the signal may be reliably analyzed.

[00211] In some examples, via therapy manager 16, 371 (Figs. 1B, 9), the respiratory-dependent stimulation function 456 can be disabled so that therapy is selectively applied entirely via the independent stimulation function 14 (Fig. 2A), 454 (Fig. 12). Of course, in some examples as previously described, the respiratory-dependent stimulation function 456 is not even present with the independent stimulation function 14, 454 being the sole mechanism to apply nerve stimulation.

[00212] Figure 14 is a diagram 470 schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol 454 (Fig. 12) and the respiration-dependent stimulation protocol 456 (Fig. 12), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection in diagram 470 can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram 470 can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least Figures11B-13.

[00213] In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols 454, 456. In some examples, an independent stimulation protocol 454 is applied for a predetermined period of time, as shown at 472 in Figure 14. The predetermined period of time corresponds at least to an amount of time for a stable respiration period to be established, which may be ensured based on the independent

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stimulation of the airway-patency-related nerve. In some examples the first predetermined period of time corresponds to a period sufficient to establish a steady state in which filtering is established, inspiration and expiration are being detected reliably, signal gain control is realized, etc.

[00214] In some examples, operation of the first independent stimulation protocol during at least the first predetermined period of time is not a test mode, such as a mode that may otherwise be dedicated to diagnosing or evaluating the operational fitness of the stimulation system. Rather, the first independent stimulation protocol operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

[00215] In some examples, by applying stimulation protocol(s) via the independent stimulation, a stable respiratory waveform is achieved, thereby increasing the likelihood of being able to transition to operation in the respiratory-dependent stimulation at 478 than if independent stimulation at 472 were not deployed prior to the activation of the respiratory-dependent function at 478.

[00216] With further reference to Figure 14, based on monitoring of the sensed respiratory waveform, at repeating intervals, at 474 it is queried whether the respiratory waveform is sufficiently stable to support activation of the respiratory-dependent stimulation . If the answer to the query at 474 is NO, then pathway 476 directs continued operation of independent stimulation at 472. However, if the answer to the query at 474 is YES, then pathway 477 directs initiation of operation of respiratory-dependent stimulation at 478 of Figure 14. During operation of respiratory-dependent stimulation at 478, the query at 474 is periodically implemented. If the answer to the query (at 474) is NO, then operation in respiratory-dependent stimulation n (456 in Fig. 12) at 478 in Figure 14 is terminated as operation is returned (i.e. reverts) via pathway 476 to independent stimulation at 472 in Figure 14 for at least the predetermined period of time.

[00217] For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in independent stimulation at 472 without converting to operation in respiratory-dependent stimulation 478.

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[00218] In some examples, the query at 474 is performed generally continuously by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc. Upon one or more of these parameters failing to meet the sensor signal quality criteria, then the answer to the query (at 474) would be registered as NO. Upon meeting the sensor signal quality criteria, the answer to the query at 474 is YES.

[00219] In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a first parameter as an average peak-to-peak respiratory amplitude above a threshold, where the average is computed from the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a second parameter as a peak-to-peak respiratory amplitude variability below a threshold, where the threshold is referenced to an average computed over the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a third parameter as a respiratory duration variability below a threshold, where threshold is reference to an average computed of the previous 60 seconds. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via a fourth parameter as an average inspiratory phase duration above a threshold, where the average is computed of the previous two respiratory cycles. In some examples, meeting the signal quality criteria (e.g. answer to query is YES) can be defined via various combinations of the respective first, second, third, and fourth parameters, including but not limited to, a combination of all four parameters. It will be understood that the sensor signal quality criteria and/or meeting the sensor signal quality criteria is not exclusively defined by the respective four parameters.

[00220] Figure 15A is block diagram of a stimulation protocol element 490, according to one example of the present disclosure. In some examples, stimulation protocol element 490 includes at least some of substantially the same features and attributes as stimulation protocol element 450 as previously described in association with at least Figures 12-14, while further including at least the features shown in Figure 15A.

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[00221] As shown in Figure 15A, stimulation protocol element 490 includes an override function 492 to take abrupt and sustained action to achieve a stable respiratory pattern. For instance, in some examples, persistent sleep disordered breathing is observed, which includes a series of unresolvable/intractable respiratory events (e.g. persistent apnea) that occur despite stimulation via either the independent stimulation function 454 or the respiratory-dependent function 456. In some examples, the override function 492 is activated when a stable respiratory pattern has not been detected for a predetermined period of time, such as 5 or 10 minutes. In some examples, the predetermined period of time is less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes.

[00222] Upon activation of the override function 492, therapy that was being implemented via the independent stimulation function 454 or via the respiratory-dependent function 456 is terminated or converted over to operation via a continuous stimulation function 494 (Fig. 15A) in which nerve stimulation is applied continuously (a 100 % duty cycle) for a predetermined period of time. As previously described, in some examples, continuous stimulation refers to a train of stimulation pulses which occur in a relatively short time frame. For instance, in some examples, continuous stimulation corresponds to at least a finite number (e.g. 5, 10, etc.) of stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 20 stimulation pulses per second. In some examples, continuous stimulation corresponds to at least 30 stimulation pulses per second. In some examples, the number of stimulation pulses per second is selectable by an operator via a control portion (e.g. 56 in Figure 2C). In some examples, during such continuous stimulation, each stimulation pulse within a train of stimulation pulses includes a primary stimulation pulse followed by a separate recharge pulse, which is in turn followed by a non-stimulation phase before the next primary stimulation pulse.

[00223] In some examples, the override function 492 is implemented via an "other" function, in which nerve stimulation is applied that is not continuous but which has an intensity and duration substantially greater than implemented via the stimulation protocols

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of one of the independent stimulation function 454 (Fig. 12) or the respiratory-dependent function 456 (Fig. 12).

[00224] In some examples, operation via the override function 492 is maintained until at least one of a time limit, and/or the therapy manager detecting (via the sensed respiratory waveform) at least one respiratory cycle exhibiting an absence of sleep disordered breathing behavior as measured by a number of respiratory cycles and/or a severity threshold (in one example). In some examples, the time limit is 100 seconds, such as about 20 breaths. However, in some examples, the time limit can be much lower, such as 30 to 40 seconds. In some examples, the continuous stimulation is applied until detected sleep disordered breathing is absent for at least three consecutive respiratory cycles, i.e. a successful inspiration occurs for at least three consecutive respiratory cycles or some operator-selectable quantity (e.g. 2, 4) of consecutive respiratory cycles for a particular patient.

[00225] In some examples, the continuous stimulation is applied up to a predetermined maximum period. In some examples, the predetermined maximum period is at least 120 seconds. In some examples, the predetermined maximum period is selectable by an operator and can have values greater or less than 120 seconds, such as 130 seconds, 110 seconds, 90 seconds, etc. In general terms, the predetermined maximum period corresponds to an expired time by which fatigue of the stimulated muscle is complete or nearly complete.

[00226] In some examples, upon a determination that detected sleep disordered breathing behavior meets or exceeds the severity threshold, the therapy manager terminates operation in the respective independent and respiratory-dependent stimulation modes and initiates operation in a third mode including a stimulation protocol of a stimulation period and a non-stimulation period in a proportion of at least 3 to 1 wherein the stimulation period has a duration equal to or greater than a duration of at least four respiratory cycles.

[00227] In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 10 seconds. In some examples, the duration of the stimulation period is about 30 seconds and the duration of the non-stimulation period is about 5 seconds.

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[00228] Upon determination that a stable respiratory period has been established, operation in the override function 492 terminates and operation is resumed via the independent stimulation function 454 (Fig. 12) consistent with the functionality previously described in association with at least Figs. 12-14.

[00229] Figure 15B is a diagram 500 schematically illustrating aspects of selecting a stimulation protocol, according to one example of the present disclosure. In some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram 500 can be embodied as a method while in some examples, at least some aspects of selecting a stimulation protocol as expressed in diagram 550 can be embodied as operational aspects of a stimulation protocol management associated with a therapy manager 16 as described in association with at least Figures 1-15A.

[00230] As shown at 502, respiratory information can be periodically sensed during a treatment period and without synchronization to stimulation. In other words, in at least some instances, this periodic sensing is not related to and/or does not result in synchronizing stimulation to sensed respiratory information. Rather, such periodic sensing can be used to enhance and/or evaluate the effectiveness of the stimulation, among other uses for such periodically sensed respiratory information.

[00231] As shown at 504 in Figure 15B, if the duration of the sensed respiratory cycles (among a sample of respiratory cycles) is less variable from cycle-to-cycle than a duration variability criteria, then a stimulation protocol is adopted in which a repeating stimulation cycle is applied and which has a duration different than a duration of the reference respiratory cycle for this patient. This arrangement introduces an intentional stagger or offset between the duration of the stimulation cycle and the duration of respiratory cycle, which may ensure overlap of at least some stimulation periods (of the stimulation cycles) with the actual inspiratory phases of the respiratory cycles of the patient a majority of the time.

[00232] In some examples, the duration variability criteria establishes a measure of the variability of a duration of sensed respiratory cycles. The variability can be measured by a frequency of changes in the duration during an observation period and/or a magnitude of

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change in such durations during the observation period. Further details regarding the observation period are identified below.

[00233] In some examples, the duration variability criteria is based on several factors, including but not limited to, a duration of a typical stable respiratory period (e.g. 3-6 seconds, depending on the patient), the minimum duration of an apnea (e.g. 10 seconds), and/or an observation period (e.g. 5 minutes) following a change in stimulation parameters. In some examples, the observation period can more than 5 minutes while in some examples, the observation period can be less than 5 minutes, such as when some number (e.g. 3 apneas) of apneas are detected prior to reaching 5 minutes. In some examples, the duration variability criteria is further based on a standard deviation of respiratory periods of less than 1 second and a sample period of at least 4 minutes.

[00234] With further reference to 504 in Figure 15B, in some examples, this arrangement is implemented via stimulation protocol 210 in Figure 3B in which a respiratory waveform is represented via a series 202 of respiratory cycles 204A-204H. Moreover, in this example, the duration of the stimulation cycle (4 stimulation periods plus 1 non-stimulation period) is less than a duration (R) of the reference respiratory cycles, such that the repeating stimulation cycle has a duration different than a duration (R) of the reference respiratory cycle.

[00235] This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number (e.g. 2, 3, 4) of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase 162 of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

[00236] In some examples, other example stimulation protocols are used for implementation. For instance, example stimulation protocols 220, 230 as described in association with at least Figures 3C, 3D can be used. It is noted that stimulation protocols 220, 230 include stimulation cycles having a duration greater than a duration (R) of the

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reference respiratory cycle as shown in the respective legends 229, 239 of Figures 3C, 3D, respectively.

[00237] As shown at 506 in Figure 15B, if the duration of the sensed respiratory cycle (of a sensed sample of respiratory cycles) is more variable than the duration variability criteria noted above, then a repeating stimulation cycle is applied and which has a duration generally matching a duration of a reference respiratory cycle. In this instance, the natural variability of the duration of the patient's respiratory cycle can be used to introduce a stagger or offset relative to the duration of the stimulation cycle, which may ensure an overlap of at least some stimulation periods relative to at least some of the inspiratory phases of the patient's live respiratory cycles at least a majority of the time.

[00238] In some examples, the reference respiratory cycle is defined by a patient-specific average respiratory cycle obtained at an earlier point in time. In some examples, the reference respiratory cycle is defined by a multi-patient specific average respiratory cycle obtained from a database.

[00239] In some examples, this arrangement is implemented via stimulation protocol 240 in Figure 3E in which a respiratory waveform is represented via a series 244 of respiratory cycles 245A-245M. Accordingly, Figure 3E models the situation in which the duration (R1) of the respiratory cycles has varied (relative to the duration R of its base/stable respiratory cycle) by more than a threshold. In some examples, the threshold includes R changing (increasing or decreasing) in duration by 5 percent. In this instance the duration R1 represents about an 8 percent change from the duration R because the respiratory cycles 245A-245M have a duration R1 of 6 ½ time units whereas duration R is equal to 6 time units. It will be understood, of course, that other numeric values that are more or less than 5 percent can be used as the threshold.

[00240] While Figure 3E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in preceding respiratory cycles. Accordingly, at least with respect to the method of Figure 15B, duration R1 should not be

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viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

[00241] It will be further understood that variations in the duration of the respiratory cycle may be exhibited as decreases (instead of increases) and that variations in the duration of the respiratory cycle are not permanent but may last some finite number of respiratory cycles before reverting to a baseline or changing to yet another non-R duration.

[00242] In the example of Figure 3E, the duration of the stimulation cycle (4 stimulation periods plus 2 non-stimulation periods) is less than a duration (R1) of the respiratory cycles but with the duration of the stimulation cycles being equal to the duration (R) of the reference respiratory cycle (which is based on a historical baseline in at least some examples).

[00243] With this arrangement, because the duration (R1) of the sampled respiratory cycle (obtained via periodic sensing) has varied relative to a reference duration R, the therapy manager 16 utilizes a stimulation cycle having a duration to match the duration of the reference respiratory cycle, which in turn introduces the above-mentioned intentional stagger or offset.

[00244] This arrangement ensures that no matter when the stimulation protocol is generally activated, no more than a finite number of respiratory cycles would occur without a stimulation period significantly coinciding with an inspiratory phase of the respective respiratory phases. This phenomenon occurs, at least in part, because of a sufficiently large difference between the duration of the stimulation cycle and the duration of the respiratory cycle, and in view of the relative proportion of the stimulation period to the non-stimulation period.

[00245] Accordingly, as represented at block 506, when the duration of the periodically sensed respiratory cycle varies more than a duration variability criteria, the therapy manager ensures an appropriate level of stimulation coinciding with the inspiratory phases of the respiratory cycles by intentionally not adjusting the duration of the stimulation cycle to match the modified duration R1 exhibited by the periodically sensed respiratory cycles.

[00246] While Figure 3E exhibits a duration R1 which remains constant at least for the illustrated series of respiratory cycles, it will be understood that duration R1 may have a

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different value (e.g. longer or shorter) in subsequent respiratory cycles and/or that duration R1 may have had different values (e.g. longer or shorter) in at least some preceding respiratory cycles. Accordingly, at least with respect to the method of Figure 15B, duration R1 should not be viewed as being indefinitely static, but rather as having a particular value at one snapshot in time.

[00247] Figure 15C is a block diagram schematically illustrating a stimulation protocol selector element 520, according to one example of the present disclosure. In some examples, the stimulation protocol selector element 520 includes, and enables, selection between a first function 522 and a second function 524. In some examples, a selection via element 520 between first function 520 and second function 522 can be implemented in association with the aspects of block 502 in Figure 15B. In some examples, first function 520 can be implemented via at least some of the aspects of stimulation selection as described in association with block 504 in Figure 15B while second function 522 can be implemented via at least some of the aspects of stimulation selection as described in association with block 506 in Figure 15B.

[00248] Figure 15D is a diagram 550 schematically illustrating a relationship between, and automatically selection between, the independent stimulation protocol 454 (Fig. 12) and the respiration-dependent stimulation protocol 456 (Fig. 12), according to one example of the present disclosure. In some examples, at least some aspects of stimulation protocol selection 551 in diagram 550 can be embodied as a method while in some examples, at least some aspects of stimulation protocol selection in diagram 550 can be embodied as operational aspects of a stimulation protocol manager of a therapy manager, as described in association with at least Figures11B-13.

[00249] In some examples, operation of the at least partially implantable stimulation system is implemented via providing cooperation or complementary deployment of the respective stimulation protocols 454, 456 (at least Figs. 11B-13). Accordingly, as shown at 552 in Figure 15D, operation starts in a respiratory-dependent stimulation protocol.

[00250] With further reference to Figure 15D, based on monitoring of the sensed respiratory waveform, at repeating intervals, at 554 it is queried whether the respiratory waveform is

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sufficiently stable to support continued operation of respiratory-dependent stimulation at 552. If the answer to the query at 554 is YES, then pathway 556 affirms continued operation of respiratory-dependent stimulation at 552. However, if the answer to the query at 554 is NO, then pathway 557 directs initiation of operation of independent stimulation at 558 of Figure 15D for at least a predetermined period of time. The first predetermined period of time is defined in substantially the same manner as previously described in association with at least Figure 14, and the operation of the independent stimulation function at 558 is not a test mode. Rather, the independent stimulation (at 558) operates for at least the predetermined period of time to apply therapeutic stimulation to achieve a stable respiratory behavior and a stable respiratory waveform.

[00251] Upon operation of independent stimulation at 558 for at least the predetermined period of time, the query at 554 is periodically implemented. If the answer to the query (at 554) is YES, then operation in independent stimulation at 558 in Figure 15D is terminated as operation is returned via pathway 556 to respiratory-dependent stimulation at 552 in Figure 15D. For at least the current example, it will be understood that, in the event that no stable respiratory waveform is established, the operation would remain in the independent stimulation at 558 without reverting operation into respiratory-dependent stimulation at 552.

[00252] In some examples, the query at 554 is performed by monitoring parameters indicative of respiratory signal sensing quality (i.e. sensor signal quality criteria), such as but not limited to, peak to peak amplitude, inspiratory duty cycle, respiratory rate, etc.

[00253] Figure 16A is diagram 640 schematically illustrating a nerve stimulation protocol 641, according to one example of the present disclosure.

[00254] In one aspect, diagram 640 omits a representative respiratory waveform relative to the stimulation protocol because, in at least some examples, operation according to independent stimulation function 14 (Fig. 1A) occurs regardless of whether a sensed respiratory waveform is available or reasonably stable. Accordingly, diagram 640 illustrates stimulation periods relative to predetermined time periods instead of relative to inspiratory and expiratory phases of a normal respiratory pattern, as further described and illustrated below.

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[00255] As shown in Figure 16A, a nerve stimulation protocol 641 comprises stimulation segments 642 and non-stimulation segments 648, 649 (i.e. rest periods), which may occur within a time frame (T). In this arrangement, the time frame T comprises a series of eight time units with each time unit having a duration t, as shown in Figure 16A. In some examples, a combination of two consecutive time units have a duration R that generally corresponds to a duration of a respiratory cycle. In one aspect, the duration of one time unit (t) comprises one-half of duration R.

[00256] As shown in diagram 640, stimulation protocol 641 includes a repeating sequence of continuous stimulation segments 642 and non-stimulation segments 648, 649. Each stimulation segment 642 has a duration of 3 time units (t), each non-stimulation segment 648 has a duration of two time units, and each non-stimulation segment 649 has a duration of one time unit. This pattern is represented by legend 645 as 3:SK2:3:SK1, where SK represents "skip" to indicate skipping stimulation.

[00257] As further shown by diagram 640, as this stimulation cycle pattern (3:SK 2:3:SK 1) is repeated through a series of time frames T (with each time frame T including 8 time units), one can identify the number of stimulation time units that occurs within each time frame T. For example, the first time frame includes 6 stimulation time units out of 8 total time units, followed by three time frames T including 5 stimulation time units out of 8 total time units, followed by two "six stimulation time unit" time frames T, and then three "five stimulation time unit" time frames T. With this in mind, one can express a pattern of the stimulation time units for the first twelve consecutive time frames as 6:5:5:5:6:6:5:5:5.

[00258] Via the stimulation protocol 641, a therapeutic nerve stimulation regimen is applied in which no period of four consecutive respiratory cycles will transpire without a stimulation period coinciding with an expected inspiratory phase of a respiratory cycle. In this stimulation protocol, the duration of stimulation periods exceeds the duration of non-stimulation periods.

[00259] Figure 16B is a diagram 651 schematically illustrating a stimulation protocol 650, according to one example of the present disclosure. In some examples, protocol 650 exhibits at least some of substantially the same features and attributes as the stimulation protocols,

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as previously described in association with at least Figs. 3B-3E. In general terms, via stimulation protocol 650, via stimulation element 12 (Fig. 1A) and/or therapy manager 16 (Fig. 1B) the independent stimulation function 14 implements asynchronous nerve stimulation which to promote stable respiration despite potential sleep disordered breathing.

[00260] As illustrated in Figure 16B, the stimulation protocol 650 operates according to stimulation cycles in which the duration (D) of each stimulation cycle is less than the duration (R) of the reference respiratory cycles 654A, 654B. Moreover, in some examples, the stimulation cycle has a duration (D) which is significantly less (at least half or less) than the duration (R) of the reference respiratory cycles 654A, 654B. In one of these examples, a duration (D) of the stimulation cycle is less than 30 percent of the duration (R) of the reference respiratory cycles 654A, 654B. In one of these examples, a duration (D) of the stimulation cycle is less than 20 percent of the duration (R) of the reference respiratory cycle 654A, 654B. In one such instance, as illustrated in Figure 16B, the duration (D) of the stimulation cycle is about 1 second, whereas the duration (R) of the reference respiratory cycle is about 6 seconds.

[00261] In some examples of implementing stimulation protocol 650, within a given stimulation cycle the stimulation period (e.g. 652A, 652B, etc.) and the non-stimulation period (e.g. 658A, 658B, etc.) are in a proportion of 4 to 1 to yield a stimulation duty cycle of 80 percent (for each stimulation cycle). In such examples, each stimulation cycle lasts about 1 time unit (t), including a continuous stimulation period of 4 "1/5" time units followed by a non-stimulation period of a single "1/5" time unit, with this stimulation cycle being repeated continuously when nerve stimulation via stimulation protocol 650 is implemented. Accordingly, in some examples, the duration of the entire stimulation cycle (e.g. 4 "1/5" time units of stimulation and a single "1/5" time unit of non-stimulation) is 1 time unit (t), which is significantly less than the duration R of the respiratory cycle, which is 6 time units in this example.

[00262] However, it will be understood that in some examples, the duration of the stimulation period need not coincide with a discrete number (e.g. 4) of fractional time units

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(e.g. "1/5" time units) and the duration of the non-stimulation period need not coincide with a discrete number (e.g. 1) of fractional time units (e.g. "1/5" time units).

[00263] In some examples, the duration (R) of the reference respiratory cycles (e.g. 654A, 654B, etc.) can be selected to be more or less than 6 time units (t), as shown in Fig. 16B. In some examples, the duration (D) of each stimulation cycle (including a stimulation period, such as 652A and a non-stimulation period, such as 658A) can be selected to be more or less than one time unit (t).

[00264] In Figure 16B, the first end 653 of stimulation period 652A is shown as coinciding with the beginning of an inspiratory phase 162 of the respiratory cycle 654A. However, it will be understood that the beginning 653 of the stimulation period 652A is not synchronized relative to the inspiratory phase 162. Rather, the beginning 653 of stimulation period 652A is shown as coinciding with the beginning of inspiratory phase 162 for illustrative simplicity in juxtaposing the stimulation protocol 650 relative to the reference respiratory cycles 654A, 654B, etc. Accordingly, it will be understood that when stimulation (according to stimulation protocol 650) is initiated during a treatment period, the beginning of the stimulation period 652A may coincide with a different portion of the reference respiratory cycle (e.g. 654A) than shown in Figure 16B.

[00265] As further shown in Figure 16B, in one aspect, each respective non-stimulation period (e.g. 658A, 658B, etc.) has a duration significantly less than (e.g. at least less than half) a duration of each respective stimulation period (e.g. 652A, 652B, etc.). In one aspect, the duration of each stimulation period (e.g. 652A, 652B, etc.) is also significantly less than (e.g. at least less than 30%) a duration (R) of the respective reference respiratory cycles (e.g. 654A, 654B, etc.). In some examples, in stimulation protocol 650, the duration (D) of each stimulation period (e.g. 652A, 652B, etc.) is significantly less than a duration (I) of the inspiratory phase 162 of an individual respiratory cycle (e.g. 654A) such that multiple, different stimulation periods occur during a single inspiratory phase 162. Accordingly, with this arrangement, several stimulation cycles will be repeated within a single reference respiratory cycle.

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[00266] In some examples, the relatively short duration of the stimulation cycle causes a successive stimulation period (e.g. 652B) to begin at a different place within the inspiratory phase 162 of the reference respiratory cycle than prior stimulation period (e.g. 652A), such that the stimulation pattern is considered to be independent of (i.e. not synchronized relative to) the characteristics of the respiratory cycle. Rather, the asynchronous nature of stimulation protocol 650 is further exhibited via the stimulation periods 652C-652F occurring during the expiratory phase 170 of respiratory cycle 654A because the same stimulation cycle is repeated regardless of where the stimulation periods falls relative to different portions of the reference respiratory cycle.

[00267] Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 650 is started relative to a series of respiratory cycles, the short duration (D) of the stimulation cycle (relative to the longer duration R of the respiratory cycle) ensures that at least a portion of two stimulation periods (e.g. 652A, 652B) will significantly overlap (at least a majority) the inspiratory phase 162 of the respective reference respiratory cycles throughout the portion of the treatment period during which stimulation protocol 650 is applied.

[00268] In some examples, via therapy manager 16 (Fig. 1B) a clinician can set a criteria how many respiratory cycles through which the stimulation protocol 650 will be applied before stimulation terminates and/or before a different stimulation protocol is implemented. In some examples, the criteria are based on a predetermined amount of time and/or a predetermined number of respiratory cycles for a particular patient.

[00269] It will be understood that each inspiratory phase 162 of each respiratory cycle (204A-204H) is shown in its ideal form in Figure 3B, and that in some instances where the inspiratory phase 162 at least partially coincides with one of the respective non-stimulation periods (e.g. 218D), the inspiratory phase may sometimes have an irregular shape compared to the idealized shape shown in Figure 3B.

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[00270] Accordingly, via stimulation protocol 650, the independent stimulation function 14 of therapy manager 16 (Fig. 1B) employs asynchronous nerve stimulation to achieve stable respiration despite potential sleep disordered breathing.

[00271] In some examples, the stimulation protocol 650 (and similar protocols described above) is implemented via the "other" function 496 (Fig. 15A) of override function 492 to help overcome the type of persistent sleep-disordered breathing that does not become controlled via less intensive stimulation protocols. Accordingly, stimulation protocol 650 provides stimulation, which is not continuous but which has an intensity substantially greater than implemented via the stimulation protocols of one of the independent stimulation function 454 (Fig. 12) or the respiratory-dependent function 456 (Fig. 12), as previously illustrated in association with at least Figs. 3B-3E.

[00272] However, unlike a continuous stimulation pattern such as provided via continuous function 494 (Fig. 15A) of override function 492, stimulation protocol 650 regularly provides non-stimulation periods to enable the targeted nerve and/or muscle to rest somewhat among the stimulation periods, while still achieving an overall 80% stimulation duty cycle. In this arrangement, multiple stimulation periods can occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase. In one aspect, such an arrangement may contribute to more favorable patient comfort or tolerance for the implementation of the "other" override function and/or contribute to diminishing any potential nerve or muscle fatigue.

[00273] In some examples, variations of stimulation protocol 650 are implemented in which the duration (D) of the stimulation cycle is significantly less than the duration (R) of the reference respiratory cycle, and the stimulation duty cycle is about 60 percent or 70 percent (instead of 80 percent). In such an arrangement, multiple stimulation periods can still occur during each inspiratory phase of the repeating reference respiratory cycles such that no inspiratory phase occurs without stimulation occurring during at least a majority of any given inspiratory phase, but with more non-stimulation available. In one aspect, such an arrangement may provide more comfort for some patients and/or potentially less muscle

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fatigue, as compared to the illustrated example stimulation protocol 650 having an 80% stimulation duty cycle (with relatively short duration stimulation cycles).

[00274] As with the other example stimulation protocols described herein, stimulation protocol 650 can be modified by an operator via the various parameters, functions, and components as previously described in association with at least Figures 4-5 can be selected and/or adjusted via a control portion (56 in Fig. 2C; 360 in Fig. 9; 380 in Fig. 10) in association with user interface (396 in Fig. 11A; 400 in Fig. 11B).

[00275] Figure 17A is a flow diagram 700 of a method 701 of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method 701 is performed using the components, elements, systems, etc. previously described and illustrated in association with Figures 1-16B. In some examples, method 701 is performed using components, elements, systems, etc. other than those previously described and illustrated in association with Figures 1-16B.

[00276] As shown in Figure 17A, at 705 method 701 includes asynchronously stimulating an airway-patency-related nerve, according to a first stimulation protocol of stimulation cycles including a stimulation period and a non-stimulation period.

[00277] Figure 17B is a flow diagram 720 of a method 721 of nerve stimulation to treat sleep disordered breathing, according to one example of the present disclosure. In some examples, method 721 is performed using the components, elements, systems, etc. previously described and illustrated in association with Figures 1-16B. In some examples, method 721 is performed using components, elements, systems, etc. other than those previously described and illustrated in association with Figures 1-16B.

[00278] As shown in Figure 17B, in cooperation with the method 701 of Figure 17A, method 721 includes performing nerve stimulation via the therapy manager providing automatic convertible operation between the independent stimulation mode/function of Figure 17A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at 724. With this arrangement, the therapy manager causes operation in the first mode for at least a first predetermined period of time (726) and converts operation into the second mode upon at

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least one parameter of the sensed respiratory waveform meeting a sensor signal quality criteria (728). Upon the at least one parameter of the sensed respiratory waveform failing to meet the sensor signal quality criteria (730), operation reverts into the first mode for at least the first predetermined period of time In this example, the first mode acts as the default mode of operation.

[00279] In some examples, the sensor signal quality criteria is indicative of the system's ability to actually deliver stimulation at the targeted portion of the respiratory period with a high degree of confidence. In some examples the system may define an obstructive event (e.g. apnea/hypopnea) as lasting at least 10 seconds, then the above-mentioned high degree of confidence would correspond to not missing the target portion of the respiratory period twice in consecutive respiratory cycles.

[00280] In some examples, the sensor signal quality criteria can be indicative of a patient's real-time condition either in the absence of or in the presence of stimulation. In some examples, the sensor signal quality criteria can be indicative of sensor noise, thereby indicating how well the sensor signal correlates with the patient's real-time condition.

[00281] However, in some examples, the second mode can act as the default mode of operation. Accordingly, as shown in Figure 17C, in cooperation with the method 701 of Figure 17A, method 771 includes performing nerve stimulation via the therapy manager providing convertible operation between the independent stimulation mode/function of Figure 17A and a second stimulation mode of stimulating the airway-patency-related nerve synchronous with a characteristic of the sensed respiratory waveform, as shown at 774. With this arrangement, the therapy manager causes operation in the second mode (776), and upon at least one parameter of the sensed respiratory waveform failing to meet a sensor signal quality criteria, operation converts into the first mode for at least a first predetermined period of time (778). At 780, upon the at least one parameter of the sensed respiratory waveform meeting the sensor signal quality criteria, operation reverts back into the second mode.

[00282] In some examples, with respect to at least Figures 17B and 17C, the conversion between the first stimulation mode and the second stimulation mode is automatic.

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[00283] With respect to selection of the first mode or the second mode in association with Figures 17B and 17C, in some examples a therapy manager 800 includes a default mode selector function 802 (as shown in Figure 18) to enable user selection of either the first mode or the second mode as a default mode. In some examples, the therapy manager 800 also comprises at least some of the features and attributes as therapy manager 16 (Fig. 1B) and other examples of a therapy manager, as previously described in association with at least Figures 1-17C.

[00284] With respect to selection of the first mode or the second mode in association with Figures 17B and 17C, in some examples a therapy manager 850 includes a manual conversion function 852 (as shown in Figure 19) to selectively cause conversion between the two different stimulation modes. In one aspect, such selective conversion can be implemented during operator titration of the therapeutic treatment as the operator adjusts parameters of the stimulation protocols for a particular patient. In some examples, the therapy manager 850 also comprises at least some of the features and attributes as therapy manager 16 (Fig. 1B) and other examples of a therapy manager, as previously described in association with at least Figures 1-17C. Accordingly, at least some examples of the present disclosure provide for a robust scheme to increase the effectiveness of nerve stimulation to treat sleep disordered breathing.

[00285] Although specific examples have been illustrated and described herein, it will be appreciated by those of ordinary skill in the art that a variety of alternate and/or equivalent implementations may be substituted for the specific examples shown and described without departing from the scope of the present disclosure. This application is intended to cover any adaptations or variations of the specific examples discussed herein.

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Electronic Patent Application Fee Transmittal

Application Number:	
Filing Date:	
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Attorney Docket Number:	I618.118.104

Filed as Large Entity

Filing Fees for Utility under 35 USC 111(a)

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
UTILITY APPLICATION FILING	1011	1	300	300
UTILITY SEARCH FEE	1111	1	660	660
UTILITY EXAMINATION FEE	1311	1	760	760
Pages:				
Claims:				
CLAIMS IN EXCESS OF 20	1202	4	100	400
Miscellaneous-Filing:				
LATE FILING FEE FOR OATH OR DECLARATION	1051	1	160	160

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Miscellaneous:				
		Total in USD ($)		**2280**

Electronic Acknowledgement Receipt

EFS ID:	40476709
Application Number:	17012481
International Application Number:	
Confirmation Number:	3270
Title of Invention:	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING
First Named Inventor/Applicant Name:	Darrell Wagner
Customer Number:	25281
Filer:	PAUL STEVEN GRUNZWEIG/Justina Perez
Filer Authorized By:	PAUL STEVEN GRUNZWEIG
Attorney Docket Number:	I618.118.104
Receipt Date:	04-SEP-2020
Filing Date:	
Time Stamp:	13:26:33
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$2280
RAM confirmation Number	E202094D26554325
Deposit Account	
Authorized User	
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File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Application Data Sheet	2020-09-04ADS.pdf	1823392 dd61d20843e5baec4c62feb51f62e474be7d7206	no	9
Warnings:					
Information:					
2	Drawings-only black and white line drawings	2020-09-04FIGS.pdf	1167502 30e4e36d96d10f83208258bd1ea2bf8a0116c6c5	no	13
Warnings:					
Information:					
3	Power of Attorney	2020-09-04POA.pdf	345362 66e4bd33b0818e7a968c934d94379fe2b7dc33a9	no	2
Warnings:					
Information:					
4		2020-09-04CONAppln.pdf	269034 73f890a7051c6c0c7654f3b9bff409a86112877b	yes	70

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Abstract	70	70
	Claims	66	69
	Specification	1	65

Warnings:					
Information:					
5	Fee Worksheet (SB06)	fee-info.pdf	38208 8a095713962895ac854b62eb70ec8d78eed27a17	no	2

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Information:	
Total Files Size (in bytes):	3643498

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.
This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.

Secrecy Order 37 CFR 5.2:

☐ Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)

Inventor Information:

Inventor 1 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Darrell		Wagner	

Residence Information (Select One) ● US Residency ○ Non US Residency ○ Active US Military Service

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Address 2	Suite 1600

City	State/Province	Postal Code	Country
Golden Valley	MN	55416	US

Inventor 2 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Quan		Ni	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

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City	State/Province	Postal Code	Country
Golden Valley	MN	55416	US

Inventor 3 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	John		Rondoni	

Residence Information (Select One) ◉ US Residency ○ Non US Residency ○ Active US Military Service

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

City	Plymouth	State/Province	MN	Country of Residence	US

Mailing Address of Inventor:

Address 1	6500 Wayzata Blvd.
Address 2	Suite 1600

City	Golden Valley	State/Province	MN
Postal Code	55416	Country	US

Inventor 4 — Remove

Legal Name

Prefix	Given Name	Middle Name	Family Name	Suffix
	Dave		Dieken	

Residence Information (Select One) (•) US Residency ( ) Non US Residency ( ) Active US Military Service

City	Minneapolis	State/Province	MN	Country of Residence	US

Mailing Address of Inventor:

Address 1	6500 Wayzata Blvd.
Address 2	Suite 1600

City	Golden Valley	State/Province	MN
Postal Code	55416	Country	US

All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the **Add** button. Add

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below.
For further information see 37 CFR 1.33(a).

☐ **An Address is being provided for the correspondence Information of this application.**

Customer Number	25281		
Email Address	USPTO.PATENTS@dbclaw.com	Add Email	Remove Email

Application Information:

Title of the Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING		
Attorney Docket Number	I618.118.104	Small Entity Status Claimed	☐
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	13	Suggested Figure for Publication (if any)	3B

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not** be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32).
Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	● Customer Number	US Patent Practitioner	○ Limited Recognition (37 CFR 11.9)
Customer Number	25281		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.
When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
	Continuation of	15/562714	2017-09-28

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

Prior Application Status	Pending		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
15/562714	a 371 of international	PCT/US2016/022611	2016-03-16
Prior Application Status	Expired		Remove
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
PCT/US2016/022611	Claims benefit of provisional	62/135305	2015-03-19
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the **Add** button.			Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)[i] the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

			Remove
Application Number	Country[i]	Filing Date (YYYY-MM-DD)	Access Code[i] (if applicable)
Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.			Add

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.
NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant 1 — Remove

If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

Clear

● Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest	

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	INSPIRE MEDICAL SYSTEMS, INC.		
Mailing Address Information For Applicant:			
Address 1	5500 Wayzata Blvd.		
Address 2	Suite 1600		
City	Golden Valley	**State/Province**	MN
Country	US	Postal Code	55416
Phone Number		Fax Number	
Email Address			

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Assignee Information including Non-Applicant Assignee Information:

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

Assignee 1

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Remove

If the Assignee or Non-Applicant Assignee is an Organization check here. ☒

Organization Name	INSPIRE MEDICAL SYSTEMS, INC.

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1	5500 Wayzata Blvd.		
Address 2	Suite 1600		
City	Golden Valley	**State/Province**	MN
Country i	US	Postal Code	55416
Phone Number		Fax Number	
Email Address			

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. Add

Signature:

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This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Paul S. Grunzweig/			Date (YYYY-MM-DD)	2020-09-04
First Name	Paul S.	Last Name	Grunzweig	Registration Number	37143

Additional Signature may be generated within this form by selecting the Add button. Add

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	I618.118.104
	Application Number	
Title of Invention	STIMULATION FOR TREATING SLEEP DISORDERED BREATHING	

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The information provided by you in this form will be subject to the following routine uses:

1 The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3 A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent CooperationTreaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Exhibit 1002
NYXOAH, INC., et al. v. INSPIRE MEDICAL SYSTEMS, INC.
01643

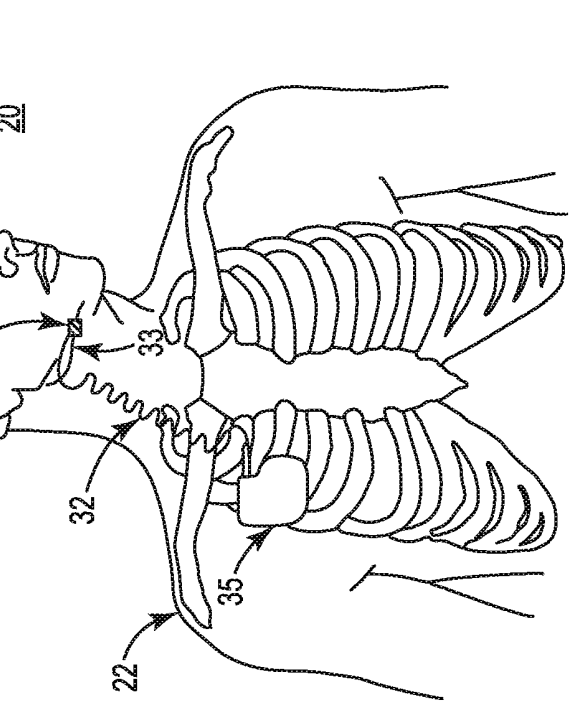


Fig. 2A

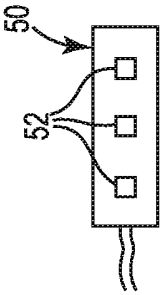


Fig. 2E

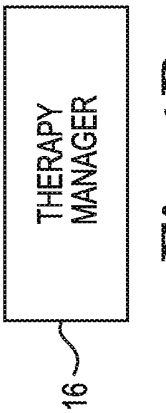


Fig. 1B

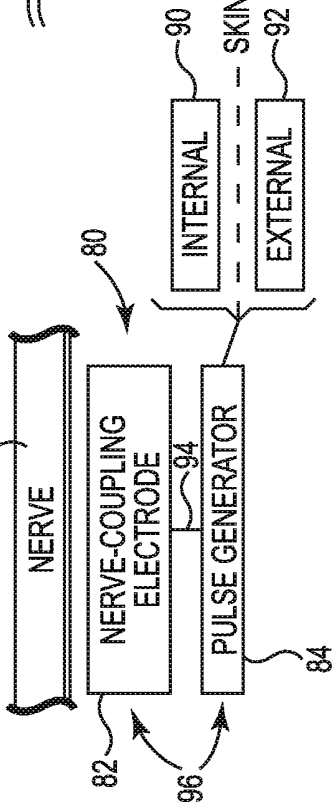


Fig. 2D

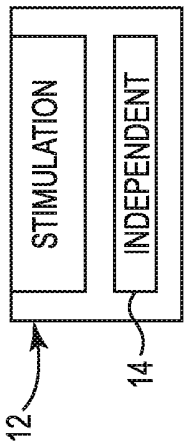


Fig. 1A

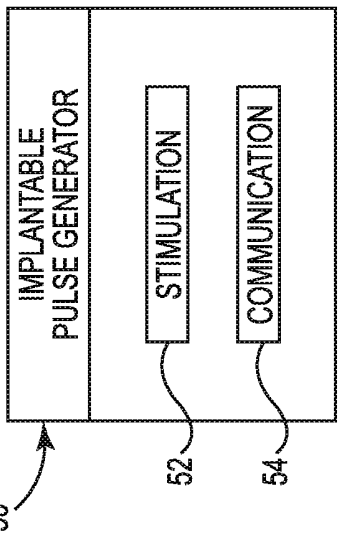


Fig. 2B

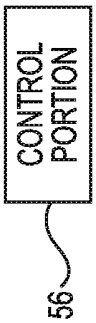


Fig. 2C

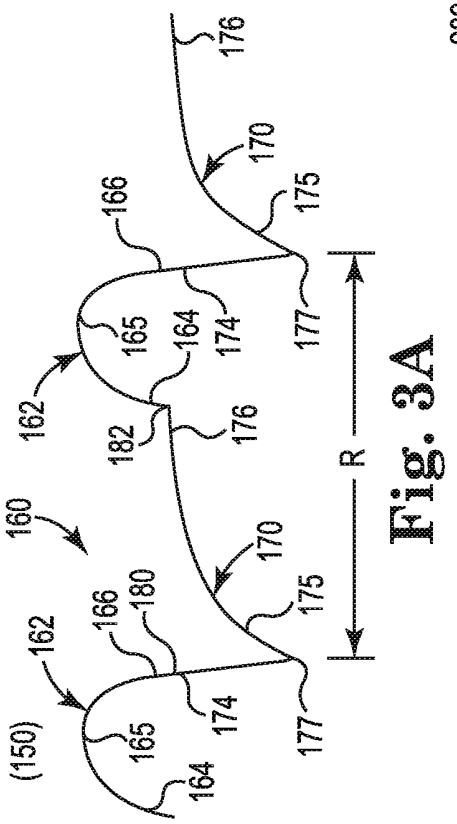

(150)
160
162
164
165
166
174
175
176
177
180
182
170
R

Fig. 3A

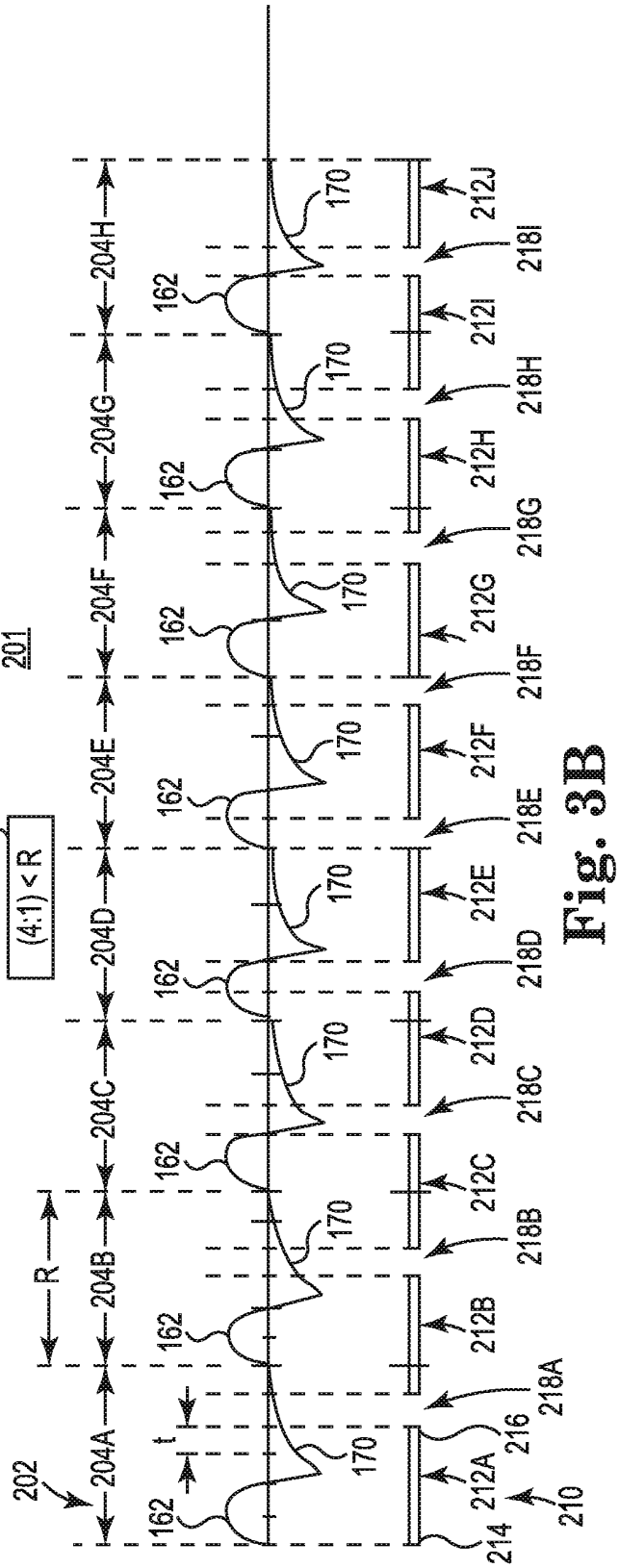

201
209
(4:1) < R
R
t
202
204A
204B
204C
204D
204E
204F
204G
204H
162
170
210
212A
212B
212C
212D
212E
212F
212G
212H
212I
212J
214
216
218A
218B
218C
218D
218E
218F
218G
218H
218I

Fig. 3B

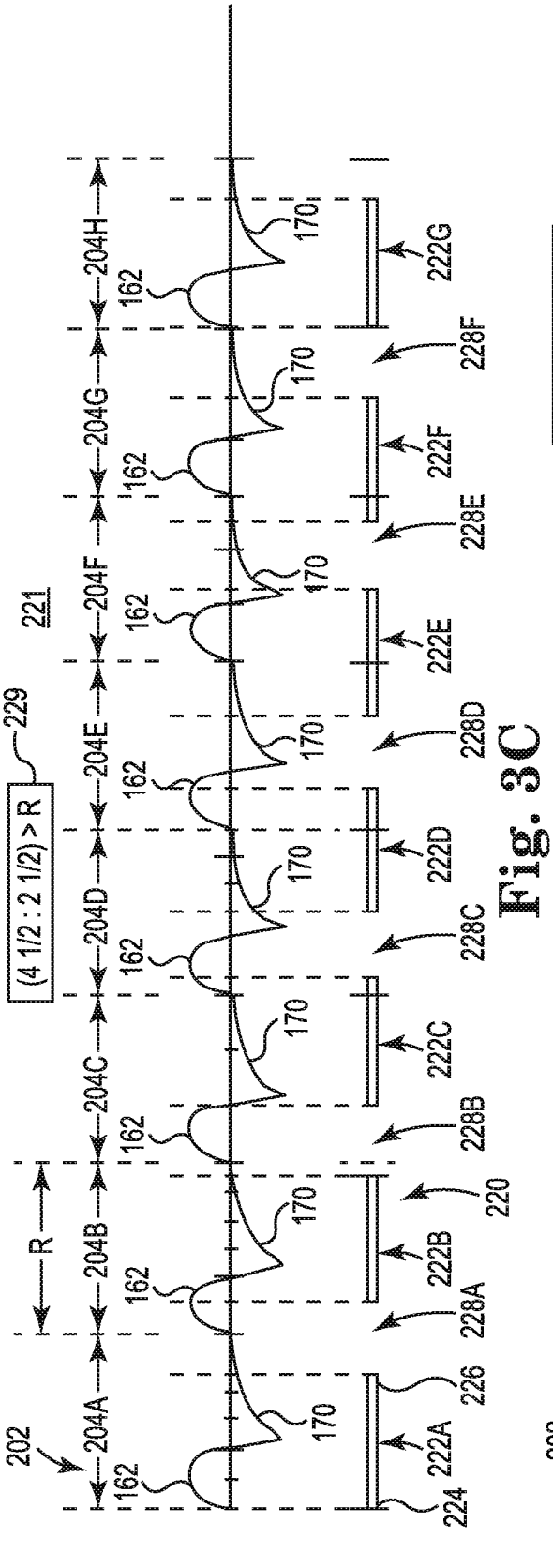

202
204A
204B
204C
204D
204E
204F
204G
204H
R
(4 1/2 : 2 1/2) > R
229
221
162
170
222A
222B
222C
222D
222E
222F
222G
224
226
228A
228B
228C
228D
228E
228F
220

Fig. 3C

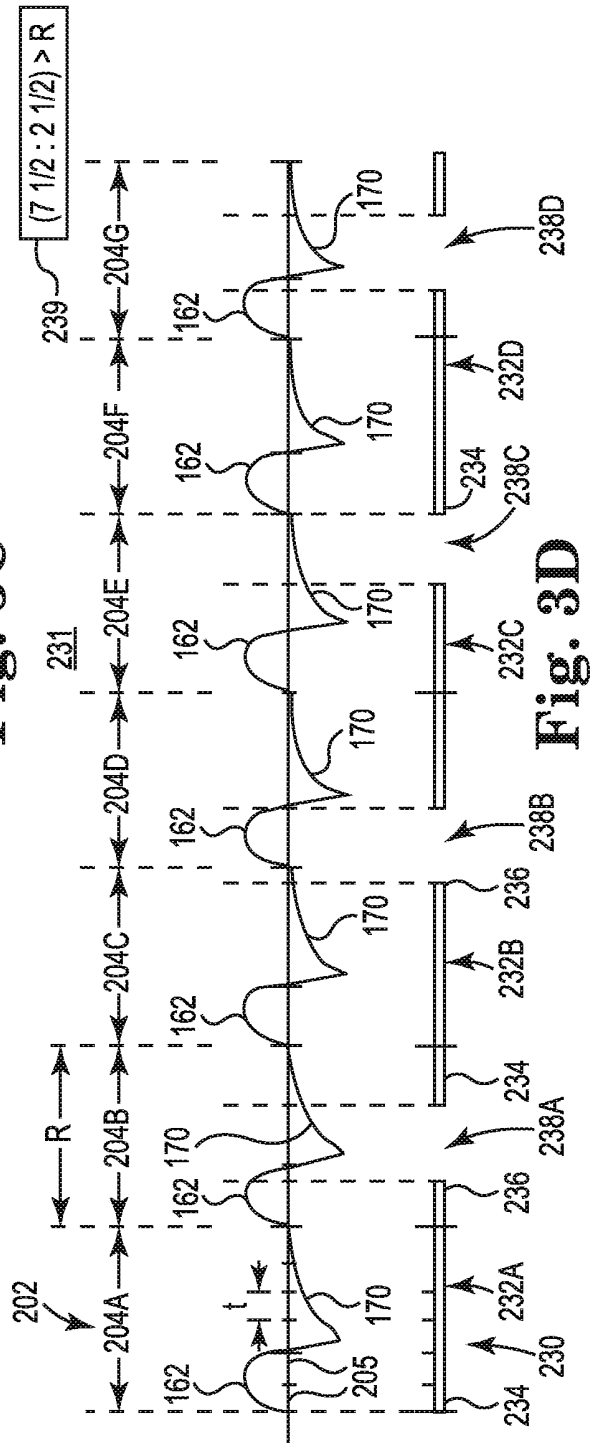

202
204A
204B
204C
204D
204E
204F
204G
R
(7 1/2 : 2 1/2) > R
239
231
162
170
205
t
230
232A
232B
232C
232D
234
236
238A
238B
238C
238D

Fig. 3D

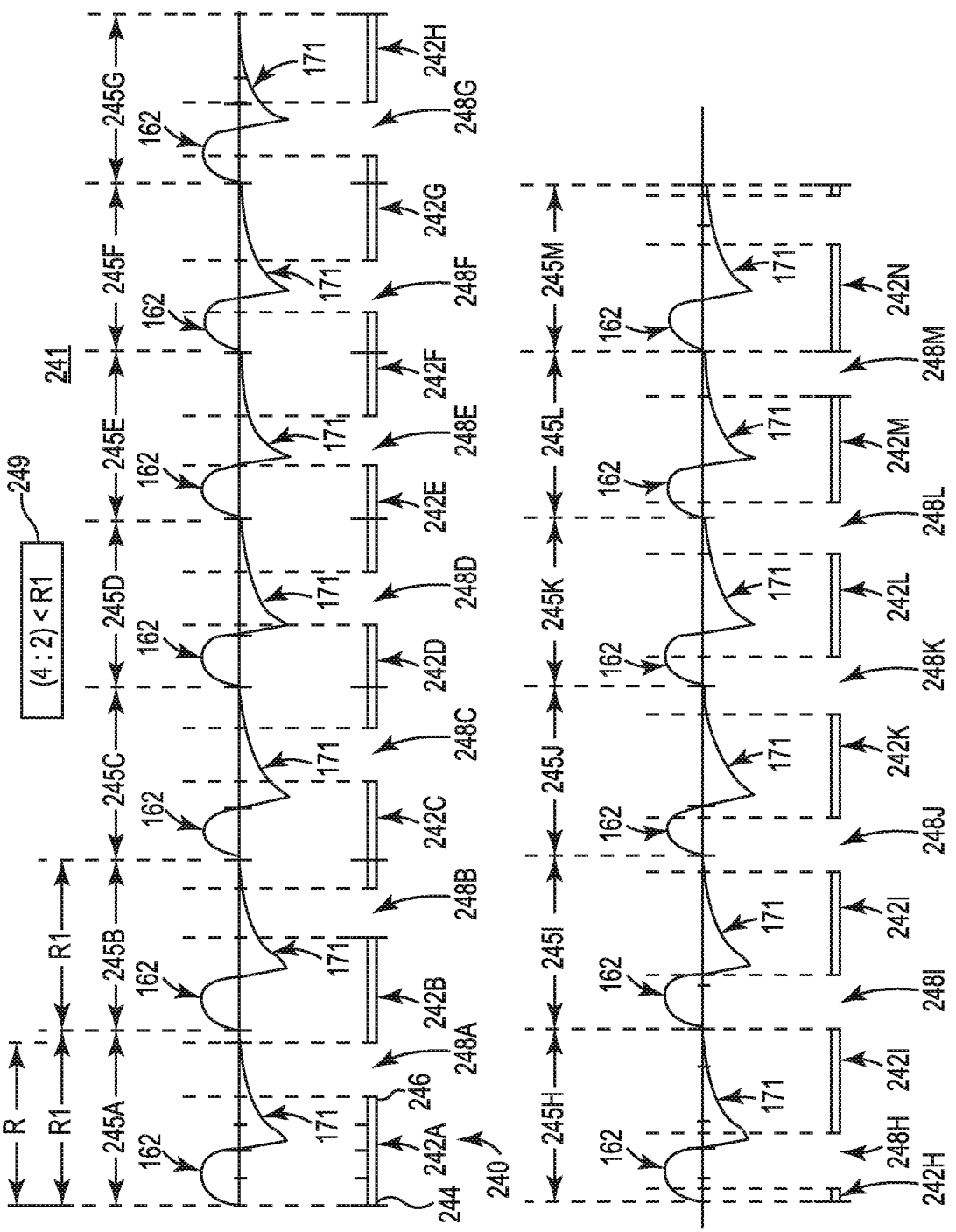

R
R1
R1
245A
245B
245C
245D
245E
245F
245G
245H
245I
245J
245K
245L
245M
241
249
(4 : 2) < R1
162
171
246
240
244
242A
242B
242C
242D
242E
242F
242G
242H
242I
242K
242L
242M
242N
248A
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248I
248J
248K
248L
248M

Fig. 3E

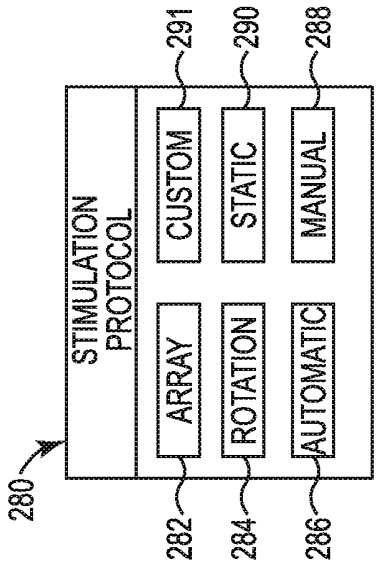


Fig. 5

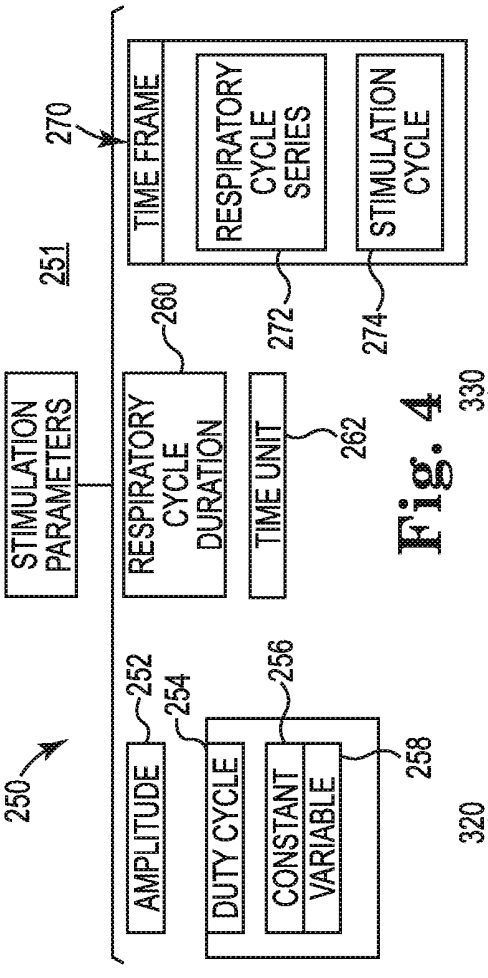


Fig. 4

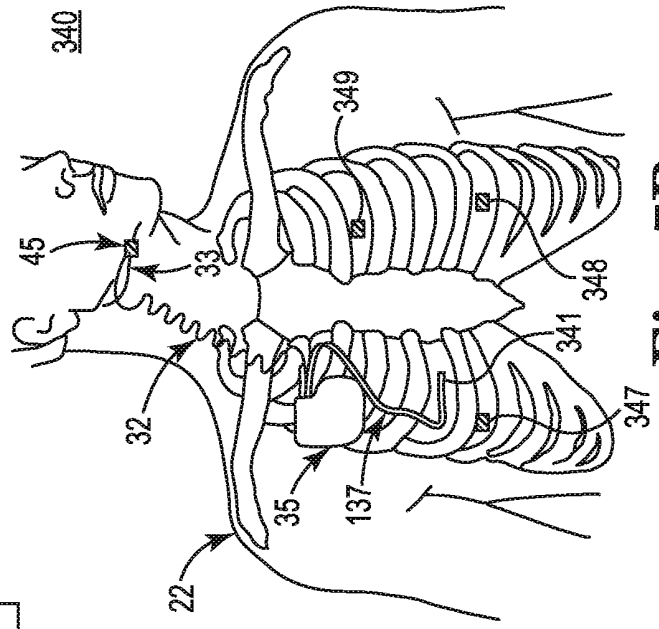


Fig. 7B

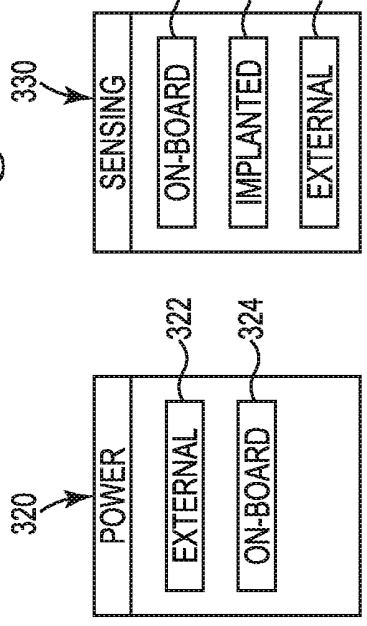


Fig. 7A

Fig. 6

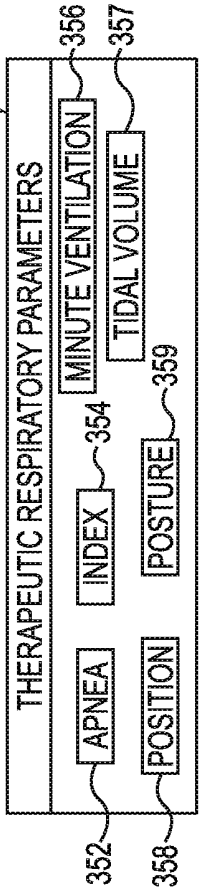


Fig. 8

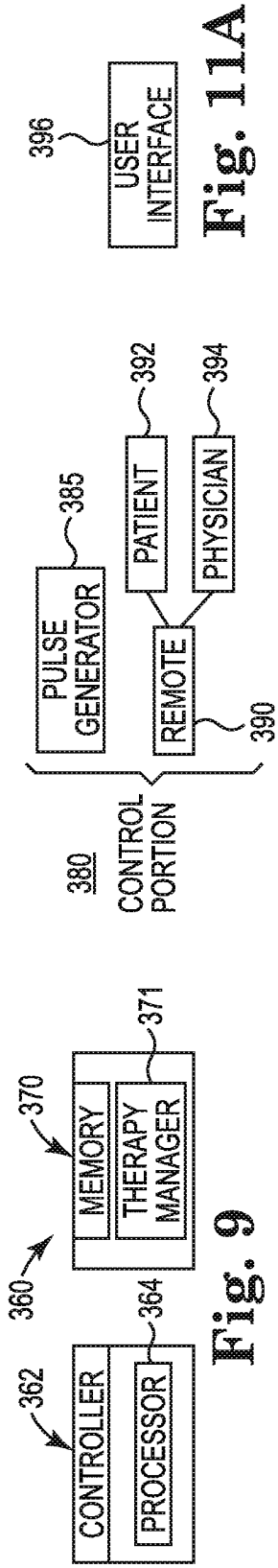


Fig. 9

Fig. 10

Fig. 11A

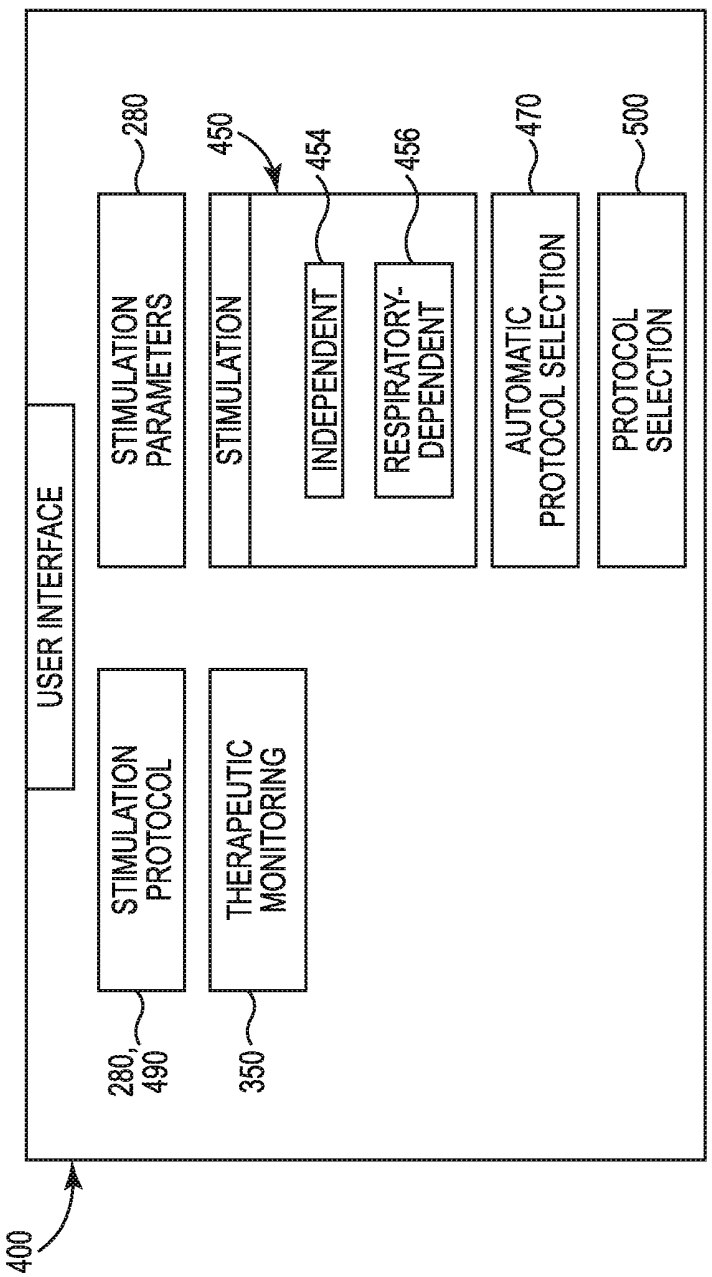


Fig. 11B

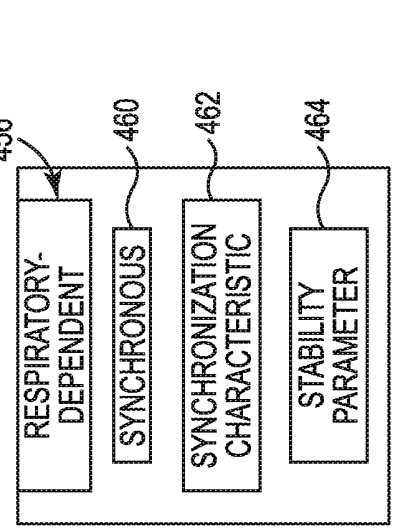


Fig. 13

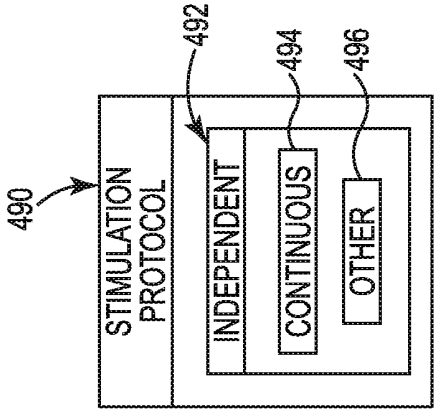


Fig. 15A

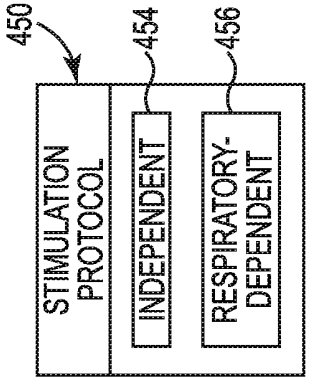


Fig. 12

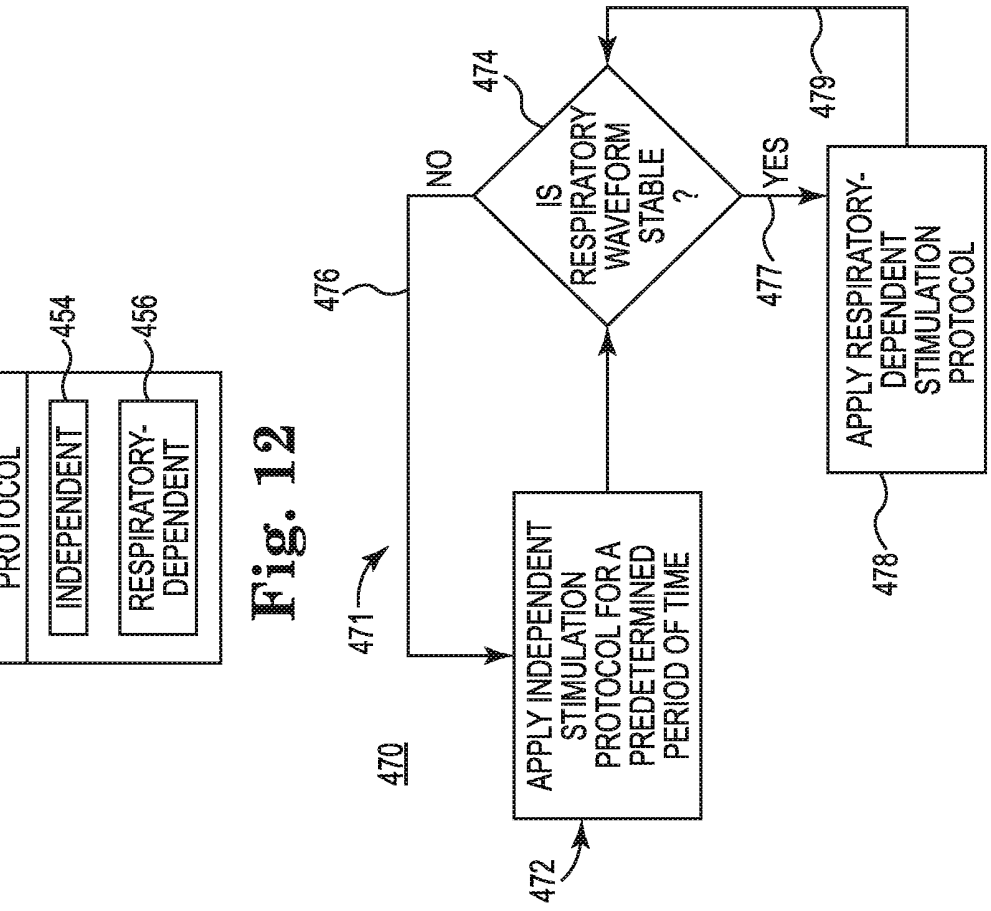


Fig. 14

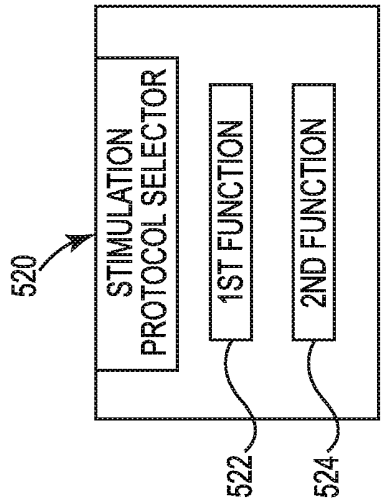


Fig. 15C

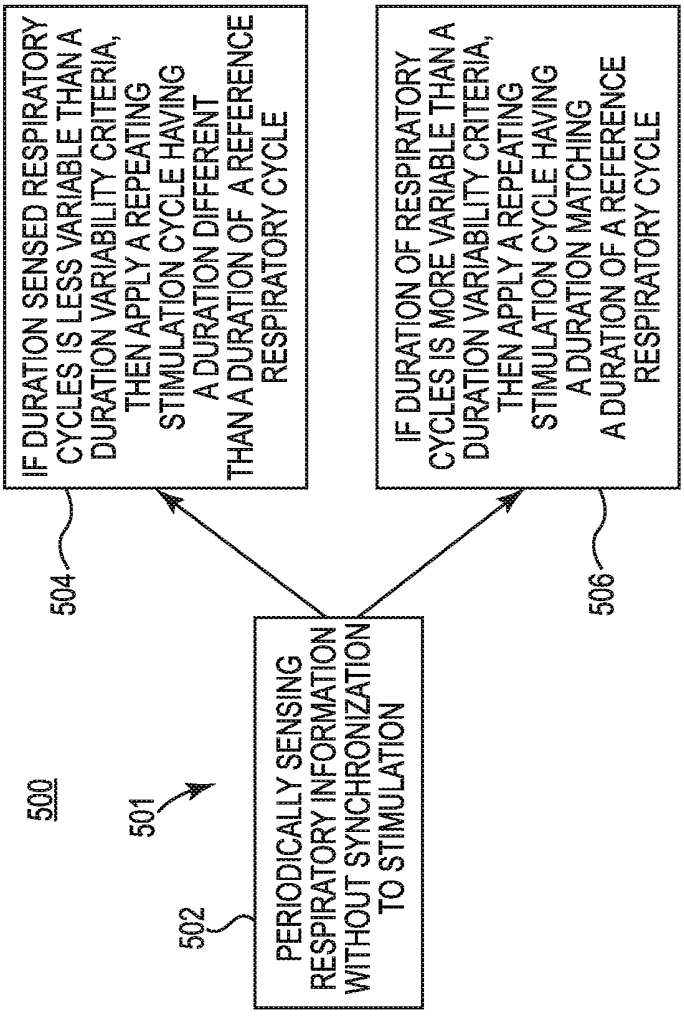


Fig. 15B

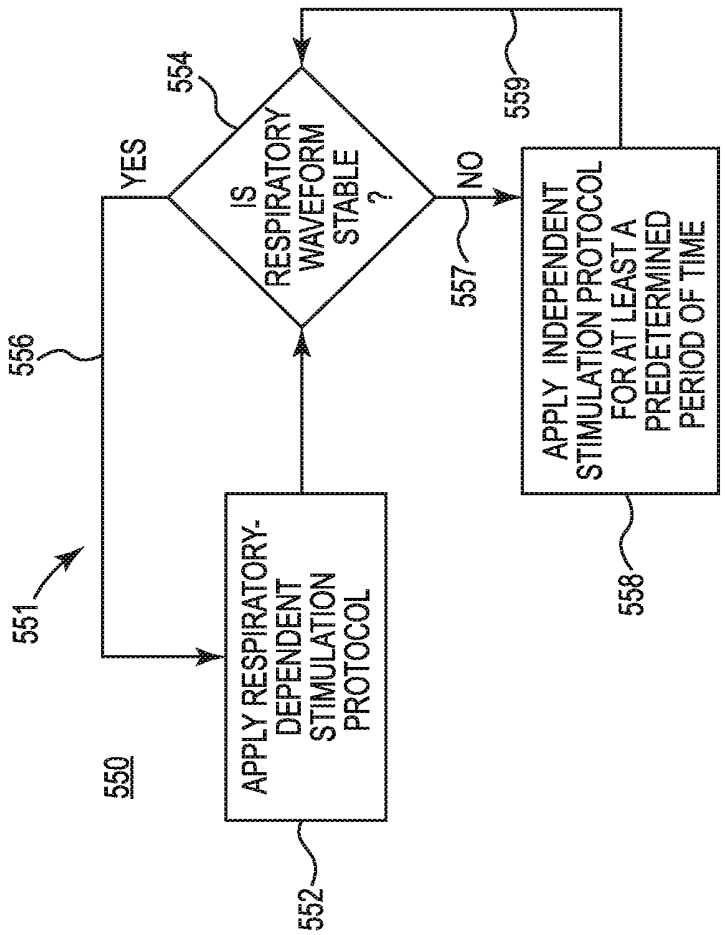

550
551
552
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559
YES
NO
IS RESPIRATORY WAVEFORM STABLE ?
APPLY RESPIRATORY-DEPENDENT STIMULATION PROTOCOL
APPLY INDEPENDENT STIMULATION PROTOCOL FOR AT LEAST A PREDETERMINED PERIOD OF TIME

Fig. 15D

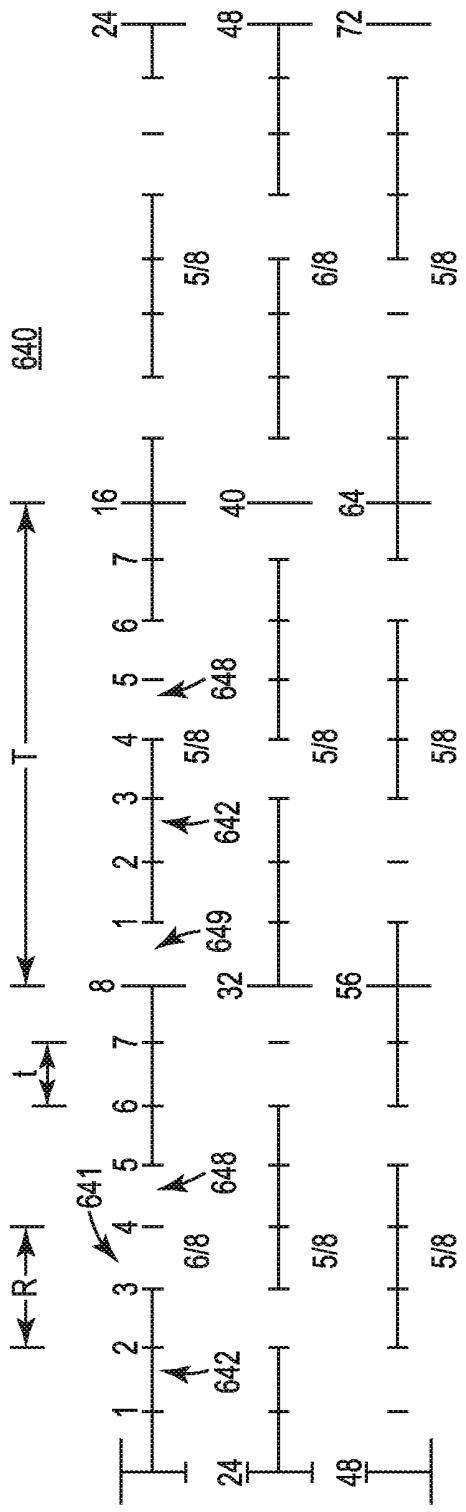


Fig. 16A

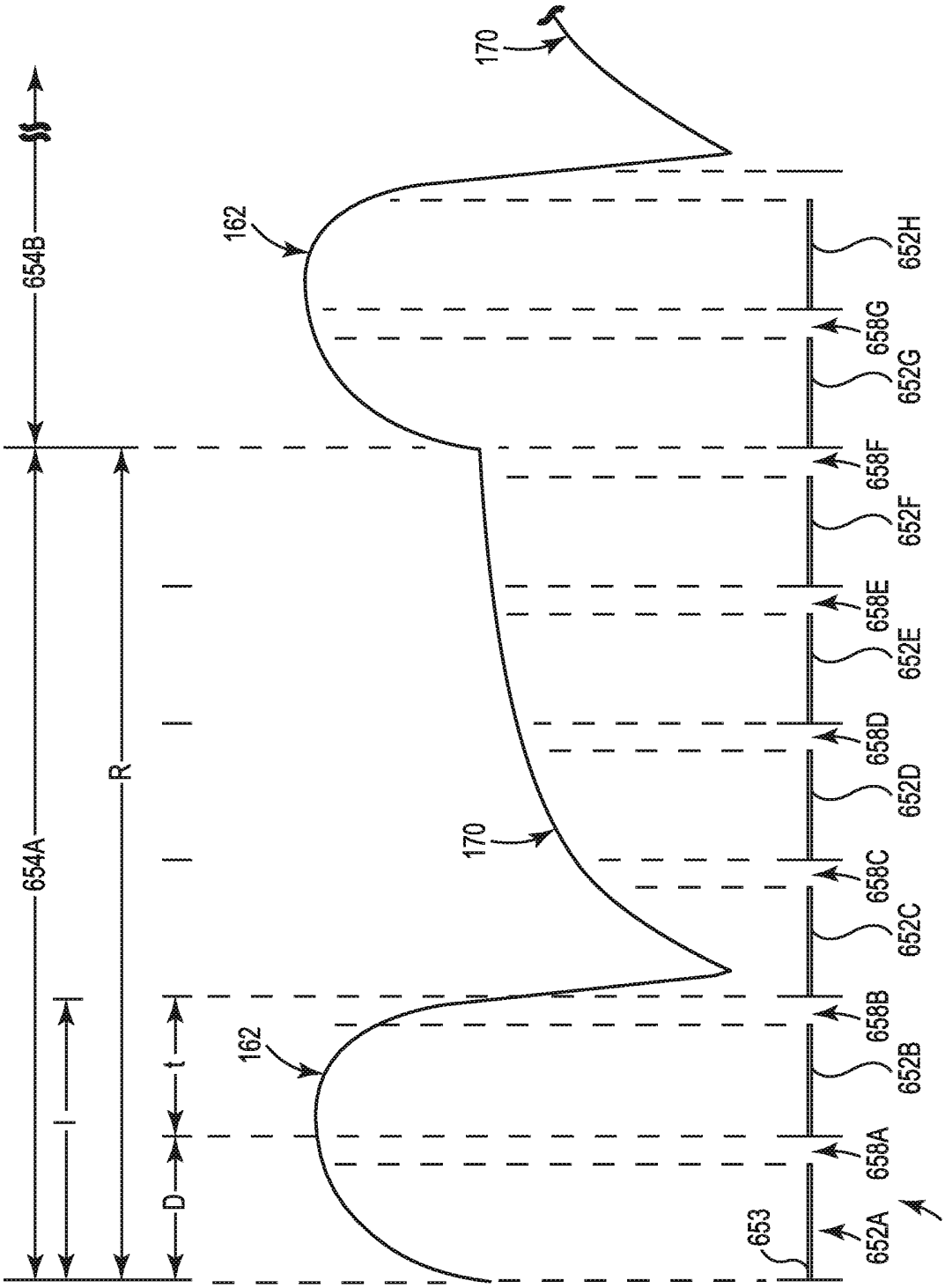

654B
654A
R
l
t
D
162
162
170
170
653
652A
658A
652B
658B
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652E
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658G
652H
650

Fig. 16B

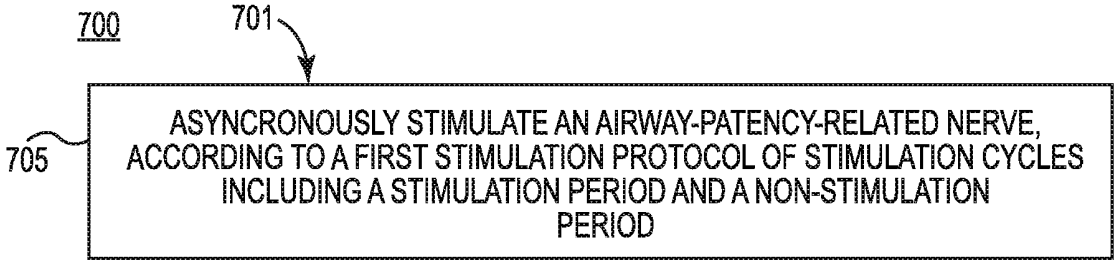


Fig. 17A

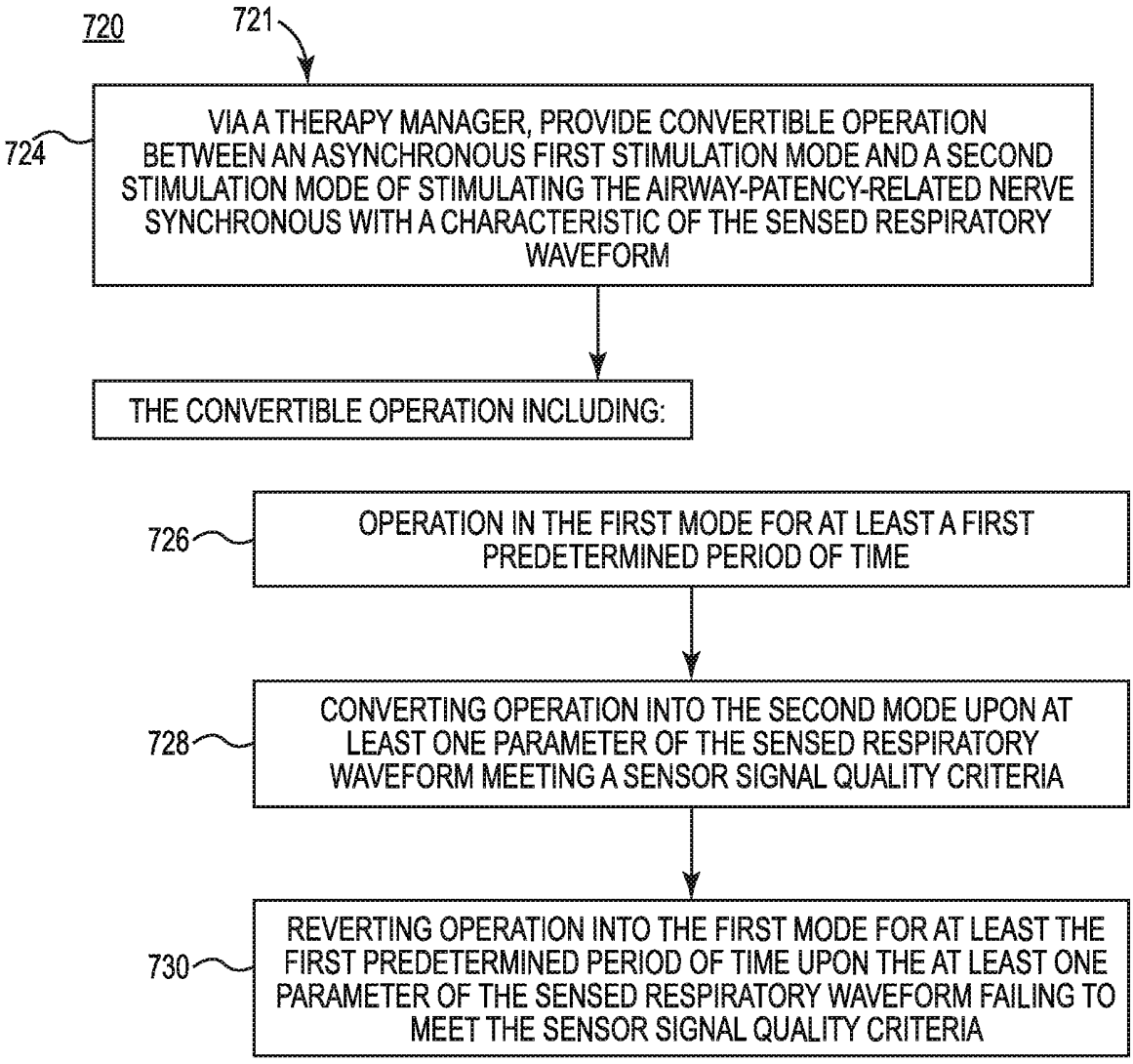


Fig. 17B

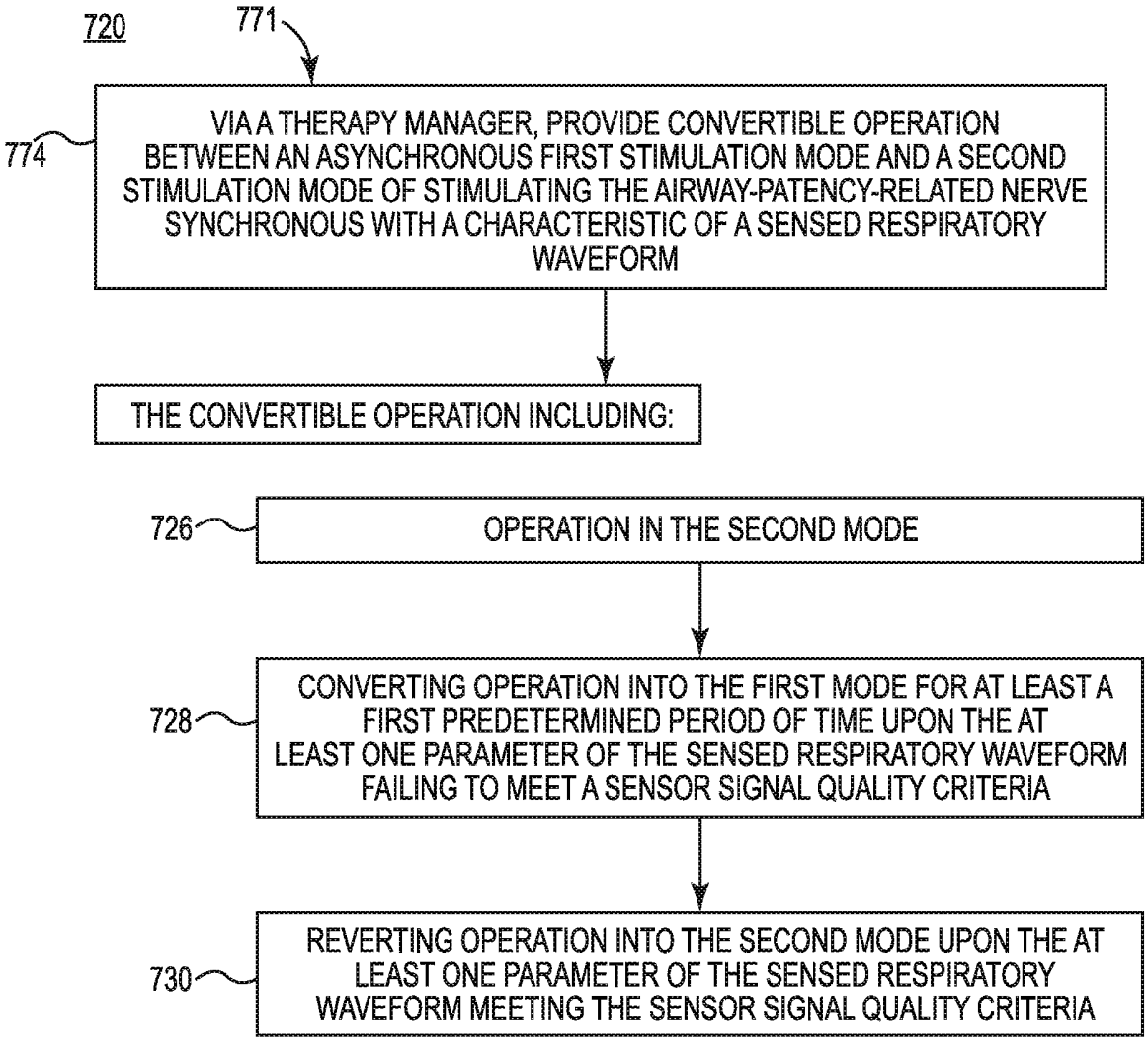


Fig. 17C

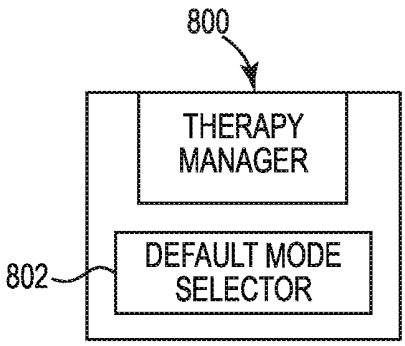


Fig. 18

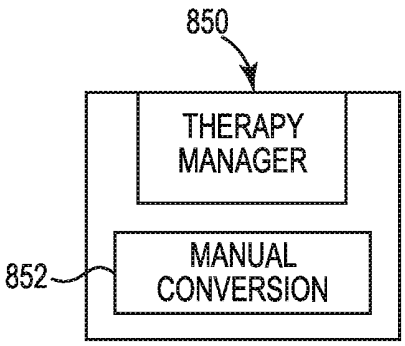


Fig. 19