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METHODS AND SYSTEMS FOR DELIVERY OF FLUIDS, AEROSOLS AND ACOUSTIC ENERGY TO TISSUE SURFACES, CAVITIES AND OBSTRUCTED PASSAGES SUCH AS INTRANASAL OSTIA

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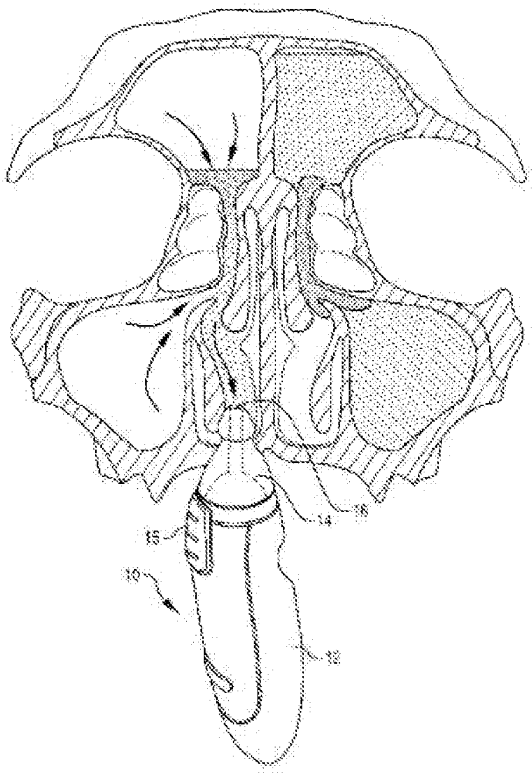
Abstract of WO2010077980 (A1)

Methods and systems for delivering fluids, aerosols, and/or ultrasound energy to target sites on tissue surfaces and within body cavities or lumens, obstructions or undesired materials associated with body cavities and tissue surfaces and, particularly, target sites on tissue surfaces or at obstructions within natural orifices, such as ear, nose and

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throat passages and, particularly, nasal passages and cavities are provided. In one aspect, methods and systems for delivering fluids and/or aerosols to target sites such as nasal passages at generally high frequency (e.g., ultrasound) pulsation rates and at multiple, alternating pulsation rates are provided. In another aspect, methods and systems for delivering high frequency acoustic energy, including high intensity ultrasound and high intensity focused ultrasound, directly to tissue, or to obstructions in passages or cavities such as nasal passages, sinuses and sinus ostia are provided.

FIG. 2B



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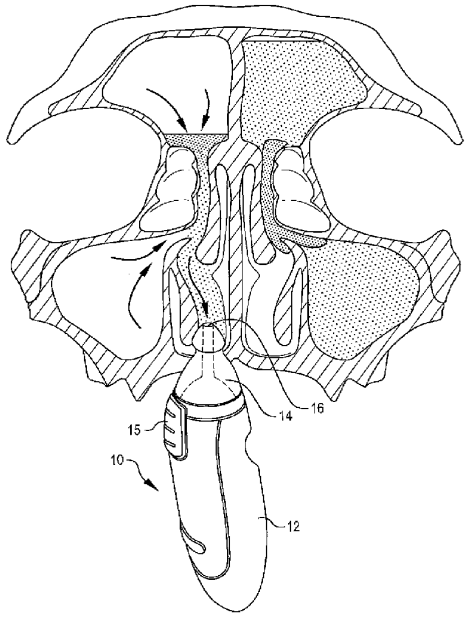
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FIG. 2B



(57) Abstract: Methods and systems for delivering fluids, aerosols, and/or ultrasound energy to target sites on tissue surfaces and within body cavities or lumens, obstructions or undesired materials associated with body cavities and tissue surfaces and, particularly, target sites on tissue surfaces or at obstructions within natural orifices, such as ear, nose and throat passages and, particularly, nasal passages and cavities are provided. In one aspect, methods and systems for delivering fluids and/or aerosols to target sites such as nasal passages at generally high frequency (e.g., ultrasound) pulsation rates and at multiple, alternating pulsation rates are provided. In another aspect, methods and systems for delivering high frequency acoustic energy, including high intensity ultrasound and high intensity focused ultrasound, directly to tissue, or to obstructions in passages or cavities such as nasal passages, sinuses and sinus ostia are provided.

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METHODS AND SYSTEMS FOR DELIVERY OF FLUIDS, AEROSOLS AND ACOUSTIC ENERGY TO TISSUE SURFACES, CAVITIES AND OBSTRUCTED PASSAGES SUCH AS INTRANASAL OSTIA

Technical Field

The present invention relates to methods and systems for delivering fluids, aerosols, and/or acoustic energy to tissue surfaces, body cavities or lumens, obstructions or undesired materials associated with body cavities or on tissue surfaces, and particularly to tissue surfaces on or near natural orifices, such as ear, nose and throat passages and, particularly, nasal and sinus passages and cavities. In one aspect, the present invention relates to methods and systems for delivering fluids and/or aerosols to tissue surfaces, body cavities or lumens and obstructions, such as to nasal passages, at generally high frequency (e.g., sonic and/or ultrasound) pulsation rates. In another aspect, the present invention relates to methods and systems for delivering acoustic energy (e.g., sonic and/or ultrasound energy, and including high intensity ultrasound (HIU) and high intensity focused ultrasound (HIFU)) directly to tissue, or to obstructions in passages or cavities such as nasal passages, sinuses and sinus ostia.

Background

Rhinitis is produced by irritation and inflammation of the mucous membranes of the nasal cavities and is generally caused by allergic reactions, environmental irritants, bacteria and/or viruses. Symptoms of rhinitis include runny nose, nasal congestion and post-nasal drip. Rhinitis has been associated not only with discomfort, congestion and nasal conditions, but also sleeping problems, ear conditions and learning challenges. Treatment generally involves administration of antihistamines, leukotriene antagonists, nasal corticosteroids, decongestants, allergen immunotherapies, or saline irrigation of sinus cavities.

Sinusitis is produced by a number of pathologic processes, including inflammation of the sinus cavities, poor mucus transport, obstruction of passages from inflammatory debris and growth of biofilms within the sinuses and their drainage systems (ostea). Additionally, resulting stagnation, edema and poor blood flow in the surrounding tissue further decreases the ability of blood borne assistance in the form of immune modulators and antibiotics to reach the site. Microorganisms encased in biofilms are notoriously difficult to treat, since the biofilm matrix is highly resistant both to the action

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of the immune system and to treatment with antibiotics. Sinusitis therapy may involve saline irrigation and administration of aerosols, as well as the administration of drugs such as antibiotics, decongestants, antihistamines and nasal steroids, sinus surgery, balloon sinuplasty and administration of nebulized antibiotics. Response rates for current therapies are generally relatively low, both on a short term and a long term basis. This is likely because of the multifactorial nature of this disease as described above. Each individual therapy used as standard treatment for sinusitis does not address all pathophysiologic causes that accumulate to cause the disease, sinusitis. This is true for other diseases such as chronic ear infections, recurrent skin infections, chronic wounds, vascular plaques, gastroenterologic obstructions and solid tumors.

Nasal irrigators for application of both solutions and aerosols are well known and are used to relieve symptoms of sinusitis and rhinitis, such as nasal congestion. Routine nasal irrigation generally improves symptoms in adults with chronic rhinosinusitis, as well as children with allergic rhinitis. Irrigating fluid, such as saline, may improve nasal ciliary motility and may additionally reduce airway edema and soften the mucus, which allows more effective aspiration. Irrigation and aspiration, or suctioning, is typically performed in hospital or medical office environments using installed, wall suction systems that are quite powerful and can be quite effective. Manual irrigating and/or aspirating devices that are available for home use are generally low flow rate, low aspiration pressure devices. Neti pots and squeeze bottles, for example, are used to irrigate nasal passageways manually and, while they temporarily relieve symptoms, they provide little long term comfort.

U.S. Patent Publication US 2008/0154183 A1 discloses self-contained, motorized devices that provide continuous or intermittent suction, as well as continuous or intermittent, on-demand delivery of irrigating fluid to nasal passages. U.S. Patent Publications US 2009/0281454 A1, 2009/0281482 A1, 2009/0281483 A1 and 2009/0281485 A1 disclose additional features of irrigation and aspiration devices. The disclosures of these patent publications are incorporated herein by reference in their entireties.

Commercial devices provide pulsed mist and/or a pulsating rinse to nasal passages using misting wands. Recent product improvements include a flex tip allowing 360° rotation with a tip locking and release feature, variable, stepless pressure control and a calibrated pulse rate. Different wands may be provided for the pulsed mist and pulsating rinse modes.

Delivery of liquid rinses and mists to nasal passages is described in the patent literature. U.S. Patent Publication US 2007/0299396 A1 discloses a pulsatile irrigation

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device producing a calibrated pulsatile rinse of 1200—1250 pulses/min, driven by a piston driven pump assembly. Atomization to droplets of about 15-25 microns is accomplished using a bolt encased in the end of the tip. U.S. Patents 4,776,990, 4,805,614 and WO 2007/129297 disclose devices for home and office use that provide water-saturated, pressurized, heated air to nasal passages.

Many different types of nebulizers and aerosol generators have been developed. Some devices employ ultrasound transducers to nebulize solutions or generate aerosol droplets. U.S. Patent 3,774,602, for example, discloses a disposable, cartridge-type single shot ultrasonic nebulizer for inhalation therapy. U.S. Patent 4,109,863 discloses another apparatus for ultrasonic nebulization of liquid samples or suspensions. U.S. Patent 4,319,144 discloses a nebulization control system for a piezoelectric ultrasonic nebulizer. U.S. Patent 6,357,671 discloses another ultrasonic nebulizer that is controllable to vary the amplitude of the ultrasonic output.

Liquid aerosols may also be produced using micropumps, including electronic micropumps. In one system, a dome-shaped aperture plate or diaphragm having many tapered holes is vibrated at a high rate (e.g., 100,000 times per second). The rapid vibration causes each aperture to act as a micropump, drawing liquid through the holes and ejecting consistently sized droplets.

Liquid projection apparatus having addressable nozzles are also known. U.S. Patent 6,394,363 discloses a device having multiple transducers associated with multiple nozzles for projecting liquid as jets or droplets from selected nozzles. Related liquid projection apparatus are described in PCT International Publications WO 2008/044069 A1, WO 2008/044070 A1, WO 2008/0044071 A1, WO 2008/0044072 A1 and WO 2008/0044073 A1.

Application of ultrasound directly or indirectly to the nasal passages, or to tissue in the nasal passages, has also been proposed. Experimental studies administering low intensity (1 W/cm^2), pulsed (1:9) and continuous therapeutic ultrasound at a frequency of 1 MHz to sinuses by application of an ultrasound soundhead to the skin of the cheeks and forehead were conducted to ascertain the effect on chronic sinusitis and chronic rhinosinusitis. Ansari et al., Therapeutic ultrasound as a treatment for chronic sinusitis, *Physiotherapy Research International*, 9(3) 144-146 (2004); Ansari et al., Physiotherapty for chronic rhinosinusitis: The use of continuous ultrasound, *International Journal of Therapy and Rehabilitation*, July 2007, Vol 14, No 7; Ansari et al., A preliminary study into the effect of low-intensity pulsed ultrasound on chronic maxillary and frontal sinusitis, *Physiotherapy Theory and Practice*, 23(4):211-218, 2007.

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The use of high intensity focused ultrasound (e.g., HIFU) is well known for ablation or remodeling of various types of tissue. Ultrasound catheter systems for delivering ultrasound energy for ablating obstructions within blood vessels using an ultrasound transmission wire or ultrasound transmission member are described, for example, in U.S. Patents 7,297,131 and 5,989,208.

A handheld, focused ultrasonic therapeutic device for treating skin lesions involved with gynecological disorders is described in U.S. Patent Publication US 2005/0080359. A supersound treatment apparatus suitable for treatment of rhinitis is described in PCT International Patent Publication WO 2008/009186. Devices targeting ultrasound beams on subepithelial layers of nasal mucosa in the nasal turbinates have been reported to reduce the volume of inferior turbinates, while increasing the volume of nasal ventilation.

U.S. Patent Publication US 2008/0027423 discloses a system for treatment of nasal tissue by application of ultrasound energy directly to tissue regions beneath the surface of the turbinate tissue. Fluid may be infused or injected directly into the turbinate tissue being treated, e.g. to enlarge the size of the turbinates and ensure delivery of ultrasound energy directly to the tissue. U.S. Patent Publications 2007/0144529 and 2008/0027423 relate to injecting fluid into the nasal turbinate using retractable needles at the end of a wand and then delivering ultrasound energy into the turbinate tissue. The treatment is accomplished using frequencies of from 0.5 to 12 MHz, generally from 5 to 12 MHz. Cooling fluid and/or radio frequency (RF) energy may also be delivered from the ultrasound and infusion probe.

Other modalities, including surgical techniques, are also used for treating tissue in intranasal passages. Somnoplasty uses controlled, low-power radiofrequency energy to create one or several submucosal volumetric lesions, which are resorbed over a period of several weeks to reduce unwanted tissue volume and stiffen remaining tissue in desired areas. Electrosurgical techniques are used for ablating, shrinking, coagulating or otherwise modifying tissue, including enlarged or hypertrophied nasal turbinates. In some systems, an active electrode of an electrosurgical probe is positioned in proximity to target tissue in the presence of an electrically conductive fluid. When a high frequency voltage is applied, tissue in proximity to the electrode is ablated, severed, or modified. Endoscopic techniques such as balloon sinuplasty, in which a sinus balloon catheter is positioned across a blocked ostium and inflated to restructure the blocked ostium, are also used for opening blocked passageways. Placement of stents and other implantable devices in sinus passageways is also performed to maintain patency.

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Rhinitis and sinusitis remain widespread throughout many populations despite the many devices and systems described in the prior art. Effective and long-lasting reduction of mucus and accumulated inflammatory debris and reduction in the growth of biofilms within the nasal passages, sinuses and their drainage systems, remain challenging despite the proliferation of treatment options. The disclosure presented herein is directed, in part, to providing improved methods and systems for delivery of fluids, aerosols and ultrasound energy to tissue surfaces, cavities and obstructed sites in passages, lumens or cavities such as nasal passages, sinuses and sinus ostia.

Summary

Methods and systems of the present invention employ the application of acoustic energy, such as generally high frequency (e.g., sonic and/or ultrasound) acoustic energy, directly and/or through the delivery of pulsed irrigation fluids and/or aerosol flows, to address a range of pathophysiological processes that accumulate, and interact, to cause various illnesses and conditions, and to produce undesired symptoms. Methods and systems of the present invention may be applied for the treatment of tissue sites such as skin surfaces, organs and internal tissue surfaces, and to obstructions on tissue surfaces or within body cavities, lumens or the like, for disruption and/or removal of the obstruction(s). Some embodiments involve the delivery of acoustic energy directly to tissue or to obstructions, or delivery of pulsed irrigation fluids and/or aerosol flows, and employ multiple modes of administration, such as delivery of acoustic energy and/or irrigation fluid(s) or aerosol(s) at multiple frequencies (e.g. ultrasound and/or sub-ultrasound frequencies), intensities, pulse durations, pulse repetition rates, duty cycles, and the like. Yet other embodiments involve the administration of acoustic energy, or delivery of pulsed irrigation fluids and/or aerosol flows, according to single or multiple modes of operation, in combination with another treatment modality such as administration of an antimicrobial or therapeutic agent, application of electromagnetic radiation, an electrical field, radio frequency energy, laser energy, microwave energy, or the like.

In one aspect, methods and systems of the present invention produce a liquid stream and/or aerosol particles and/or aerosol droplets and deliver the liquid and/or aerosol to a tissue surface, or to a cavity or lumen or an obstruction, at generally high frequency pulsations (generally >1500 Hz) in "sonic" (sub-ultrasound) and/or ultrasonic frequency range(s) and at a generally low pressure. The tissue surface may be an external tissue surface, such as a skin surface or a wound, or it may be a tissue surface in a body cavity or lumen, such as in the vascular system, the respiratory system, the

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gastrointestinal system, the reproductive system, or a natural orifice such as the mouth and/or throat, the ear, the nose, including the nasal cavity and nasal passageways. The obstruction may be an obstruction in a body cavity, such as a nasal cavity or passageway or in another natural orifice, or at another internal or external body location and may comprise pathological tissue, cellular debris, or the like. The aerosol may comprise a suspension of fine solid particles, or liquid droplets, or a mixture of solid particles and liquid droplets, and it may be generated using a variety of systems known in the art for generating aerosols.

In some embodiments, delivery of an irrigating liquid and/or aerosol may be accomplished using multiple and/or alternating pulsations having different frequencies, intensities, pulse durations, pulse repetition rates and/or duty cycles. Pulsed delivery using generally high frequency pulsations, or alternating pulsations of different frequencies, may preferentially provide cavity entry (e.g., by Helmholtz principle), biofilm dissolution or reduction, degradation of pathological tissue, acoustic enhancement of delivery of medications or other treatment modalities, improvement of circulation, local immune modulation, and other desired effects. Different operating modalities providing delivery of acoustic energy at multiple frequencies may be provided, and may be selectable by the user, to preferentially promote various functionalities.

Liquid streams and aerosol droplets delivered to tissue surfaces such as skin, natural orifice cavities such as intranasal passages, and to obstructions at a variety of tissue sites by means of generally high frequency pulsations are preferably aqueous and may consist of saline, or may consist essentially of saline (with small amounts of active or inactive compositions dissolved in or carried by the saline). Liquid streams and aerosol droplets delivered using high frequency pulsations may alternatively, or additionally, comprise saline or another carrier solution comprising antibiotics, antimicrobial agents, drugs, or the like, dissolved or suspended in the liquid solution and/or delivered as aerosol particles or droplets. Suitable medications for delivery in a liquid stream or as aerosol particles or droplets may comprise (and are not limited to), in addition to saline, hypertonic saline, lactated ringer's solution, dead sea salt solution, antibiotics, midazolam, fentanyl, insulin, growth hormone, one or more growth factors, gentamycin, clindamycin, ciprofloxacin, cefuroxime, levofloxocin, tobramycin, ampicillin+sulbactam, amphotericin, tobramycin/amphotericin combinations, cefotaxime, ceftriaxone, fluticasone, budesonide, mometasone furoate monohydrate, xylitol, eucalyptus, tea tree oil, capsaicin, grapefruit seed extract, oil of wintergreen, and the like.

Devices of the present invention for delivery of an irrigating liquid and/or aerosol to a desired site on the skin or within the respiratory system or a natural orifice are

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generally handheld devices comprising a handle and at least one solution and/or aerosol discharge port. Source liquid for discharging onto tissue surfaces, or for generation of aerosol droplets, may be stored in a reservoir or device assembly separate from the handheld device and provided to the handheld device using appropriate tubing, conduits, and the like. Alternatively, devices of the present invention may incorporate a refillable liquid reservoir for storing source liquid, or mate with a disposable cartridge or liquid reservoir that may be provided in a pre-filled or fillable format and is attachable to and detachable from the device, generally at the handle portion. Device features and configurations, including irrigation and aspiration features, nozzle features, dual function switch features, articulating head features, pump and fluid control features and aspiration features may be similar to those described in U.S. Patent Publications 2008/0154183 A1, US 2009/0281454 A1, 2009/0281482 A1, 2009/0281483 A1 and 2009/0281485 A1, the disclosures of which are incorporated herein by reference in their entireties.

In another aspect, methods and systems of the present invention deliver generally high frequency (e.g., ultrasound) acoustic energy for application directly to tissue surfaces or to obstructions within body cavities or lumens, including blocked sites or obstructions in orifices or lumens such as in nasal passages. In one embodiment, devices of the present invention comprise an insertion wand sized and configured for insertion into at least a portion of a body cavity or lumen, or for contacting a target site on a tissue surface or at an obstruction within a body cavity or lumen, and an acoustic energy delivery member associated with the insertion wand for conveying generally high frequency acoustic energy (e.g., ultrasound energy, including high intensity ultrasound (HIU) and high intensity focused ultrasound (HIFU)) directly to tissues or obstructed sites, such as within nasal passages. Delivery of high frequency acoustic energy provides mechanical and cavitational effects that promote opening of blocked passages and lumens, such as nasal passages, sinuses and sinus ostia. High frequency, generally high intensity acoustic energy may be provided directly to an obstructed site, such as an intranasal passage or another body lumen or cavity, to preferentially disrupt and/or ablate pathological tissue, obstructions, cellular debris and the like, including inflammatory buildup, bony hypertrophy, various types of plaque, and biofilms.

In some embodiments, delivery of acoustic energy at particular frequencies, intensities, pulse durations, pulse repetition rates, and/or duty cycles, may be selected to promote effects such as immune modulation, improved vascularization, bioacoustic effects and improved efficacy of administered agents such as antibiotic, antimicrobial and other agents. Systems and methods of the present invention may also provide delivery of one or more sequences of acoustic energy, with each sequence providing delivery of

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acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, and/or duty cycle. Multiple sequences may be programmed in the device as multiple programmed protocols may be selectable by a user. In some embodiments, each acoustic energy delivery sequence, or each programmed protocol may target a specific effect, tissue type, administered agent, or the like.

In yet another aspect, methods and systems of the present invention provide delivery of an irrigating liquid and/or generally high frequency acoustic energy (e.g., ultrasound energy) to a desired internal site of a subject using a catheter assembly. In these embodiments, irrigating fluid and/or acoustic energy is provided to a tissue site, or an obstruction, at an internal target site, such as a site in the vascular system, the respiratory system, the gastrointestinal system, the reproductive system, or the like, using an acoustic energy delivery system for delivery of acoustic energy and tubular structures for delivery of an irrigating liquid. Various systems and methods for delivery acoustic energy to internal body sites for purposes of treatment, disruption, ablation and/or removal of undesired tissue or obstructions, and the like, are known in the art and may be used in systems and methods of the present invention. Various types of catheters employing ultrasound transducers are disclosed, for example, in U.S. Patents 5,362,309, 5,318,014, 5,315,998, 5,269,291, 5,197,946, 5,735,811, 5,197,946, 5,989,208, 6,001,069, 6,024,718, 6,623,444, 6,855,123 and 7,297,131, the disclosures of which are incorporated herein by reference in their entireties.

In some embodiments, delivery of an irrigating liquid and/or acoustic energy at particular frequencies, intensities, pulse durations, pulse repetition rates, and/or duty cycles using a catheter-based system, may be selected to promote effects such as immune modulation, improved vascularization, bioacoustic effects and efficacy of administered agents such as antibiotic, anti-restonosis and other agents. Delivery of one or more sequences of acoustic energy, with each sequence providing delivery of acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, and/or duty cycle may be provided and multiple sequences may be programmed in a catheter-based system as multiple programmed protocols selectable by a user.

Fluid and/or aerosol particles and/or droplets may be supplied in addition to delivery of high frequency acoustic energy through acoustic energy delivery systems of the present invention, in a continuous or pulsed delivery protocol, to tissue surfaces or to obstructions to promote penetration of blocked sites such as nasal passages, disruption and opening of undesired blockages, and/or to provide cooling of the target site during or following delivery of high frequency (e.g., ultrasound) acoustic energy. Pulsed delivery using high frequency pulsations promotes entry (e.g. by Helmholtz principle), biofilm

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dissolution and acoustic enhancement of medications delivered in the liquid stream and/or aerosol droplets.

Devices of the present invention may incorporate one or more aspiration ports for removal of materials from a working site prior to, during or following delivery of fluid and/or aerosol particles/droplets and/or generally high frequency acoustic energy. Multiple delivery ports may be provided for delivery of multiple (different) fluids, or for delivery of multiple types of aerosol particles/droplets, sequentially or simultaneously. Visualization and/or illumination of intranasal target sites may be provided using optical, acoustic, or other types of visualization and illumination systems incorporated in devices of the present invention. An endoscopic port may be provided for delivery of diagnostic and/or therapeutic tools, agents, and the like. Systems for delivering additional diagnostic and/or treatment modalities such as electromagnetic radiation, radio frequency radiation, laser radiation, microwave radiation, and the like, may also be provided in connection with methods and systems of the present invention.

Devices of the present invention may also incorporate one or more systems, such as one or more discrete receptacle(s), for collection of material removed by aspiration. The collected tissue, obstruction and/or debris samples may be subjected to various types of diagnostic testing, characterization, and the like. Multiple collection receptacles may be provided for collection of samples at different stages of a protocol.

Brief Description of the Drawings

Fig. 1 shows a schematic illustration showing a handheld device of the present invention for delivering fluid and/or aerosol particles or droplets to a tissue surface or an obstruction, the device being shown inserted into a user's nostril and the illustration showing, in cross-section, the internal anatomy of the nasal passageways.

Figs. 2A and 2B show schematic diagrams illustrating the use of a device shown in Fig. 1, with Fig. 2A showing insertion of the device into a nostril and operation of the device to distribute an irrigating fluid and/or aerosol pulsed at high frequency in the area of clogged nasal passageways, and Fig. 2B showing aspiration of the loosened material from the passageways following delivery of the irrigating fluid and/or aerosol.

Fig. 3 shows a schematic drawing illustrating another embodiment of a device of the present invention for delivering fluid and/or aerosol particles or droplets and/or high frequency acoustic energy (e.g., ultrasound energy) to a tissue surface.

Fig. 4 shows a schematic drawing illustrating the device of Fig. 3 inserted into a user's nasal passageway to deliver fluid and/or aerosol particles or droplets and/or high frequency acoustic energy (e.g., ultrasound energy) to a tissue surface in the nasal

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passageway and shows, schematically in cross-section, the internal anatomy of the nasal passageways.

Fig. 5 shows a schematic drawing illustrating a device similar to that shown in Fig. 3 for placement and expansion of an expandable member (e.g., balloon) in a body cavity and shows, schematically in cross-section, the internal anatomy of the nasal passageways.

Fig. 6 shows a schematic drawing of another device of the present invention inserted into a user's nasal passageway to deliver high frequency acoustic energy (e.g., ultrasound energy) to a tissue surface in the nasal passageway, with or without delivery of fluid and/or aerosol particles or droplets and shows, schematically in cross-section, the internal anatomy of the nasal passageways.

Fig. 7 shows a schematic drawing of another device of the present invention for delivering high frequency acoustic energy (e.g., ultrasound energy) to a tissue surface, with or without delivery of fluid and/or aerosol particles or droplets.

Figs. 8A -8E show schematic diagrams illustrating the use of a device similar to that shown in Figs. 6 and 7, with Fig. 8A showing insertion of the device into a nostril; Fig. 8B showing extension of an active therapeutic component for delivering generally high frequency acoustic energy (e.g., ultrasound energy) to a blockage in a nasal passageway; Fig. 8C schematically showing delivery of acoustic energy through the active therapeutic component to disrupt the blockage; Fig. 8D showing aspiration of debris from the site; and Fig. 8E showing cleared nasal passageways following treatment.

Like numbers have been used to designate like parts throughout the several drawings to provide a clear understanding of the relationship of the various components and features, even though different views are shown. It will be understood that the appended drawings are not necessarily to scale, and that they present a simplified, schematic view of many aspects of systems and components of the present invention. Specific design features, including dimensions, orientations, locations and configurations of various illustrated components may be modified, for example, for use in various intended applications and environments.

Detailed Description

Specific methods and systems of the present invention for pulsed delivery of liquids and/or aerosols, and/or for delivery of generally high frequency, generally high intensity acoustic energy (e.g., ultrasound) to intranasal areas such as nasal passages, sinuses and sinus ostia, are described with reference to the accompanying drawings. It will be appreciated that these specific embodiments are illustrative, and that systems and

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methods of the present invention may be used in a variety of applications, as described elsewhere in this specification.

Fig. 1 shows a schematic illustration of one embodiment of device for pulsed delivery of liquids and/or aerosols to a subject's nasal passages. As shown in Fig. 1, device 10 comprises a handle 12, a nostril interface member 14 and a discharge port 16. Handle 12 has a size and configuration that facilitates holding in one or both hands and may include ridges, indentations, curved contours, and the like, to enhance the ergonomic feel and secure handling of the device. Handle 12 may include at least one activation mechanism, such as control 15, for activating one or more device functions. In one embodiment, for example, control 15 may be operated by a user to activate, or inactivate, a pulsatile flow of liquid and/or aerosol from discharge port 16 in nostril interface member 14.

Handle 12 may also house power supply and control elements for operating the device. Power may be supplied to device 10 by physical connection to an electrical power source such as a separate control unit or an electrical outlet by means of a conventional power cord, as is well known in the art. Power may alternatively be supplied by a battery source mounted in the handle. Battery power sources may be provided as replaceable or rechargeable components. Battery charging may be accomplished by direct coupling of battery terminals, or conductive elements provided on the housing, with a power source, or by indirect coupling using, for example, an inductive charging system. Handle 12 may also house control mechanisms, such as mechanical or electronic switches, microprocessors, power supplies, and the like, and may house an aerosol generation device and/or the system for generating pulsatile discharge of liquid and or aerosol droplets.

Handle 12 and nostril interface member 14 may be provided in an integrated, single piece construction, or they may be provided as separate components that are detachable from one another. Nostril interface member 14 comprises at least one discharge port 16 at a distal end of the member, and generally has a size and configuration that permits insertion of a distal end of the interface member and discharge port 16 into the nostril of a user. The distal end of the nostril interface member may have a generally curved or tapered configuration, with a smaller diameter area at the discharge outlet, such that the discharge outlet and distal end of the interface member may be inserted into the nostril, while more proximal surfaces of the nostril interface member contact the nostril opening and effectively "seal" the opening during use of the device. In some embodiments, the nostril interface member may be flexible and may comprise a telescoping structure that permits extension and retraction of the member, or adjustment

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of the member to different sizes or configurations. In some embodiments, the nostril interface member may be articulatable with respect to the handle.

In one embodiment, devices of the present invention are capable of delivering a liquid stream in a generally high frequency pulsatile flow. In another embodiment, devices of the present invention are capable of generating aerosol particles and/or droplets, and delivering the aerosol particles and/or droplets in a generally high frequency pulsatile flow. In yet another embodiment, devices of the present invention are capable of selectively delivering a liquid stream, aerosol particles and/or aerosol droplets, simultaneously or sequentially, in a generally high frequency pulsatile flow. Liquid, aerosol particles and/or aerosol droplets may be delivered from a common discharge port sequentially and intermittently, or from multiple, dedicated discharge ports, simultaneously or sequentially, and on a continuous or intermittent basis.

An aspiration channel may optionally be provided for aspiration of material from a site, such as nasal passageways. Aspiration may be provided through a common port as fluid and/or aerosol delivery, or through an additional aspiration port provided in the nostril interface member 14, or through an aspiration port provided in an auxiliary device. Although an aspiration system employing a vacuum device may be provided integrally with the device and an aspiration reservoir may be incorporated into the device or used in connection with the device, aspiration may also be accomplished by interfacing an aspiration channel within the device with a vacuum or suction source provided in a medical facility. Interface tubing may be provided for this purpose.

Figs. 2A and 2B show, schematically, operation of a device as illustrated in Fig. 1. Nostril interface member 14 is inserted into and generally contacted to a user's nostril. For some applications, the nostril interface member may be sized and configured to form a substantially liquid-tight seal against a user's nostril when inserted and upon continued application of pressure in the insertion direction. After insertion and placement of the nostril interface member, the user activates a desired delivery protocol for delivery of a liquid stream, aerosol particles and/or aerosol droplets, simultaneously or sequentially, in a generally high frequency pulsatile flow, through discharge port 16. This is shown schematically by the curved dashed lines. The pulsatile delivery of liquids and/or aerosols facilitates penetration of fluids and particles through passageways and blockages and may also deliver a therapeutic effect to tissue surfaces. Liquids and other material, including debris, mucus, infected tissue, and the like may be withdrawn by aspiration using the same device following pulsatile delivery of liquids and/or aerosols, as shown schematically in Fig. 2B.

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Controls may be provided on the device handle, illustrated as actuator 15, or on an accessory device or module, allowing a user to select liquid and/or aerosol delivery modes, or allowing a user to select among various modes of operation or various pre-determined operating programs. In one embodiment, for example, a device such as that illustrated in Fig. 1 may be operated in an aerosol delivery mode whereby, upon activation, aerosol particles and/or droplets are pulsated and discharged from outlet port 16 at a generally low pressure and high frequency. In another embodiment, a single mode device may be operated in a liquid delivery mode whereby, upon activation, a high frequency pulsating liquid stream is discharged from outlet port 16, continuously or intermittently. In yet another embodiment, a user may select pulsating liquid and/or aerosol discharge modes which may also operate on a continuous or intermittent basis.

In some embodiments, multiple pulsating irrigation fluid and/or aerosol delivery options may be programmed in the device, with various operating programs being predetermined and, optionally, selectable by the user. In one embodiment, for example, a control may be actuated by a user to initiate a predetermined or selectable cycle involving multiple irrigation fluid and/or aerosol delivery protocols. Multiple different delivery protocols may involve delivery of irrigation fluid and/or aerosol at pulsation rates having a selected frequency, intensity, pulse duration, pulse repetition rate, duty cycle, and the like. Multiple different delivery protocols may additionally involve delivery of different types (e.g., composition, concentration, osmolarity, and the like) of irrigation fluids, and/or different types (e.g., composition, concentration, particle size, and the like) of aerosols.

In one embodiment, for example, a therapeutic cycle may provide delivery of from one to several different pulsation cycles that correlate with the acoustic properties of each contributing pathologic process that contributes to the disease or symptomology (e.g., sinusitis, ear infection, pneumonia, chronic skin wounds, gastroenterologic processes, tumors, and the like.) Pathologic processes that may be targeted by the therapeutic cycle may include (but are not limited to) biofilms, inflammation, mechanical obstruction, hypertrophy, poor circulation, dysfunctional immune response/modulation, and the like. In alternative embodiments, a user may select pulsating liquid rinse and/or aerosol delivery options by means of multiple selectable actuators. In any of these embodiments, multiple and selectable modes may be implemented, whereby programmed or selectable levels of liquid and/or aerosol flow or volume, aerosol particle and/or droplet size, aerosol particle and/or droplet density, pulsation frequency, temperature, and the like, may be selectable by the user.

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In one embodiment, for example, different pulsation characteristics may be provided to promote different effects. Optimal pulsation frequencies for promoting for sinus entry (resonance), biofilm dissolution, drug enhancement, immunomodulation and circulatory regulation may be different; user selectable controls may be provided for selecting pulsation frequencies or modes of operation to promote each of these functions. Alternatively, one or more pre-programmed timing sequences of application of multiple frequencies may be provided.

Aerosol generation may be accomplished using aerosol generators, such as pumps, aperture plates or diaphragms, ultrasound transducers (e.g., piezoelectric crystals), and other systems that are well known in the art. In one embodiment, solution provided at a generally low pressure is conveyed through a standard jet nebulizer to produce aerosol or finely divided liquid droplets. Aerosol droplets generated and discharged by devices of the present invention preferably have a droplet size of from about 0.5μ to about 200μ, in some embodiments from about 1μ to about 100μ, in other embodiments from about 3μ to about 60μ, and in yet other embodiments from about 5μ to about 30, entrained in gas (e.g. air).

Pulsation of the liquid and/or aerosol particles and/or droplets is generally accomplished at a frequency in excess of 100 Hz and may be accomplished at an ultrasound frequency of 20 kHz or higher. Devices of the present invention may provide either or both ultrasonic and sub-ultrasonic (sonic) oscillation of a liquid stream or aerosol as it exits the discharge outlet. A liquid flow may be pulsated at one frequency, such as a frequency less than 10 kHz, while aerosol droplets may be pulsated at a different frequency, generally at a higher frequency. Aerosol may be pulsated at frequencies in excess of about 1500 Hz, and in some embodiments in excess of about 5000 Hz, and generally at frequencies less than 10 MHz. In some embodiments, aerosol is pulsated at frequencies in excess of about 10 kHz, from about 10 kHz to about 100 kHz, in some embodiments from about 15 kHz to about 50 kHz, and in yet other embodiments from about 20 kHz to about 40 kHz.

Aerosol particles or droplets may alternatively be pulsated at two or more alternating frequencies. In one embodiment, aerosol may be pulsated at multiple alternating, sub-ultrasonic frequencies. In another embodiment, aerosol is pulsated at two or more alternating frequencies, with one or both of the frequencies being an ultrasonic frequency. According to one embodiment, for example, aerosol delivery is provided by pulsation at multiple frequencies, such as at an ultrasonic frequency of from about 20 kHz to about 40 MHz and at one or more additional ultrasonic or sub-ultrasonic frequencies.

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The pulsation frequency of delivery of liquid and/or aerosol streams may be alternated by providing multiple pulsation generators, or by operating a single pulsation generator differently. Various cycles may be implemented and, in some embodiments, a user may selectively control aerosol generation and pulsation, while in other embodiments, predetermined cycles of aerosol generation and pulsation may be provided. In one embodiment, for example, a column of mist is generated in the space between the transducer and an aerosol discharge orifice when the transducer is operated at the aerosol generation frequency, and the column of mist is then pulsated as it exits the discharge orifice when the device is operated at the pulsation frequency. Cycles may be established, and predetermined, to operate the transducer in an aerosol generation mode for a time sufficient to generate a suitable aerosol column, and then to operate the transducer in the pulsation mode for a time sufficient to discharge the aerosol from the column.

According to some embodiments, a single piezoelectric crystal or another ultrasound generating device may be operated in different modes, sequentially, to produce both aerosol and high frequency pulsations of liquid and/or aerosol. In another embodiment, multiple ultrasound transducers (e.g., two piezoelectric crystals) may be operated in aerosol generation and pulsation modes, respectively, simultaneously or intermittently, to generate aerosol and then to pulsate the generated aerosol at a generally high frequency. A dedicated aerosol generation transducer may be operable, for example, in a single operating condition or in multiple operating conditions, and a dedicated pulsation transducer may, similarly, be operable at a single pulsation frequency, or at multiple selectable pulsation frequencies.

In one embodiment, an aerosol generation system (e.g., a piezoelectric crystal or ultrasound transducer) and an aerosol pulsation system (e.g., an ultrasound transducer) are located separately. An aerosol generation transducer may be located at a liquid solution interface, for example, to generate a column of aerosol droplets extending above the liquid solution interface. An aerosol pulsation system, such as an ultrasound transducer, may be located along an aerosol column or in proximity to an aerosol discharge orifice, providing pulsatile discharge of aerosol from a discharge port.

In another embodiment wherein ultrasound transducers are used both for aerosol generation and pulsation, an aerosol generation transducer and an aerosol pulsation transducer may be located in proximity to one another. Multiple transducers may be collocated, for example, with an aerosol generation transducer provided in a central position, and a pulsation transducer provided as an annular transducer positioned around the central aerosol generation transducer to provide pulsation of the aerosol at discharge.

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Multiple transducers may be operated simultaneously to both generate and pulsate aerosol simultaneously. Alternately, an aerosol generator may be operated to generate a column of aerosol and the aerosol pulsation transducer may be operated independently to pulsate the generated aerosol. The aerosol generation transducer may be immersed in liquid and in direct contact with the liquid, or it may be in indirect contact with liquid through a flexible membrane or diaphragm.

Devices of the present invention may additionally incorporate a heater, or a thermostat for controlling the temperature of liquid discharged in a liquid stream, of for controlling the temperature aerosol at or prior to discharge. A heating element may be provided, for example, in proximity to a wall defining the mist column to heat the mist as it moves through the column to a temperature of from about 30-50°C, in some embodiments from about 35-45°C. In some embodiments, the aerosol is heated to a temperature above the average human body temperature (37°C) prior to discharge from the device.

Figs. 3-5 show schematic illustrations of devices of the present invention for delivery of generally high frequency acoustic energy (e.g., ultrasound energy, including high intensity ultrasound (HIU) and high intensity focused ultrasound (HIFU) to tissue sites such as nasal passages. As shown in Fig. 3, device 20 comprises a handle 22, an insertion wand 24 and an acoustic energy delivery member 26. In devices intended for delivery of high frequency acoustic energy to internal sites, such as nasal passageways, insertion wand 24 is configured for insertion through a nostril opening and positioning at least partially within nasal passageways. Insertion wand 24 is generally cylindrical and may be constructed as a flexible, catheter-like structure having at least one longitudinally oriented lumen extending therethrough. External surfaces of the insertion wand may be provided with a surface texture, or coating, such as a hydrophilic or hydrophobic coating, to ease passage of the insertion wand though nasal passages and improve deliverability. External surfaces of the insertion wand may also be provided with antibacterial coatings or coatings through which drugs or other agents are provided.

Insertion wand 24 may incorporate multiple lumens, channels or the like that communicate with source liquids, aerosol particles and/or droplets, vacuum sources, liquid and/or vacuum manifolds, or the like, to provide delivery of liquids, aerosol particles and/or droplets, vacuum, or the like, to intranasal passages. Multiple lumens may be co-axial with respect to one another, or they may be aligned on different axes and be non-concentric with respect to one another. In these embodiments, insertion wand 24 is generally provided with one or more discharge ports 25 in proximity to a distal area, providing intranasal delivery of a liquid and/or aerosol particles and/or droplets. Insertion

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wand 24 may, alternatively or additionally, be provided with one or more aspiration ports 27 in proximity to a distal area, providing withdrawal of delivered liquids and degraded materials from an intranasal site when an aspiration system (e.g. vacuum) is activated. A distal end of insertion wand 24 may additionally incorporate an endoscopic port and/or components of a visualization system, such as an optical or ultrasound guidance and/or visualization system.

Energy delivery member 26 may be provided at the tip of the insertion wand and configured for positioning in proximity to and/or contacting blockages within nasal passages, mucous membranes and nasal turbinates, or pathological or undesired tissue. In one embodiment, energy delivery member 26 may comprise a tapered structure, such as a generally conical structure, for focusing and concentrating high frequency and/or high intensity acoustic energy. Conical structures for delivering high intensity focused ultrasound are described, for example, in U.S. Patents 6,666,835, 6,500,133 and 6,217,530. An energy delivery member or surface may be extendible and/or retractable with respect to handle 22 and/or insertion wand 24 to provide desired positioning of the energy delivery member in contact with obstructions and/or tissues for delivery of high frequency acoustic energy.

In another embodiment, as illustrated in Fig. 5, an energy delivery member may comprise a flexible, deformable bladder or inflatable chamber 28 adapted for retaining an acoustically transmissive material, such as a liquid or gel, within its interior volume. The flexible, deformable chamber may be stored in a collapsed condition within wand 24, for example, and expanded, or inflated, at the desired target site from a distal tip of the wand by filling with an acoustically transmissive material. Expandable chamber 28 may be enlarged, at a desired target site, until the walls of the chamber contact a tissue site, or the walls of a cavity or passageway or lumen. Generally high frequency acoustic energy, e.g. ultrasound energy, may be applied to the tissue surfaces or obstructions in contact with the chamber wall by transmission through the acoustically transmissive material and the wall of the inflatable chamber.

The bladder or inflatable member(s) is constructed from a material that has generally high acoustic transmissivity properties and, when filled with an acoustically transmissive material, provides a flexible surface that is expandable and deformable to conform to contours of internal cavities or passageways, such as intranasal passages. The inflatable member may be coated with a drug or another agent, particularly an agent whose activity is enhanced in the presence of high frequency acoustic energy, such as ultrasound energy. The inflatable member may, additionally or alternatively, be permeable or porous to deliver a drug or another agent, particularly an agent whose

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activity is enhanced in the present of high frequency acoustic energy, such as ultrasound, to the target site. This embodiment provides effective delivery of ultrasound energy to tissue surfaces, cavities and obstructions over a larger surface area than point contact and provides effective access to target sites that may otherwise be difficult to access with an ultrasound applicator.

A distal end of the energy delivery member is preferably navigable to desired treatment sites, such as tissue surfaces and obstructions, such as blocked sites within nasal passages, where it can be activated to provide mechanical and cavitational effects that promote recanalization of obstructed passages. The energy delivery member may have a pre-formed shape or it may be flexible or conformable, as described above. Energy delivery members having different pre-formed shapes may also be used. A proximal end of energy delivery member 26 is connected or connectable to a generally high frequency acoustic energy generator (e.g., an ultrasound transducer) or acoustic energy coupling, providing delivery of high frequency acoustic energy (e.g., ultrasound) to the energy delivery member.

High frequency acoustic energy delivered through energy delivery member 26 generally has a frequency of greater than about 20 kHz and less than about 25 MHz; in some embodiments from about 20 kHz to about 100 kHz; in some embodiments from about 20 kHz to about 50 kHz; in other embodiments greater than about 100 kHz and less than about 1 MHz; in other embodiments from about 500 kHz to about 15 MHz; and in yet other embodiments greater than about 500 kHz and less than about 5 MHz. The acoustic energy applied through the energy delivery member may be at a generally high intensity of from about 1mW/cm^2 to about 5 W/cm^2; in some embodiments from about 50 mW/cm^2 to about 3 W/cm^2; in other embodiments from about 5-100 mW/cm^2; in yet other embodiments from about 0.1-1.5 W/cm^2. In other embodiments, the acoustic energy applied through the energy delivery member may be a generally high intensity ultrasound of greater than about 1 W/cm^2 and less than about 25 kW/ cm^2. In some embodiments, the acoustic energy applied through energy delivery member has an acoustic intensity from about 10 to about 1,000 W/cm^2; in some embodiments from about 1,000 to about 15,000 W/cm^2; and in yet other embodiments from about 3,000 to about 10,000 W/cm^2. The generally high intensity ultrasound may be sufficient to ablate tissue and/or cellular structures or debris, or it may be at a sub-ablation intensity that is sufficient to disrupt tissue and/or cellular structures or debris but not ablate. The pulse duration and repetition rate may be adjusted and matched to the frequency and intensity of acoustic energy pulses to achieve the desired effect.

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The high frequency acoustic energy may be selectably activated on a continuous basis, or ultrasound energy may be applied, through the energy delivery member, on an intermittent basis, and the frequency and/or acoustic intensity may be adjustable and selectable by the operator. Operation of the ultrasound transducer at duty cycles of less than about 80% is generally preferred; in some embodiments at duty cycles of less than 50%; and in yet other embodiments at duty cycles of less than about 30%. Enhancement and/or coupling agents promoting and/or targeting acoustic energy deposition may be used and may be provided to a target site through the insertion wand and/or the energy delivery member.

Handle 22 has a size and configuration that facilitates holding in one or both hands and may include ridges, indentations, curved contours, and the like, to enhance the ergonomic feel and secure handling of the device. Handle 22 may house power supply and control elements for operating the device. Power may be supplied to device 20 by physical connection to an electrical power source such as a separate control unit or an electrical outlet by means of a conventional power cord, as is well known in the art. Power may alternatively be supplied by a battery source mounted in the handle. Battery sources may be replaceable or rechargeable. Battery charging may be accomplished by direct coupling of battery terminals, or conductive elements provided on the housing, with a power source, or by indirect coupling using, for example, an inductive charging system. Handle 22 may also house control mechanisms, such as mechanical knobs 21A, 21B and 21C, or electronic switches, microprocessors, power supplies, and the like. Knobs 21A, 21B and 21C may provide user operable control of irrigation fluid, aerosol delivery, delivery of generally high frequency acoustic energy, selection of multiple modes of operation and/or multiple programmed protocol sequences, aspiration, other operating modalities, and the like.

Liquids and/or aerosols may be delivered through the insertion wand 24 and ports positioned along or generally at a distal end of the insertion wand, similarly to the delivery of liquids and/or aerosols described with reference to the device illustrated in Figs. 1, 2A and 2B. Aspiration may also be provided in devices such as those illustrated in Figs. 3-5, that deliver generally high frequency acoustic energy, such as ultrasound energy. Aspiration may be provided through one or more ports positioned along or generally at a distal end of the insertion wand, similarly to the aspiration feature described with reference to the device illustrated in Figs. 1, 2A and 2B.

Handle 22, insertion wand 24 and energy delivery member 26 may be provided in an integrated, single piece construction, or they may be provided as separate components that are detachable from one another. Handle 22 may be provided as a single- or

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multiple-use component. Insertion wands and/or energy delivery members may similarly be provided as integrated components or may be provided separately from one another, with appropriate interfaces for operation. Multiple configurations of insertion wands and/or energy delivery members may be provided for operation on common or multiple handles, with appropriate insertion wands and/or energy delivery members being selectable by a user depending on the circumstances of use. Insertion and energy delivery members may be provided as single- or multiple-use components, although they may generally be provided as sterile, disposable components that are mountable on a reusable handle. Device 20 may incorporate all of the components required for operation, or it may interface with a separate console, or control unit (not shown), that provides electrical power, liquid for infusion or aerosol delivery, operating control features, displays, and the like.

In some embodiments, devices of the present invention are capable of selectively delivering high frequency acoustic energy, a liquid stream, aerosol particles and/or aerosol droplets, simultaneously or sequentially, in one or a plurality of delivery modes: continuous flow; intermittent flow; or high frequency pulsatile flow. Liquid, aerosol particles and/or aerosol droplets may be delivered from a common discharge port sequentially and intermittently, or from multiple, dedicated discharge ports, simultaneously or sequentially, and on a continuous or intermittent basis. Aspiration may be provided, additionally or alternatively, through one or more ports in the insertion wand and/or energy delivery member. Insertion wand 24 may be provided with one or more channels, or lumens, for delivery of liquids, aerosol particles, and/or aerosol droplets to a desired intranasal site, and for removal of material from the site by means of aspiration.

Controls may be provided on the device handle, as illustrated, or on an accessory device or module, allowing a user to select acoustic frequency and/or intensity, liquid and/or aerosol delivery modes, aspiration modes, visualization modalities, or the like. Controls may also be provided allowing a user to select from among various modes of operation or various pre-determined or pre-set operating modes. Devices of the present invention may thus be operated, manually or by selectable automated operation, in a single mode or multiple modes.

In one embodiment, for example, a device such as illustrated in Figs. 3-5 may be operated in a high frequency acoustic energy deposition mode in which the insertion wand and energy delivery member are positioned in a nasal cavity, with the energy delivery member contacting mucus and/or debris forming an obstruction, or tissue desired to be treated. Acoustic energy delivery may be activated at a preset or selectable acoustic energy frequency and/or intensity to heat and/or cavitate and/or ablate mucus and/or

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debris forming the obstruction. In another embodiment, the energy delivery member may be positioned to contact tissue and activated at preset or selectable acoustic energy frequency and/or intensity levels to heat and/or cavitate and/or ablate selected tissue sites. Delivery of the high frequency and/or high intensity acoustic energy may be accompanied by infusion of liquids and/or aerosol particles or droplets, and/or by aspiration or liquids, wastes, mucus, and the like, from the site of energy deposition.

In some embodiments, multiple pulsating liquid rinse and aerosol delivery options, as well as multiple energy deposition options, may be programmed in the device, with various operating programs being predetermined and selectable by the user. In alternative embodiments, a user may select pulsating liquid rinse, aerosol delivery and/or energy deposition options by means of multiple selectable actuators. In any of these embodiments, multiple and selectable modes may be implemented, whereby programmed or selectable levels of liquid and/or aerosol flow or volume, aerosol particle and/or droplet size, aerosol particle and/or droplet density, pulsation frequency, temperature, acoustic energy frequency, intensity, pulse repetition rate, duty cycle, and the like, may be selectable by the user.

Figs. 6 and 7 show schematic illustrations of two embodiments of a device for delivery of generally high frequency acoustic energy to nasal passages. As shown in Fig. 6, device 40 comprises a handle 42, an insertion member 44 and an acoustic energy delivery member 46. Insertion member 44 is configured for insertion through a nostril opening and positioning at least partially within nasal passageways. Insertion member 44 is generally cylindrical and may be constructed as a flexible, catheter-like structure having at least one longitudinally oriented lumen extending therethrough. External surfaces of the insertion member may be provided with a surface texture, or coating, such as a hydrophilic or hydrophobic coating, to ease passage of the insertion member though nasal passages and improve deliverability. External surfaces of the insertion member may also be provided with antibacterial coatings or coatings through which drugs or other agents are provided.

Insertion member 44 may incorporate multiple lumens, channels or the like that communicate with source liquids, aerosol particles and/or droplets, vacuum sources, liquid and/or vacuum manifolds, or the like to provide delivery of liquids, aerosol particles and/or droplets, vacuum, or the like, to intranasal passages. Multiple lumens may be co-axial with respect to one another, or they may be aligned on different axes and be non-concentric with respect to one another. In these embodiments, insertion member 44 is generally provided with one or more discharge ports 45 in proximity to a distal area, providing intranasal delivery of a liquid and/or aerosol particles and/or droplets. Insertion

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member 44 may, alternatively or additionally, be provided with one or more aspiration ports 47 in proximity to a distal area, providing withdrawal of material from an intranasal site when an aspiration system (e.g. vacuum) is activated. A distal end of insertion member 44 may additionally incorporate components of a visualization system, such as an optical or ultrasound guidance and/or visualization system.

Energy delivery member 46 is generally provided as a structure having a smaller diameter cross-section that that of insertion member 44, providing access to smaller passages or allowing penetration of obstructions. Energy delivery member 46 is configured such that a distal end may be positioned in proximity to and/or contacting a tissue surface such as mucous membranes and nasal turbinates or polyps, bony protuberances, undesired tissue growths or accumulations or blockages within cavities such as nasal passages. In one embodiment, illustrated in Fig. 6, energy delivery member 46 comprises a generally rigid or semi-rigid wire-like structure capable of conveying, and delivering, high frequency acoustic energy (e.g., ultrasound energy, including high intensity ultrasound (HIU) and high energy focused ultrasound (HIFU) by contact with tissue or obstructive material along its length and/or at a distal end of the delivery member. In another embodiment, illustrated in Fig. 7, the energy delivery member may comprise a flexible, steerable structure 48. The energy delivery member may be extendible and/or retractable with respect to handle 42 and/or insertion member 44 to provide desired positioning of the energy delivery member in contact with obstructions and/or tissues for delivery of high frequency acoustic energy.

A distal end of the energy delivery member 46, 48 is preferably navigable to target tissue sites or target blocked sites within cavities, such as nasal passages and blocked ostea, where it can be activated to provide mechanical and cavitational effects that promote recanalization of obstructed passages. The energy delivery member 46, 48 may be extendible and retractable with respect to the insertion member 44, as shown in the simplified operational sequence schematically illustrated in Figs. 8A and 8B. Energy delivery member 46 is generally constructed from an acoustically transmissive material and may have different stiffness properties along its length, providing steerability. The energy delivery member may have a pre-formed shape, illustrated as an angled shape as shown in Fig. 6, or may be flexible or conformable, as illustrated schematically in Fig. 7. Energy delivery members having different pre-formed shapes may also be used. The energy delivery member may be constructed from metallic materials, such as Nitinol. Wire-like energy delivery members may be covered with another acoustically transmissive material, such as a resilient rubber-like material, that may function to delivery high frequency acoustic energy uniformly or in a focused fashion.

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A proximal end of energy delivery member 46, 48 is connected or connectable to a generally high frequency acoustic energy generator (e.g., an ultrasound transducer) or acoustic energy coupling, providing delivery of high frequency acoustic energy (e.g., ultrasound) along the length of and to a distal end of the energy delivery member 46, 48. In some embodiments, a guidance member, such as a guidewire-type member, may be provided and operated separately from an energy delivery member. In this embodiment, the guidance member may be advanced and positioned at a desired operating site, and the energy delivery member may then be advanced over, along-side or through the guidance member for positioning and activation at the desired operating site.

High frequency acoustic energy delivered through energy delivery members 46, 48 generally has a frequency of greater than about 20 kHz and less than about 25 MHz; in some embodiments from about 20 kHz to about 100 kHz; in some embodiments from about 20 kHz to about 50 kHz; in other embodiments greater than about 100 kHz and less than about 1 MHz; in other embodiments from about 500 kHz to about 15 MHz; and in yet other embodiments greater than about 500 kHz and less than about 5 MHz. The acoustic energy applied through the energy delivery member may be at a generally high intensity of from about 1mW/ cm^2 to about 5 W/ cm^2; in some embodiments from about 50 mW/ cm^2 to about 3 W/ cm^2; in other embodiments from about 5-100 mW/ cm^2; in yet other embodiments from about 0.1-1.5 W/ cm^2. In other embodiments, the acoustic energy applied through the energy delivery member may be a generally high intensity ultrasound of greater than about 1 W/cm^2 and less than about 25 kW/ cm^2. In some embodiments, the acoustic energy applied through energy delivery member has an acoustic intensity from about 10 to about 1,000 W/cm^2; in some embodiments from about 1,000 to about 15,000 W/cm^2; and in yet other embodiments from about 3,000 to about 10,000 W/cm^2. The generally high intensity ultrasound may be sufficient to ablate tissue and/or cellular structures or debris, or it may be at a sub-ablation intensity that is sufficient to disrupt tissue and/or cellular structures or debris but not ablate. The pulse duration and repetition rate may be adjusted and matched to the frequency and intensity of acoustic energy pulses to achieve the desired effect.

The high frequency acoustic energy may be selectably activated on a continuous basis, or ultrasound energy may be applied, through the energy delivery member, on an intermittent basis, and the frequency and/or acoustic intensity may be adjustable and selectable by the operator. Operation of the ultrasound transducer at duty cycles of less than about 80% is generally preferred; in some embodiments at duty cycles of less than 50%; and in yet other embodiments at duty cycles of less than about 30%. Enhancement and/or coupling agents promoting and/or targeting acoustic energy deposition may be

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used and may be provided to a target site through the insertion member and/or the energy delivery member.

Handle 42, insertion wand 44 and energy delivery member 46, 48 may be provided in an integrated, single piece construction, or they may be provided as separate components that are detachable from one another. Handle 42 may be provided as a single- or multiple-use component. Insertion wands and/or energy delivery members may similarly be provided as integrated components or may be provided separately from one another, with appropriate interfaces for operation. Multiple configurations of insertion wands and/or energy delivery members may be provided for operation on common or multiple handles, with appropriate insertion wands and/or energy delivery members being selectable by a user depending on the circumstances of use. Insertion and energy delivery members may be provided as single- or multiple-use components, although they may generally be provided as sterile, disposable components that are mountable on a reusable handle. Device 40 may incorporate all of the components required for operation, or it may interface with a separate console, or control unit (not shown), that provides electrical power, liquid for infusion or aerosol delivery, operating control features, displays, and the like.

In some embodiments, devices of the type illustrated in Figs. 6 and 7 are capable of selectively delivering high frequency acoustic energy, a liquid stream, aerosol particles and/or aerosol droplets, simultaneously or sequentially, in one or a plurality of delivery modes: continuous flow; intermittent flow; or high frequency pulsatile flow. Liquid, aerosol particles and/or aerosol droplets may be delivered from a common discharge port sequentially and intermittently, or from multiple, dedicated discharge ports, simultaneously or sequentially, and on a continuous or intermittent basis. Aspiration may be provided, additionally or alternatively, through one or more ports in the insertion wand and/or energy delivery member. Insertion wand 24 may be provided with one or more channels, or lumens, for delivery of liquids, aerosol particles, and/or aerosol droplets to a desired intranasal site, and for removal of material from the site by means of aspiration.

Controls may be provided on the device handle, as illustrated, or on an accessory device or module, allowing a user to select acoustic frequency and/or intensity, liquid and/or aerosol delivery modes, aspiration modes, visualization modalities, or the like. Controls may also be provided allowing a user to select from among various modes of operation or various pre-determined or pre-set operating modes. Devices of the present invention may thus be operated, manually or by selectable automated operation, in a single mode or multiple modes.

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In one embodiment, schematically illustrated in Figs. 8A-8E, a device 40 such as illustrated in Figs. 6 and 7 may be operated in a high frequency acoustic energy deposition mode in which the insertion wand 44 and energy delivery member 46 are positioned in a nasal cavity, as shown in Fig. 8A. Energy delivery member 46 may be extended, as shown in Fig. 8B, to contacting mucus and/or debris forming an obstruction within nasal passageways. Acoustic energy delivery may be activated at a preset or selectable acoustic energy frequency and/or intensity to heat and/or cavitate and/or ablate mucus and/or debris forming the obstruction, as shown schematically in Fig. 8C. In another embodiment, the energy delivery member may be positioned to contact tissue and activated at preset or selectable acoustic energy frequency and/or intensity levels to heat and/or cavitate and/or ablate selected tissue sites. Delivery of the high frequency and/or high intensity acoustic energy may be accompanied by infusion of liquids and/or aerosol particles or droplets. Extraneous materials may be aspirated during and/or following delivery of high frequency and/or high intensity acoustic energy and infusion of liquids and/or aerosol particles, as shown schematically in Fig. 8D to remove obstructions and clear passageways, as illustrated schematically in Fig. 8E.

In some embodiments, multiple pulsating liquid rinse and aerosol delivery options, as well as multiple energy deposition options, may be programmed in the device, with various operating programs being predetermined and selectable by the user. In alternative embodiments, a user may select pulsating liquid rinse, aerosol delivery and/or energy deposition options by means of multiple selectable actuators. In any of these embodiments, multiple and selectable modes may be implemented, whereby programmed or selectable levels of liquid and/or aerosol flow or volume, aerosol particle and/or droplet size, aerosol particle and/or droplet density, pulsation frequency, temperature, acoustic energy frequency, intensity, pulse repetition rate, duty cycle, and the like, may be selectable by the user.

Devices of the present invention may be provided as an integral unit that may be used once or several times and then disposed of, or an integral device may be reused on a frequent basis. Alternatively, as described above, the handle and nostril interface member or delivery wand may be detachable from one another. In a multiple component embodiment, the handle may be provided as a reusable component, while the detachable nostril interface member or delivery wand may be provided as a reusable or disposable element. Single or multiple use “covers” may be provided for covering the nostril interface member or the delivery wand, providing replaceable sterile, or antiseptic surfaces for contacting the nose and nasal passages. Such covers may be flexible and resilient and generally match the outer configuration of the nostril interface member

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and/or delivery wand, so that they may be mounted on and closely fitted over the interface member or delivery wand for multiple uses/multiple users, and the like.

The methods and devices may be used for treating common colds, nasal congestion and allergic rhinitis, as well as sinusitis and other nasal conditions. They may be used for treatment of acute or chronic conditions, and they may be used on a frequent basis to cleanse intranasal passages, thereby reducing bacterial infection and the incidence of nasal congestion, colds, sinusitis and the like.

It will be appreciated that the methods and systems of the present invention may be embodied in a variety of different forms, and that the specific embodiments shown in the figures and described herein are presented with the understanding that the present disclosure is considered exemplary of the principles of the invention, and is not intended to limit the invention to the illustrations and description provided herein. Accordingly, the descriptions provided above are considered as being illustrative and exemplary of specific structures, aspects and features within the broad scope of the present invention and not as limiting the scope of the invention.

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We claim:

1. A method for treating a target site at a tissue, within a body cavity or at an obstruction, comprising delivering at least one of fluids and aerosols to the target site using a pulsatile flow characterized by pulsations having a frequency of greater than 1500 Hz.

2. The method of claim 1, wherein the frequency of pulsations is in the ultrasound frequency range.

3. The method of claims 1 or 2, comprising delivering an aerosol to the target site at the pulsatile flow having a frequency of greater than 1500 Hz and at a pressure of more than about 10mmHg and less than about 160mmHg.

4. The method of any of claims 1-3, wherein the pulsatile flow is characterized by pulsations having at least two different frequencies.

5. The method of claim 4, wherein the at least two different frequencies include a frequency in a sub-ultrasound frequency range and a frequency in the ultrasound frequency range.

6. The method of claim 1, comprising delivering at least one of fluids and aerosols using pulsatile flows characterized by multiple modes of administration, with each mode of administration being characterized by pulsations having a different frequency, intensity, pulse duration, pulse repetition rate and/or duty cycle.

7. The method of any of claims 1-6, additionally comprising delivering at least one additional treatment modality in combination with the delivery of at least one of fluids and aerosols, wherein the additional treatment modality includes administration of an antimicrobial or therapeutic agent, application of electromagnetic radiation, application of an electrical field, application of radio frequency energy, application of laser energy, and/or application of microwave energy.

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8. The method of any of claims 1-7, additionally comprising delivering high frequency acoustic energy to the target site in combination with the delivery of at least one of fluids and aerosols.

9. The method of claim 1, wherein the fluid or the aerosol comprises at least one of the following components: saline, an antibiotic agent, a drug, hypertonic saline, lactated ringer's solution, dead sea salt solution, antibiotics, midazolam, fentanyl, insulin, growth hormone, one or more growth factors, gentamycin, clindamycin, ciprofloxacin, cefuroxime, levofloxocin, tobramycin, ampicillin+sulbactam, amphotericin, tobramycin/amphotericin combinations, cefotaxime, ceftriaxone, fluticasone, budesonide, mometasone furoate monohydrate, xylitol, eucalyptus, tea tree oil, capsaicin, grapefruit seed extract and oil of wintergreen.

10. The method of any of claims 1-9, additionally comprising aspirating material from the target site during and/or following delivery of the fluid and/or aerosol.

11. A system for delivery of at least one of fluids and aerosols to a tissue surface, cavity or obstruction, adapted to deliver a pulsatile flow of fluids and/or aerosols at a pulsation frequency of greater than 1500 Hz.

12. The system of claim 11, wherein the system comprises a handheld device having a handle and at least one fluid and/or aerosol discharge port.

13. The system of claim 11 or 12, adapted to deliver a pulsatile flow of fluids and/or aerosols at a pulsation frequency of greater than 1500 Hz and at a pressure of more than about 10mmHg and less than about 160mmHg.

14. The system of any of claims 11-13, adapted to deliver a pulsatile flow of fluids and/or aerosols at alternating pulsation frequencies corresponding to frequencies that promote entry of the fluid and/or aerosol into a tissue surface, cavity or obstruction; reduce biofilms; degrade pathological tissue; improve circulation; and/or modulate local immune responses.

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15. The system of any of claims 11-14, additionally comprising at least one aspiration port.

16. The system of claim 15, additionally comprising a system for collection of material removed by aspiration.

17. A system for delivery of high frequency acoustic energy to a target site at a tissue or at an obstruction within a body cavity or lumen, comprising an insertion wand sized and configured for insertion into a body cavity or lumen and an acoustic energy delivery member associated with the insertion wand for conveying high frequency acoustic energy.

18. The system of claim 17, wherein the acoustic energy delivery member is adapted to deliver high intensity ultrasound (HIU) or high intensity focused ultrasound (HIFU) to the target site.

19. The system of claim 17 or 18, wherein the acoustic energy delivery member is conical and is positioned at a distal portion of the delivery wand.

20. The system of claim 17 or 18, wherein the acoustic energy delivery member is a wire-like member and is extendible from the delivery wand.

21. The system of claim 17 or 18, wherein the acoustic energy delivery member is a flexible, expandable member adapted to be expanded at the target site upon by filling with an acoustically transmissive material.

22. The system of claim 21, wherein the flexible, expandable member is fluid permeable.

23. The system of any of claims 17-21, wherein the insertion wand is sized and configured for insertion into at least a portion of a nasal cavity.

24. The system of any of claims 17-21, wherein the insertion wand is sized and configured for insertion into at least a portion of the vascular system, the respiratory system, the gastrointestinal system, the reproductive system, or a natural orifice.

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25. The system of any of claims 17-24, wherein the insertion wand additionally comprises a fluid or aerosol delivery port.

26. The system of any of claims 17-25, wherein the insertion wand additionally comprises an aspiration port.

27. The system of claim 26, wherein the device additionally incorporates a system for collection of material removed by aspiration.

28. The system of any of claims 17-27, wherein the system is adapted to provide delivery of one or more sequences of acoustic energy, with each sequence providing delivery of acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, or duty cycle.

29. The system of claim 28, wherein multiple sequences are programmed in the device as multiple programmed protocols selectable by a user.

30. The system of any of claims 17-29, additionally comprising a visualization system for visualization of the target site.

31. The system of any of claims 17-30, additionally comprising an illumination system for illumination of a target site.

32. The system of any of claims 17-31, additionally comprising an endoscopic port for delivery of tools or agents to the target site.

33. A method for delivering high frequency acoustic energy to a target site at a tissue or at an obstruction within a body cavity or lumen, comprising positioning an insertion wand in proximity to the target site, positioning an acoustic energy delivery member associated with the insertion wand at the target site, and conveying high frequency acoustic energy to the target site through the acoustic energy delivery member.

34. The method of claim 33, wherein the high frequency acoustic energy is high intensity ultrasound (HIU) or high intensity focused ultrasound (HIFU).

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35. The method of claim 33 or 34, wherein the acoustic energy delivery member is a wire-like member that is extendible from the delivery wand and positioning the acoustic energy delivery member at the target site includes extending the wire-like member from the delivery wand.

36. The method of claim 33 or 34, wherein the acoustic energy delivery member is a flexible, expandable member and positioning the acoustic energy delivery member at the target site includes expanding the flexible, expandable member at the target site by filling it with an acoustically transmissive material.

37. The method of claim 33, additionally comprising delivering at least one of a fluid and an aerosol to the target site using a pulsatile flow characterized by pulsations having a frequency of greater than 1500 Hz.

38. The method of any of claims 33-37, additionally comprising aspirating material from the target site.

39. The method of any of claims 33-38, comprising delivering one or more sequences of acoustic energy, with each sequence providing delivery of acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, or duty cycle.

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AMENDED CLAIMS
received by the International Bureau onreceived by the International Bureau on
14 April 2010 (14.04.2010)

1. A method for treating a target site at a tissue, within a body cavity or at an obstruction, comprising delivering at least one of fluids and aerosols to the target site using a pulsatile flow characterized by pulsations having a frequency of greater than 1500 Hz.

2. The method of claim 1, wherein the frequency of pulsations is in the ultrasound frequency range.

3. The method of claims 1 or 2, comprising delivering an aerosol to the target site at the pulsatile flow having a frequency of greater than 1500 Hz and at a pressure of more than about 10mmHg and less than about 160mmHg.

4. The method of claims 1 or 2, wherein the pulsatile flow is characterized by pulsations having at least two different frequencies.

5. The method of claim 4, wherein the at least two different frequencies include a frequency in a sub-ultrasound frequency range and a frequency in the ultrasound frequency range.

6. The method of claim 1, comprising delivering at least one of fluids and aerosols using pulsatile flows characterized by multiple modes of administration, with each mode of administration being characterized by pulsations having a different frequency, intensity, pulse duration, pulse repetition rate and/or duty cycle.

7. The method of claims 1 or 2 or 5 or 6, additionally comprising delivering at least one additional treatment modality in combination with the delivery of at least one of fluids and aerosols, wherein the additional treatment modality includes administration of an antimicrobial or therapeutic agent, application of electromagnetic radiation, application of an electrical field, application of radio frequency energy, application of laser energy, and/or application of microwave energy.

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8. The method of claims 1or 2 or 5 or 6, additionally comprising delivering high frequency acoustic energy to the target site in combination with the delivery of at least one of fluids and aerosols.

9. The method of claim 1, wherein the fluid or the aerosol comprises at least one of the following components: saline, an antibiotic agent, a drug, hypertonic saline, lactated ringer's solution, dead sea salt solution, antibiotics, midazolam, fentanyl, insulin, growth hormone, one or more growth factors, gentamycin, clindamycin, ciprofloxacin, cefuroxime, levofloxocin, tobramycin, ampicillin+sulbactam, amphotericin, tobramycin/amphotericin combinations, cefotaxime, ceftriaxone, fluticasone, budesonide, mometasone furoate monohydrate, xylitol, eucalyptus, tea tree oil, capsaicin, grapefruit seed extract and oil of wintergreen.

10. The method of claims 1or 2 or 5 or 6, additionally comprising aspirating material from the target site during and/or following delivery of the fluid and/or aerosol.

11. A system for delivery of at least one of fluids and aerosols to a tissue surface, cavity or obstruction, adapted to deliver a pulsatile flow of fluids and/or aerosols at a pulsation frequency of greater than 1500 Hz.

12. The system of claim 11, wherein the system comprises a handheld device having a handle and at least one fluid and/or aerosol discharge port.

13. The system of claim 11 or 12, adapted to deliver a pulsatile flow of fluids and/or aerosols at a pulsation frequency of greater than 1500 Hz and at a pressure of more than about 10mmHg and less than about 160mmHg.

14. The system of claims 11 or 12, adapted to deliver a pulsatile flow of fluids and/or aerosols at alternating pulsation frequencies corresponding to frequencies that promote entry of the fluid and/or aerosol into a tissue surface, cavity or obstruction; reduce biofilms; degrade pathological tissue; improve circulation; and/or modulate local immune responses.

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15. The system of claims 14, additionally comprising at least one aspiration port.

16. The system of claim 15, additionally comprising a system for collection of material removed by aspiration.

17. A system for delivery of high frequency acoustic energy to a target site at a tissue or at an obstruction within a body cavity or lumen, comprising an insertion wand sized and configured for insertion into a body cavity or lumen and an acoustic energy delivery member associated with the insertion wand for conveying high frequency acoustic energy.

18. The system of claim 17, wherein the acoustic energy delivery member is adapted to deliver high intensity ultrasound (HIU) or high intensity focused ultrasound (HIFU) to the target site.

19. The system of claim 17 or 18, wherein the acoustic energy delivery member is conical and is positioned at a distal portion of the delivery wand.

20. The system of claim 17 or 18, wherein the acoustic energy delivery member is a wire-like member and is extendible from the delivery wand.

21. The system of claim 17 or 18, wherein the acoustic energy delivery member is a flexible, expandable member adapted to be expanded at the target site upon by filling with an acoustically transmissive material.

22. The system of claim 21, wherein the flexible, expandable member is fluid permeable.

23. The system of claim 18, wherein the insertion wand is sized and configured for insertion into at least a portion of a nasal cavity.

24. The system of claim 18, wherein the insertion wand is sized and configured for insertion into at least a portion of the vascular system, the respiratory system, the gastrointestinal system, the reproductive system, or a natural orifice.

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25. The system of claim 23 or 24, wherein the insertion wand additionally comprises a fluid or aerosol delivery port.

26. The system of claim 23 or 24, wherein the insertion wand additionally comprises an aspiration port.

27. The system of claim 26, wherein the device additionally incorporates a system for collection of material removed by aspiration.

28. The system of claim 18, wherein the system is adapted to provide delivery of one or more sequences of acoustic energy, with each sequence providing delivery of acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, or duty cycle.

29. The system of claim 28, wherein multiple sequences are programmed in the device as multiple programmed protocols selectable by a user.

30. The system of claim 18, additionally comprising a visualization system for visualization of the target site.

31. The system of claim 18, additionally comprising an illumination system for illumination of a target site.

32. The system of any of claim 18, additionally comprising an endoscopic port for delivery of tools or agents to the target site.

33. A method for delivering high frequency acoustic energy to a target site at a tissue or at an obstruction within a body cavity or lumen, comprising positioning an insertion wand in proximity to the target site, positioning an acoustic energy delivery member associated with the insertion wand at the target site, and conveying high frequency acoustic energy to the target site through the acoustic energy delivery member.

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34. The method of claim 33, wherein the high frequency acoustic energy is high intensity ultrasound (HIU) or high intensity focused ultrasound (HIFU).

35. The method of claim 33 or 34, wherein the acoustic energy delivery member is a wire-like member that is extendible from the delivery wand and positioning the acoustic energy delivery member at the target site includes extending the wire-like member from the delivery wand.

36. The method of claim 33 or 34, wherein the acoustic energy delivery member is a flexible, expandable member and positioning the acoustic energy delivery member at the target site includes expanding the flexible, expandable member at the target site by filling it with an acoustically transmissive material.

37. The method of claim 33, additionally comprising delivering at least one of a fluid and an aerosol to the target site using a pulsatile flow characterized by pulsations having a frequency of greater than 1500 Hz.

38. The method of claim 33 or 34, additionally comprising aspirating material from the target site.

39. The method of claim 33 or 34, comprising delivering one or more sequences of acoustic energy, with each sequence providing delivery of acoustic energy at a different frequency, intensity, pulse duration, pulse repetition rate, or duty cycle.

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STATEMENT ACCOMPANYING ARTICLE 19 CLAIM AMENDMENTS

Accompanying this letter, Applicants' attorneys/agent submits claim amendments under Article 19 as Replacement Sheets 27-31.

Claims 1-3, 5, 6, 9, 11-13, 16-22, 27, 29, and 33-37 are unchanged. Claims 4, 7, 8, 10, 14, 25, 26, 38 and 39 are replaced by amended claims bearing the same numbers. These claims have been amended to comply with Rule 6.4(a). Claims 15, 23, 24, 28 and 30-32 are replaced by amended claims bearing the same numbers. These claims have been amended to delete multiple dependencies.

It is the understanding of the attorney/agent that no fee is required for this request. **Transmitted herewith are 6 pages, including this letter.**

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FIG. 1

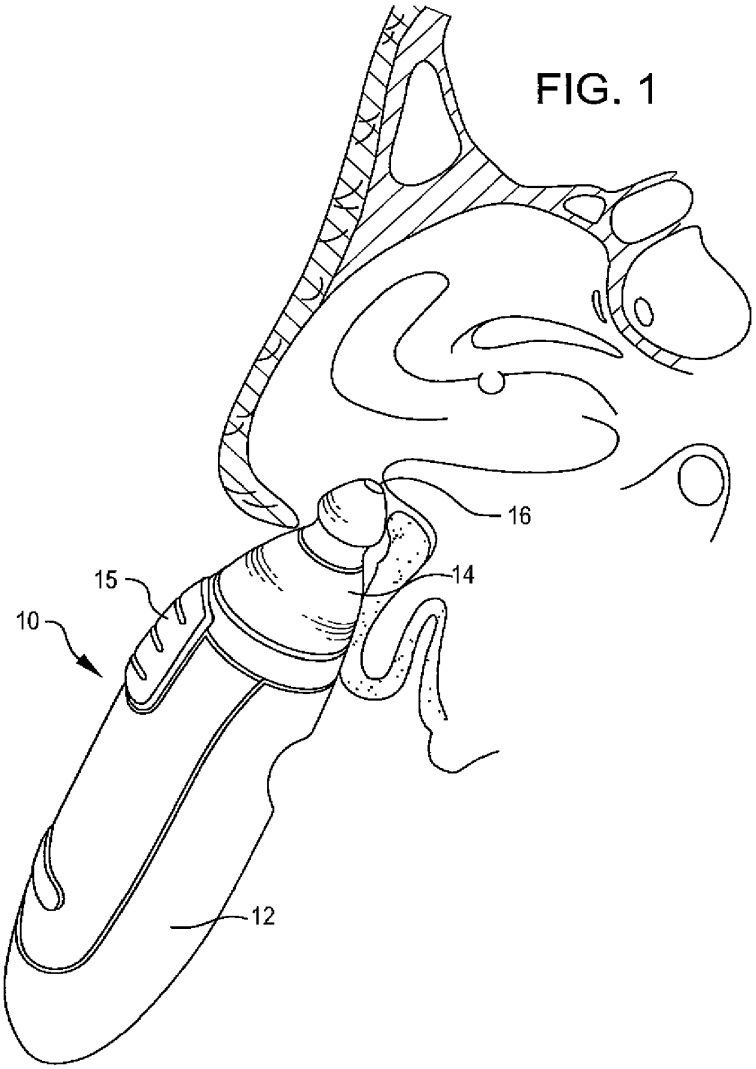


FIG. 2A

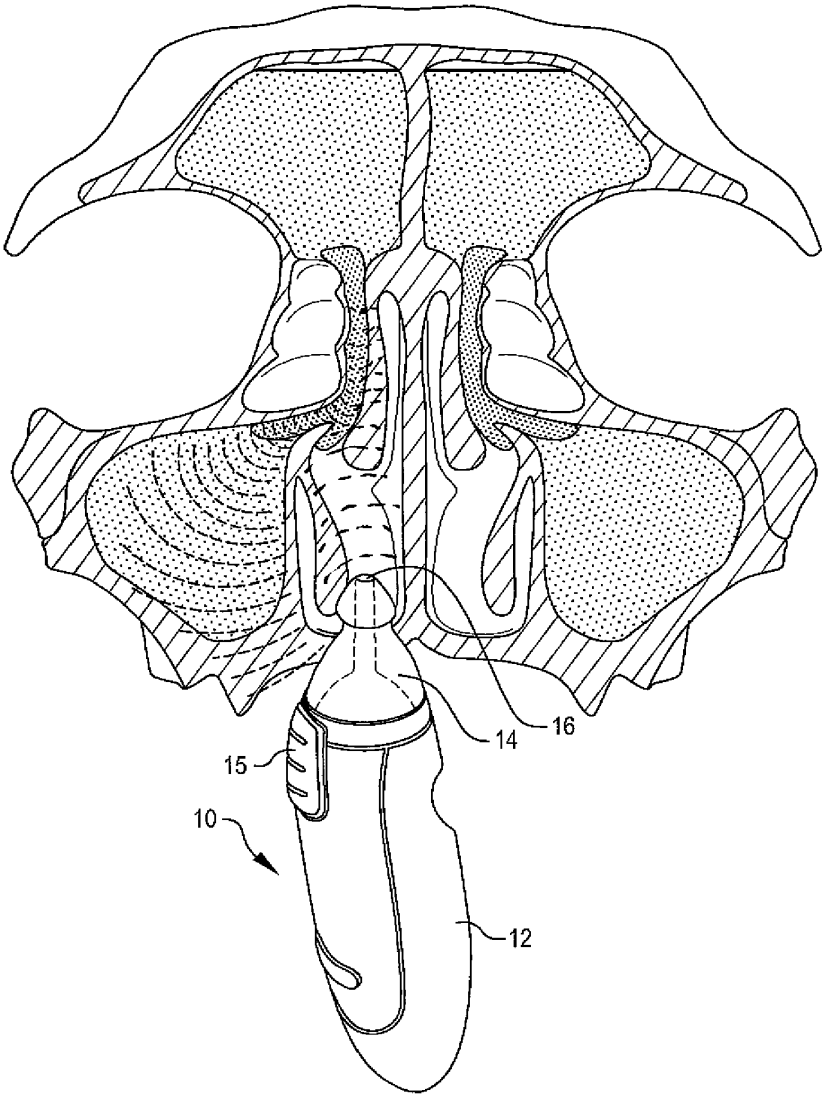


FIG. 2B

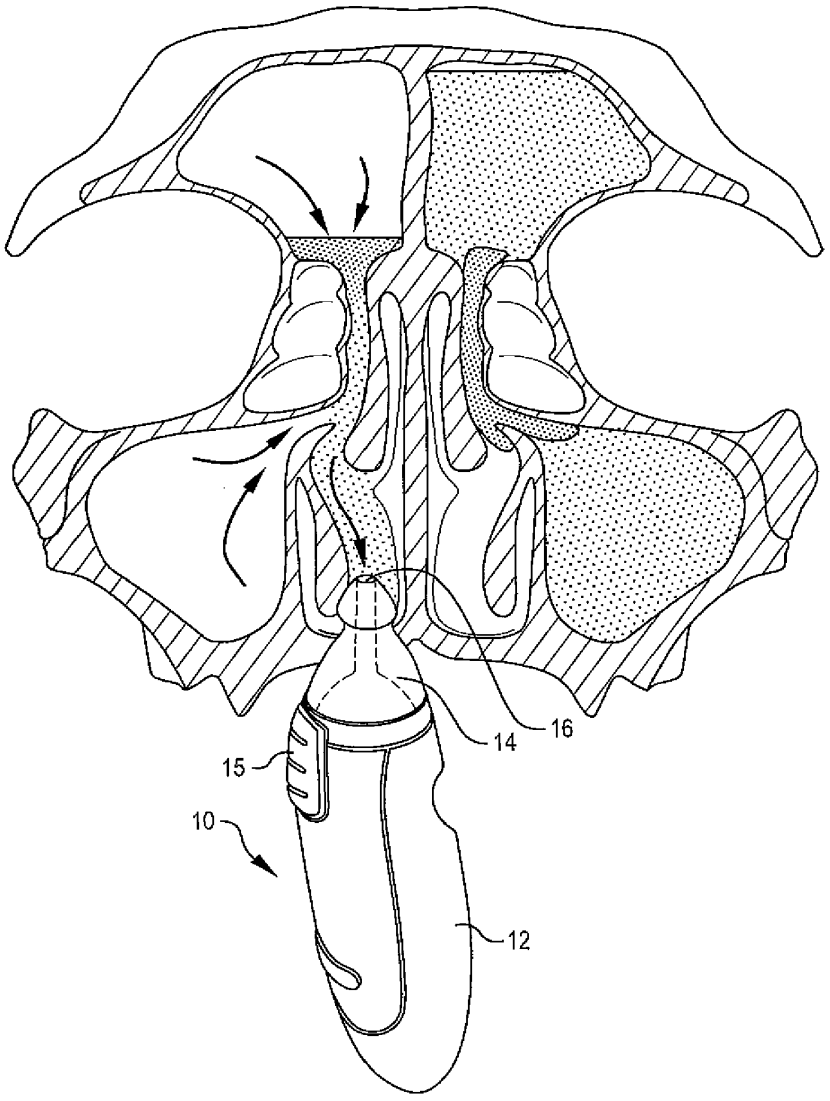


FIG. 3

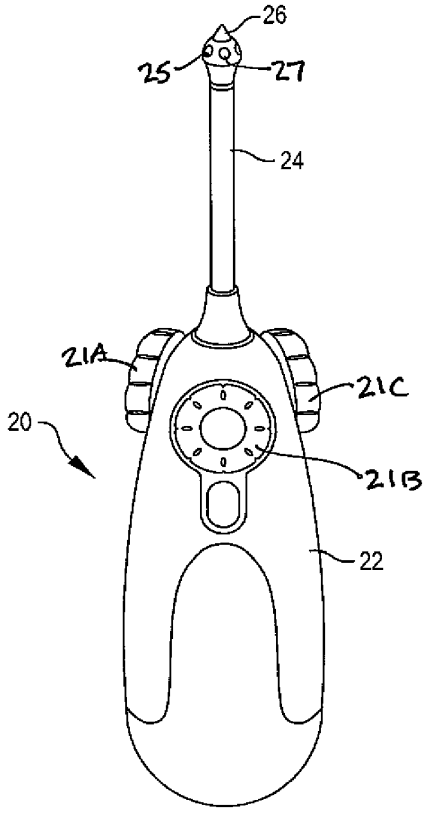


FIG. 4

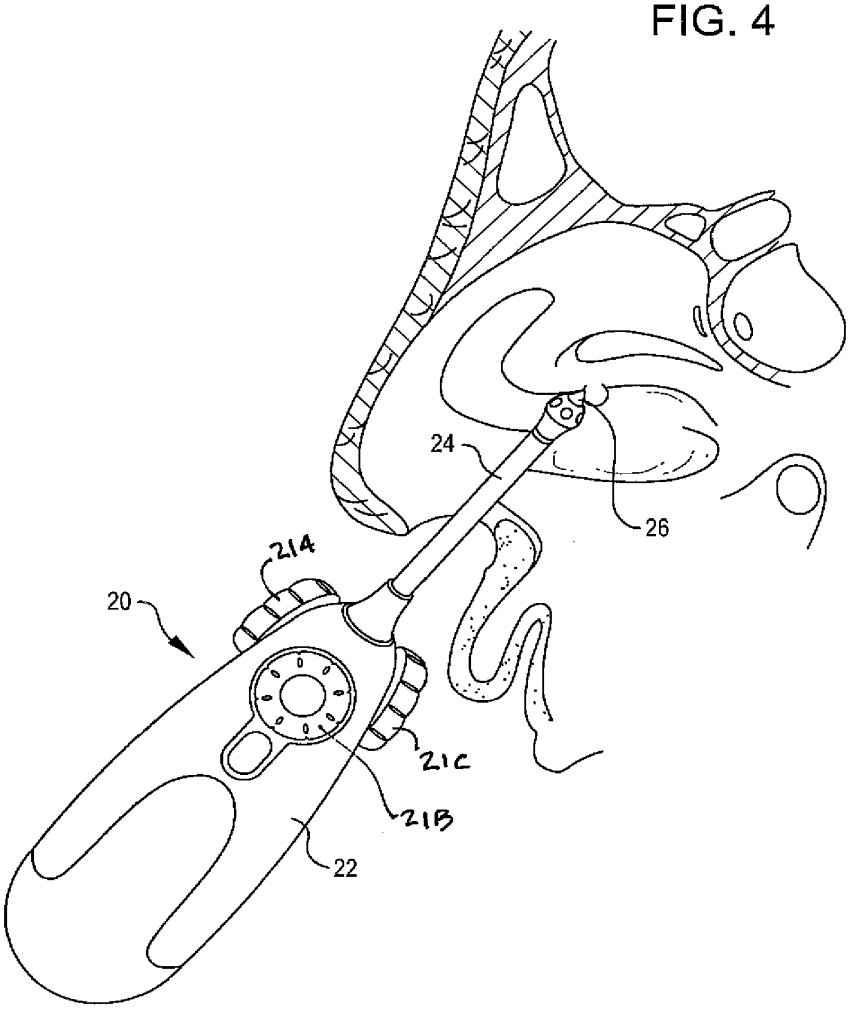


FIG. 5

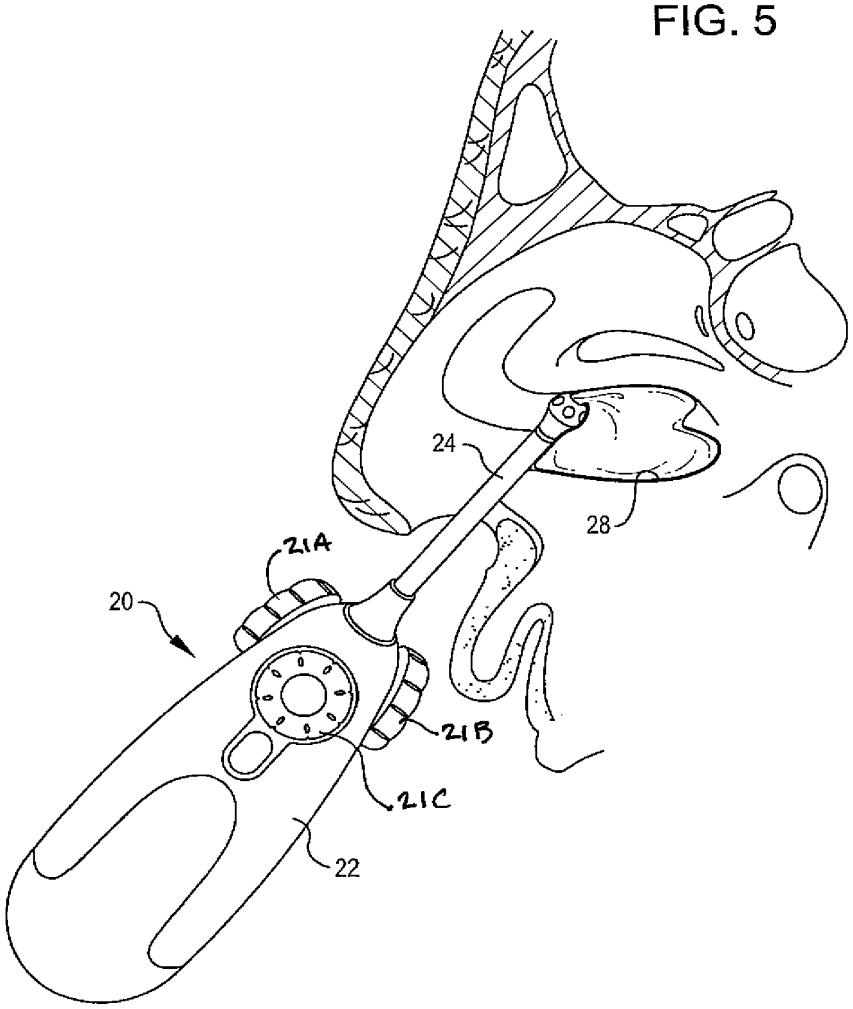


FIG. 6

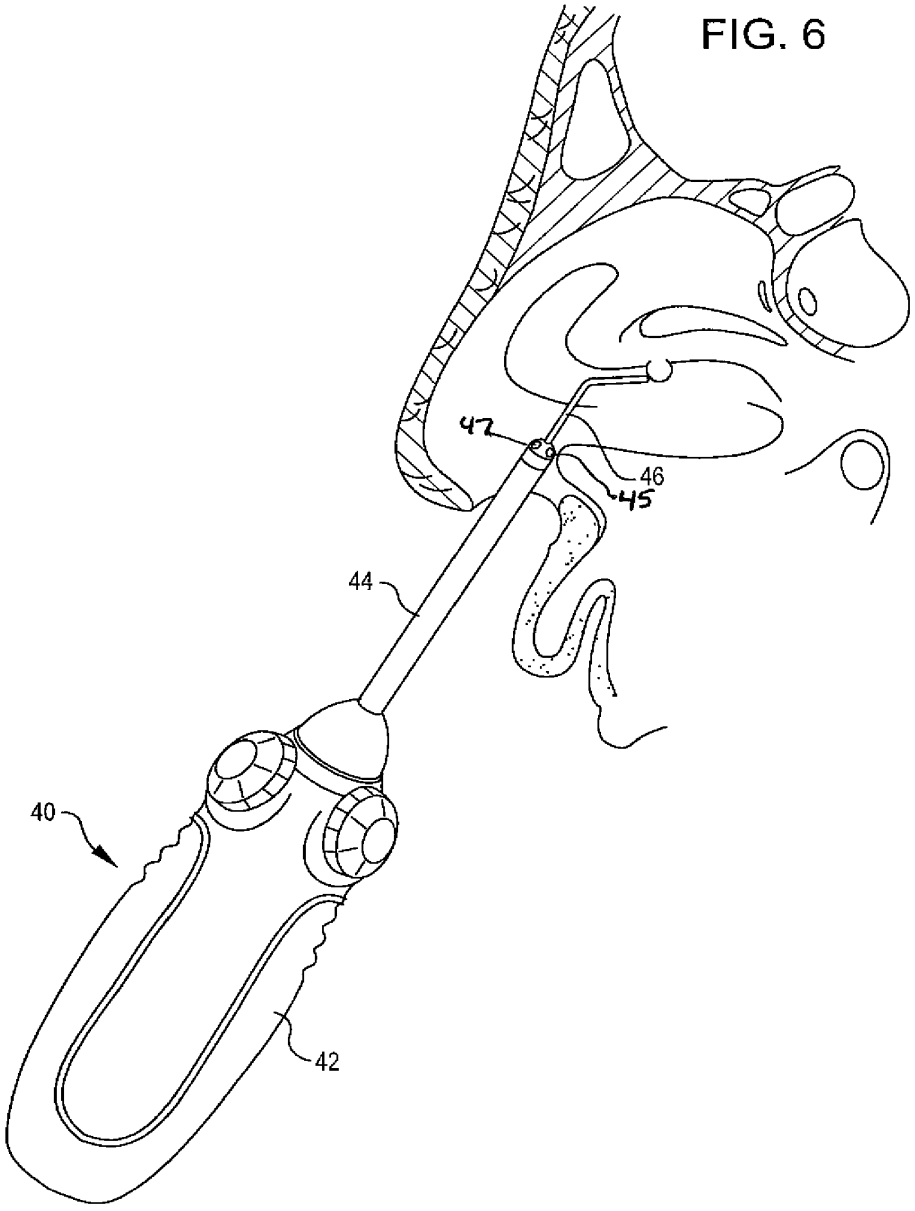


FIG. 7

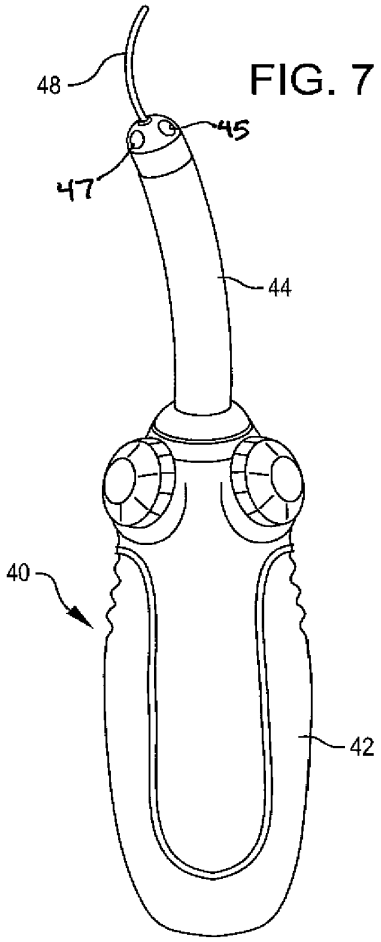


FIG. 8A

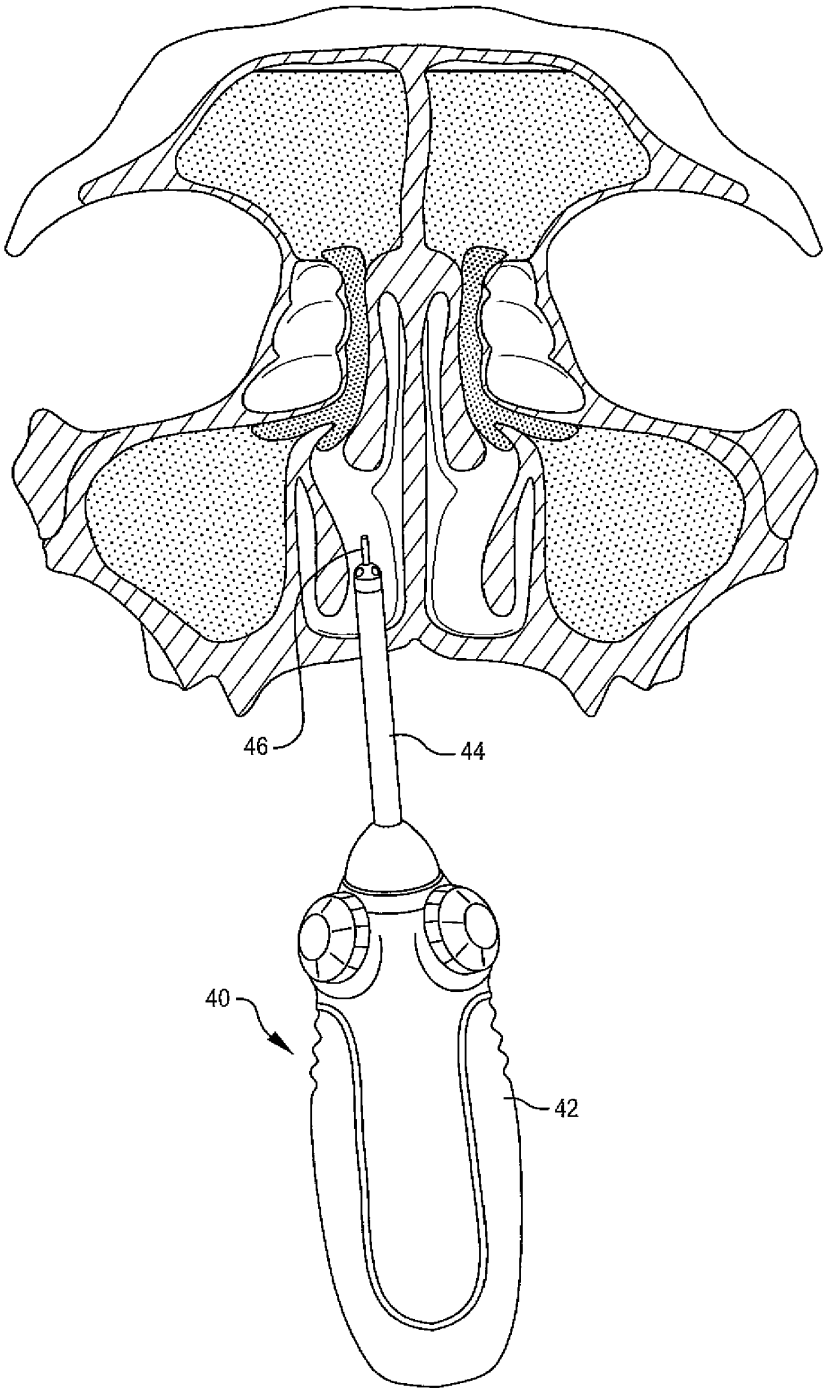


FIG. 8B

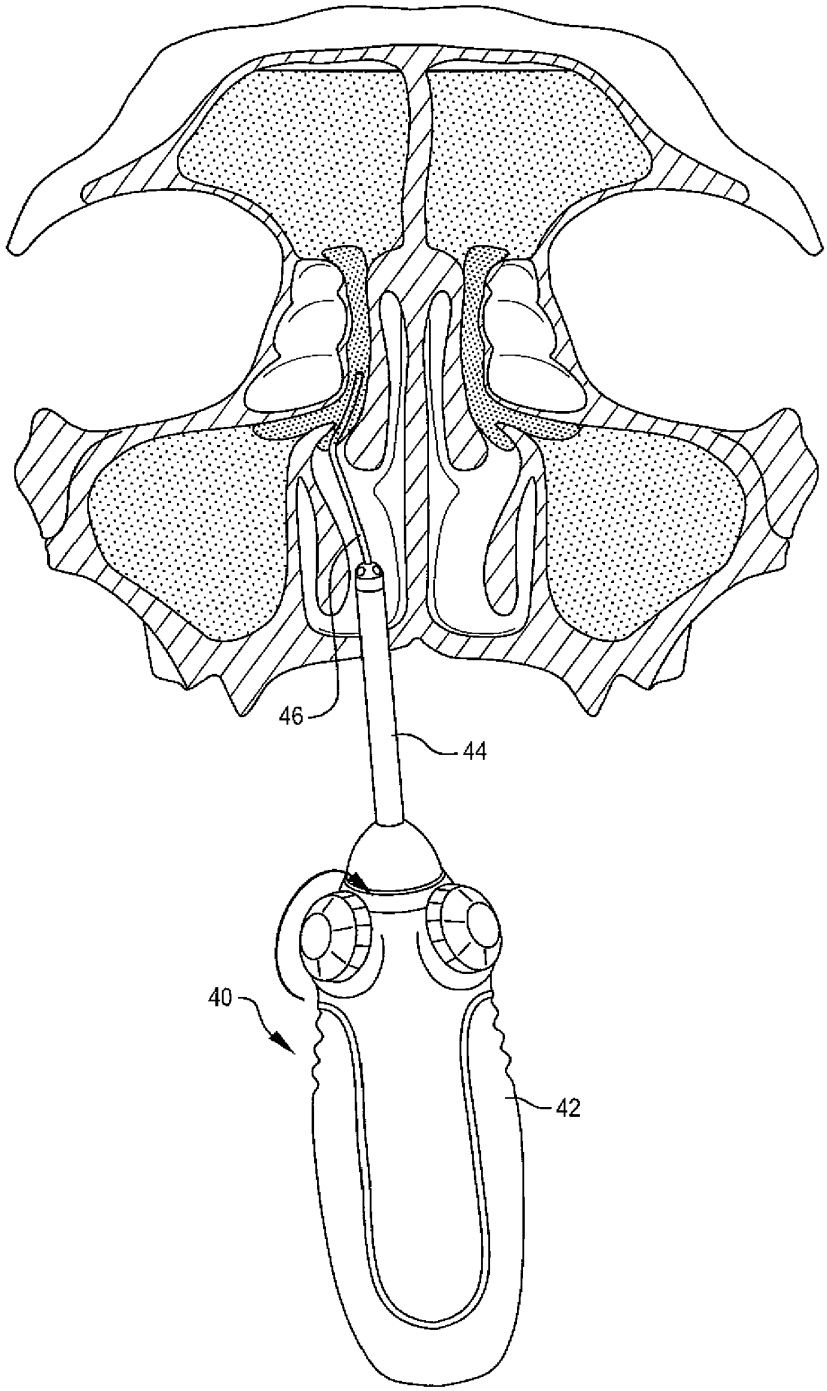


FIG. 8C

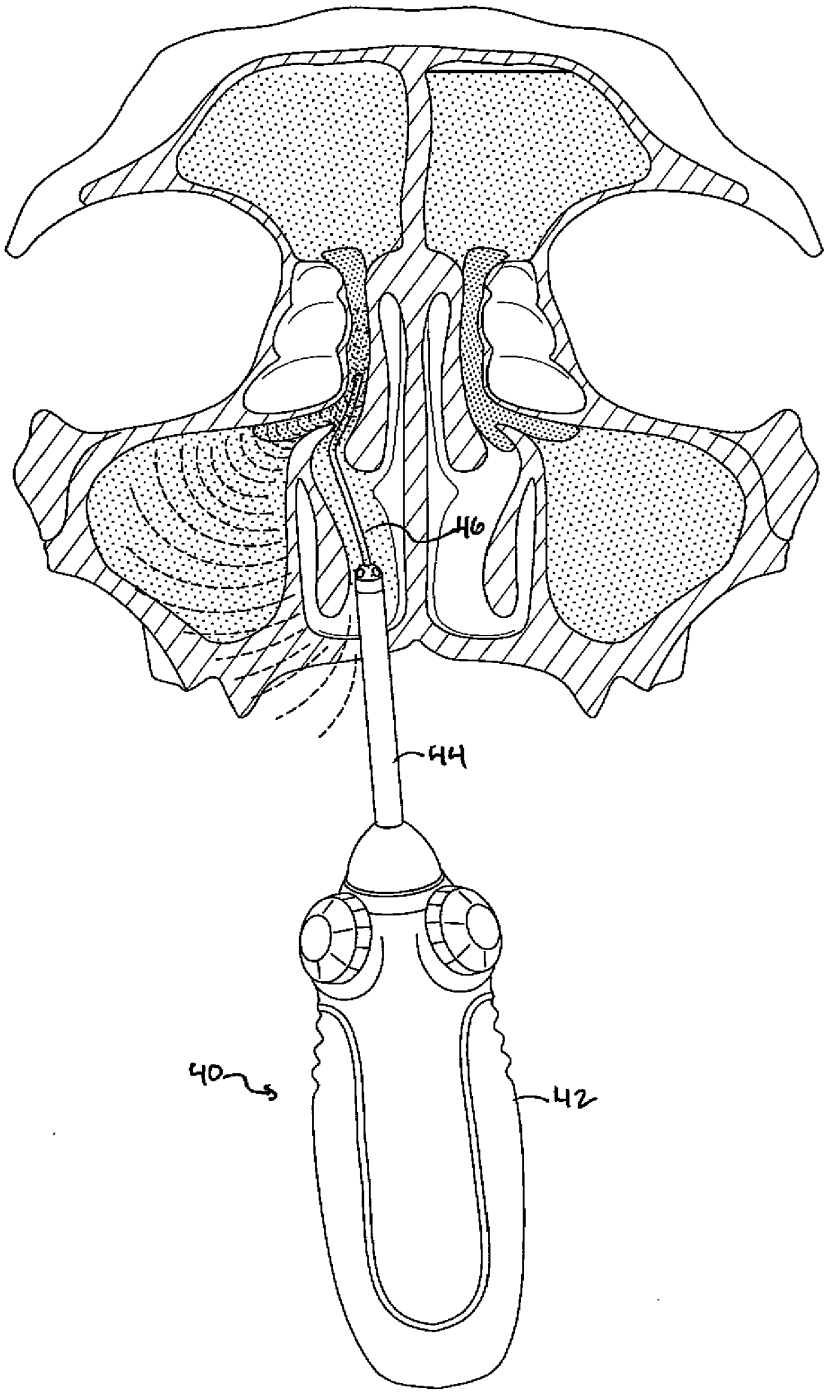


FIG. 8D

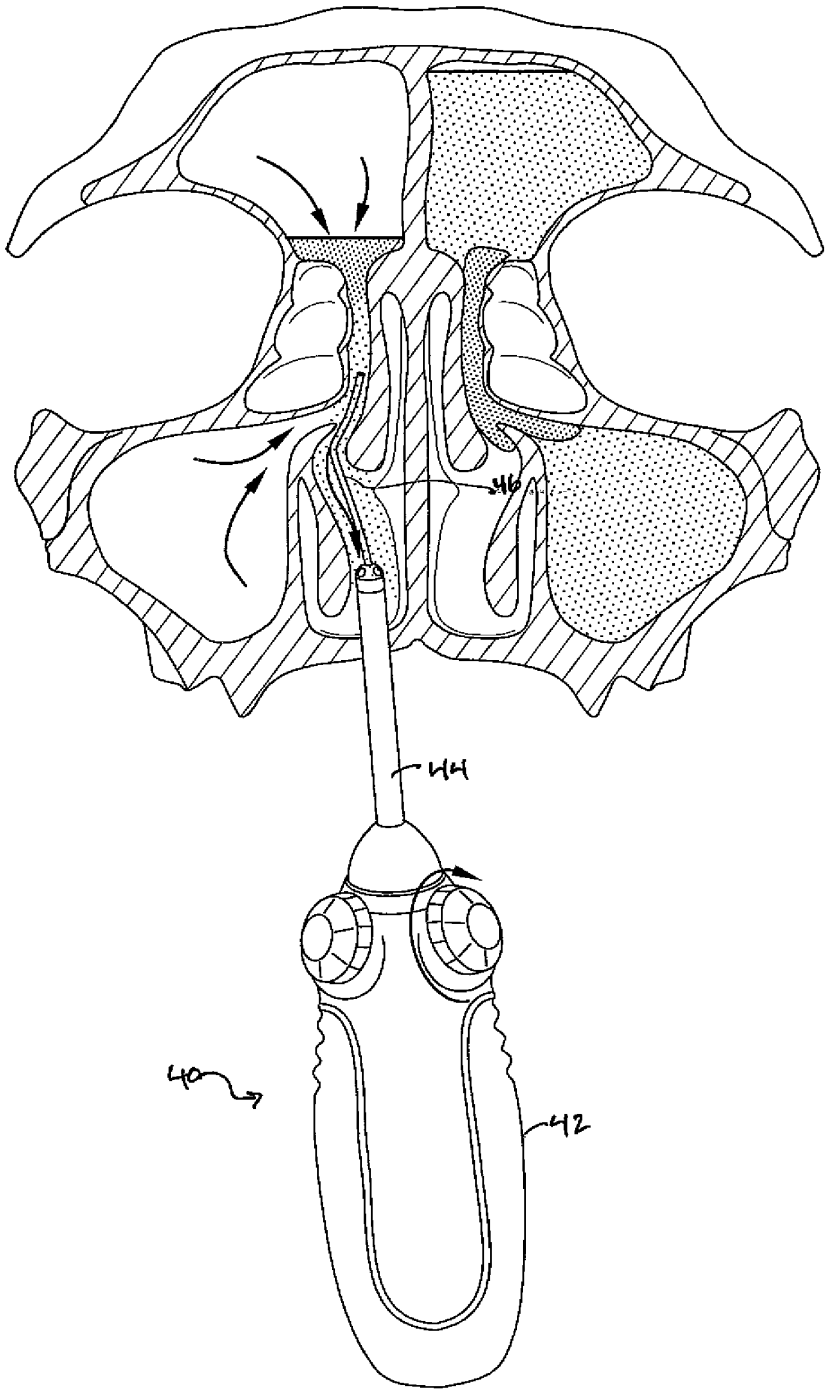
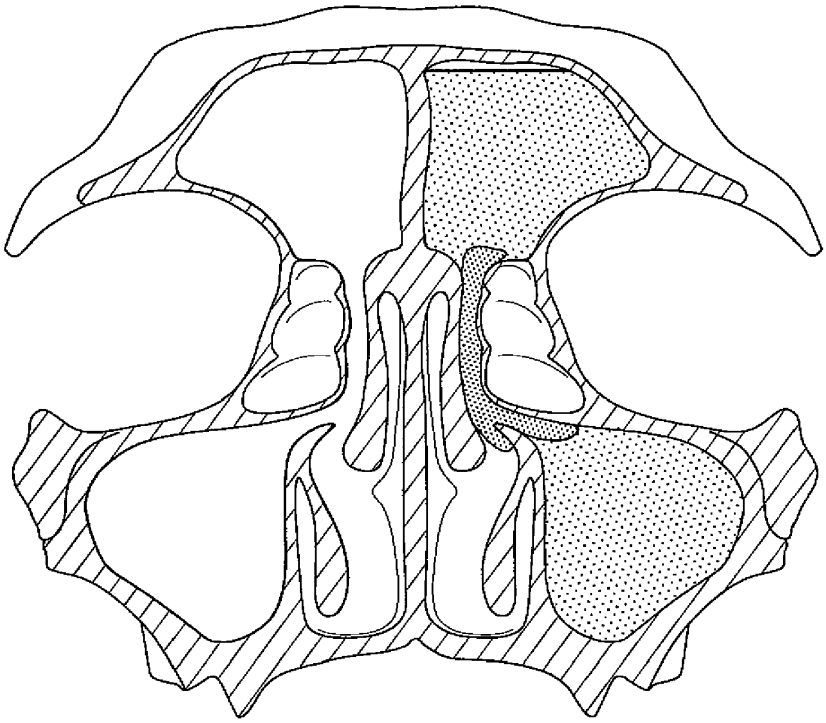


FIG. 8E



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/068309

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 17/32 (2010.01)
USPC - 604/22
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) - A61B 17/32 (2010.01)
USPC - 604/22; 606/169

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.
X -- Y	US 2002/0138036 A1 (BABAEV) 26 September 2002 (26.09.2002) entire document	1, 2, 9, 11, 12, 17, 33, 37 --- 3, 6, 13, 18-22, 34-36
Y	US 2008/0154183 A1 (BAKER et al) 26 June 2008 (26.06.2008) entire document	3, 13
Y	US 2003/0092667 A1 (TACHIBANA et al) 15 May 2003 (15.05.2003) entire document	6, 18, 34
Y	US 2004/0204728 A1 (HAEFNER) 14 October 2004 (14.10.2004) entire document	19
Y	US 2004/0024402 A1 (NITA) 05 February 2004 (05.02.2004) entire document	20, 35
Y	US 2002/0019627 A1 (MAGUIRE et al) 14 February 2002 (14.02.2002) entire document	21, 22, 36

☐ 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
11 February 2010	26 FEB 2010
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) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/068309

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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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.: 4, 5, 7, 8, 10, 14-16, 23-32, 38, 39
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 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.

Aerin Exhibit 1011, Page 604 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
Schoen, Adam M.
BROWN RUDNICK LLP
One Financial Center
Boston, MA 02111
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference NEURE-010/01WO 35242/80	Date of mailing *(day/month/year)* 24 January 2022 (24-01-2022) **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/IB2021/000597	International filing date *(day/month/year)* 31 August 2021 (31-08-2021)
Applicant NEURENT MEDICAL LIMITED	

1. [X] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

How? Directly to the International Bureau preferably through ePCT, or on paper to:
The International Bureau of WIPO, 34 chemin des Colombettes, 1211 Geneva 20, Switzerland

For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 - 9.011.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

The applicant may **submit comments on an informal basis on the written opinion of the International Searching Authority** to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer SULIS, Elisabetta Tel: +49 (0)89 2399-7922

Form PCT/ISA/220 (revised January 2020)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
NEURE-010/01WO 35242/80		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB2021/000597	31 August 2021 (31-08-2021)	31 August 2020 (31-08-2020)
Applicant		
NEURENT MEDICAL LIMITED		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. 2
      [ ] as suggested by the applicant
      [X] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Aerin Exhibit 1011, Page 606 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000597

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.: 21-40
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 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.

Aerin Exhibit 1011, Page 607 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000597

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/36 A61B18/14 A61N1/05
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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2020/107882 A1 (TOWNLEY DAVID [IE] ET AL) 9 April 2020 (2020-04-09) abstract; figures 2, 14 paragraphs [0002], [0012], [0023], [0030], [0042] - [0046], [0055], [0123] paragraphs [0066] - [0074]; figure 4 -/--	1-4, 18-20, 61, 64-70, 72-74, 76-80

[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
11 January 2022	24/01/2022

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	Molina Silvestre, A

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Form PCT/ISA/210 (second sheet) (April 2005)

Aerin Exhibit 1011, Page 608 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000597

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Anonymous: "Flexible electronics - Wikipedia", , 8 August 2020 (2020-08-08), pages 1-9, XP55877832, Retrieved from the Internet: URL:https://en.wikipedia.org/w/index.php?title=Flexible_electronics&oldid=971874913 [retrieved on 2022-01-11] the whole document	1-20, 41-95
A	US 2013/253389 A1 (JUTO JAN-ERIK [SE] ET AL) 26 September 2013 (2013-09-26) the whole document	1-20, 41-95
A	WO 2009/154456 A1 (KERPHOS B V [NL]; DE VOS GERRIT JOHANNIS [NL]) 23 December 2009 (2009-12-23) the whole document	1-20, 41-95

1

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

Aerin Exhibit 1011, Page 609 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000597

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2020107882 A1	09-04-2020	AU 2016262085 A1	04-01-2018
		AU 2021200322 A1	18-03-2021
		CA 2984207 A1	17-11-2016
		CN 107835705 A	23-03-2018
		EP 3294410 A2	21-03-2018
		HK 1252823 A1	06-06-2019
		JP 6854015 B2	07-04-2021
		JP 2018515314 A	14-06-2018
		JP 2021087861 A	10-06-2021
		US 2016331459 A1	17-11-2016
		US 2019231429 A1	01-08-2019
		US 2019239953 A1	08-08-2019
		US 2019239954 A1	08-08-2019
		US 2019239955 A1	08-08-2019
		US 2019239956 A1	08-08-2019
		US 2019239957 A1	08-08-2019
		US 2020100838 A1	02-04-2020
		US 2020107882 A1	09-04-2020
		WO 2016183337 A2	17-11-2016
US 2013253389 A1	26-09-2013	CN 104220037 A	17-12-2014
		EP 2641580 A1	25-09-2013
		JP 6175486 B2	02-08-2017
		JP 2015512279 A	27-04-2015
		US 2013253389 A1	26-09-2013
		WO 2013139644 A1	26-09-2013
WO 2009154456 A1	23-12-2009	NONE	

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/IB2021/000597

TITLE: DEVICE FOR THERAPEUTIC SINO-NASAL TREATMENT

APPLICANT: NEURENT MEDICAL LIMITED

IPC CLASSIFICATION: A61N1/36, A61B18/14, A61N1/05

EXAMINER: Molina Silvestre, A

CONSULTED DATABASES: NPL

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61N1/LOW, A61N1/36014, A61B18/1485, A61B2018/00327, A61B2018/00577, A61N1/0546

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
Claims as filed

EPO FORM P04A62

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2021/000597	31.08.2021	31.08.2020

International Patent Classification (IPC) or both national classification and IPC
INV. A61N1/36 A61B18/14 A61N1/05

Applicant
NEURENT MEDICAL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Molina Silvestre, A Telephone No. +49 89 2399-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 21-40

because:

☒ the said international application, or the said claims Nos. 21-40 relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 21-40

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☒ See Supplemental Box for further details

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-20, 41-95
	No:	Claims	
Inventive step (IS)	Yes:	Claims	5-17, 41-60, 62, 63, 71, 75, 81-95
	No:	Claims	1-4, 18-20, 61, 64-70, 72-74, 76-80
Industrial applicability (IA)	Yes:	Claims	1-20, 41-95
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

1 Reference is made to the following documents:

D1 US 2020/107882 A1 (TOWNLEY DAVID [IE] ET AL) 9 April 2020 (2020-04-09)

D2 Anonymous: "Flexible electronics - Wikipedia", , 8 August 2020 (2020-08-08), pages 1-9, XP55877832, Retrieved from the Internet: URL:https://en.wikipedia.org/w/index.php?title=Flexible_electronics&oldid=971874913 [retrieved on 2022-01-11]

2 **Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

3 No opinion has been established for claims 21-40 with regard to novelty, inventive step and industrial applicability because the subject-matter of these claims includes methods for treatment of the human or animal body by therapy in the sense of Rule 39.1(iv) PCT. This is because the step of treating a condition within a sino-nasal cavity constitutes such a method.

4 **Re Item V**

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

4.1 The application does not meet the requirements of Article 6 PCT, because claim 81 is not clear.

This is because the following technical feature is unclear:

F81.1: "wherein at least two of the struts are connected by a cross member"

In turn, F81.1 is unclear because the term "cross member" lacks a generally-acknowledged definition and is not defined in the claim.

For the purposes of the present document, claim 81 has been interpreted as if this unclear term had been clarified by stating that the cross member comprises a flexible PCB.

4.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 does not involve an inventive step in the sense of Article 33(3) PCT.

D1 is regarded as being the prior art closest to the subject-matter of claim 1, and discloses a device (fig. 14 (1402)) for treating a condition within a sino-nasal cavity of a patient, the device comprising: an end effector (fig. 14 (1412)) including one or more flexible circuit members (fig. 14 (1476)) for delivering energy to one or more target sites within the sino-nasal cavity of the patient (D1, abstract; figures 2, 14; paragraphs [0002], [0012], [0023], [0030], [0042] - [0046], [0055], [0123]).

The subject-matter of claim 1 therefore differs from this known device in that the flexible circuit member is a flexible printed circuit board (PCB) member.

D1 does not disclose in detail how the disclosed flex circuit is implemented. The problem to be solved by the present invention may therefore be regarded as filling this gap in the disclosure of D1.

The solution proposed in claim 1 of the present application cannot be considered to involve an inventive step (Article 33(3) PCT). This is because flexible PCBs are a very well-known and widely-used possibility for implementing flex circuits and is therefore a possibility that the skilled person would consider when filling this gap. This is all the more the case in view of the fact that D1 suggests creating "complex electrode arrays" (paragraph [0123]) and incorporating thermocouples and other circuitry (paragraph [0123]), aspects for which a flex PCB would be particularly well-suited.

4.3 Analogously, the present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 61 does not involve an inventive step in the sense of Article 33(3) PCT.

D1 is regarded as being the prior art closest to the subject-matter of claim 1, and discloses the provision of an end effector (balloon - fig. 14 (1470)) dimensioned to be at least partially deployed inside a sino-nasal cavity of a patient; and the attachment of a flexible circuit member (fig. 14 (1476)) to the end effector, the flexible circuit configured to deliver energy to a target site within the sino-nasal cavity (D1, abstract; figures 2, 14; paragraphs [0002], [0012], [0023], [0030], [0042] - [0046], [0055], [0123]).

The subject-matter of claim 61 therefore differs from this known method in that the flexible circuit member is a flexible printed circuit board (PCB) member.

D1 does not disclose in detail how the disclosed flex circuit is implemented. The problem to be solved by the present invention may therefore be regarded as filling this gap in the disclosure of D1.

The solution proposed in claim 61 of the present application cannot be considered to involve an inventive step (Article 33(3) PCT). This is because flexible PCBs are a very well-known and widely-used possibility for implementing flex circuits and is therefore a possibility that the skilled person would consider when filling this gap. This is all the more the case in view of the fact that D1 suggests creating "complex electrode arrays" (paragraph [0123]) and incorporating thermocouples and other circuitry (paragraph [0123]), aspects for which a flex PCB would be particularly well-suited.

4.4 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 76 does not involve an inventive step in the sense of Article 33(3) PCT.

D1 is regarded as being the prior art closest to the subject-matter of claim 76, and discloses the provision of providing a single piece of metal (each of the individual struts - fig. 4 (440)); and dimensioning the single piece of metal to form an end effector dimensioned for insertion into a sino-nasal cavity of a subject (D1, paragraphs [0066] - [0074]; figure 4)

The subject-matter of claim 76 therefore differs from this known device in that the single piece of metal is dimensioned by cutting.

D1 does not disclose in detail how the pieces of metal are dimensioned. The problem to be solved by the present invention may therefore be regarded as filling this gap in the disclosure of D1.

The solution proposed in claim 76 of the present application cannot be considered to involve an inventive step (Article 33(3) PCT). This is because cutting is a very well-known and widely-used possibility for dimensioning pieces of metal.

4.5 Dependent claims 2-4, 18-20, 64-70, 72-74, 77-80 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, the reasons being as follows:

4.5.1 In respect of each of claims 2, 4, 18, this is because its technical features are also anticipated by the disclosure of D1 (see D1 citations under 4.2 above). The subject-matter of each of these claims therefore differs from the disclosure of D1 in the same way the subject-matter of claim 1 does and hence lacks an inventive step for the same reasons. In respect of claim 4 the disclosed balloon (fig. 14 (1470)) is held to constitute a segment as per the claim.

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4.5.2 In respect of claim 3, this is because its subject-matter constitutes an obvious solution to the additional, independent partial problem of filling the gap in the disclosure of D1 with respect to how to couple the disclosed electrodes to the disclosed controller. In turn, this is because D1 already hints at using electrical communication paths on or within the flex circuit (fig. 14) and because using contacts to couple a flex circuit to other system components is a well-known and widely-used design pattern in electronics.

4.5.3 In respect of each of claims 19-20, this is because its subject-matter constitutes an obvious solution to the additional, independent partial problem of providing additional functionality for the device of fig. 14 of D1. In turn, this is because D1 already hints at the possibility of detecting tissue characteristics such as the impedance and at doing so using the same electrodes used for therapy (paragraphs [0044]-[0048], [0105]-[0111]).

4.5.4 In respect of each of claims 64-68, 70, 72, this is because its respective subject-matter constitutes an obvious solution to the problem of filling the gap in the disclosure of D1 with respect to the flex circuit implementation. In turn, this is because thermal and mechanical processes as claimed are well-known possibilities in order to achieve the adhesion disclosed in D1.

4.5.5 In respect of claim 69, this is because its subject-matter constitutes an obvious solution to the problem of filling the gap in the disclosure of D1 with respect to the flex circuit implementation. In turn, this is because single-sheet PCBs are a well-known possibility for implementing flex PCBs.

4.5.6 In respect of claim 73, this is because its technical features are also anticipated by the disclosure of D1 (see D1 citations under 4.3 above). The subject-matter of each of these claims therefore differs from the disclosure of D1 in the same way the subject-matter of claim 61 does and hence lacks an inventive step for the same reasons.

In respect of claim 74, this is because its subject-matter constitutes an obvious solution to the problem of filling the gap in the disclosure of D1 with respect to the implementation of the disclosed adhesion between the flex circuit and the balloon.

4.5.7 In respect of each of claims 77-80, this is because its technical features are also anticipated by the disclosure of D1 (see D1 citations under 4.4 above). The subject-matter of each of these claims therefore differs from the disclosure of D1 in the same way the subject-matter of claim 76 does and hence lacks an inventive step for the same reasons.

4.6 The subject-matter of each of claims 5-17, 41-60, 62, 63, 71, 75, 81-95, is neither anticipated nor rendered obvious by the available prior art. The reasons are as follows:

4.7 D1 is regarded as being the prior art closest to the subject-matter of claim 5, and discloses a device for treating a condition within a sino-nasal cavity of a patient, the device comprising an end effector including a flex circuit member and one expandable segment to which the flex circuit member is operably associated with. The subject-matter of claim 5 therefore differs from this known device in that the end effector comprises a first retractable and expandable segment comprising a plurality of first support structures upon which one or more flexible PCB members are fixedly coupled and is therefore new (Article 33(2) PCT).

The problem to be solved by the present invention may be regarded as providing for an alternative design for the device of D1.

The solution to this problem proposed in claim 5 of the present application is considered as involving an inventive step (Article 33(3) PCT). This is because, while many possibilities are conceivable to this effect, no motivation can be identified in D1 or elsewhere that would lead the skilled person to solving this problem as claimed.

4.8 Similarly, D1 is regarded as being the prior art closest to the subject-matter of claim 41, and discloses a device for treating a condition in a nasal cavity, the device comprising an end effector dimensioned for insertion into a nasal cavity and a flexible circuit member. The subject-matter of claim 41 therefore differs from this known device in that the end effector comprises at least one segment that is a unitary single piece of material comprising a plurality of individual struts the flex circuit member being attached to at least one of the struts and is therefore new (Article 33(2) PCT).

The problem to be solved by the present invention may be regarded as providing for an alternative design for the device of D1.

The solution to this problem proposed in claim 41 of the present application is considered as involving an inventive step (Article 33(3) PCT). This is because, while many possibilities are conceivable to this effect, no motivation can be identified in D1 or elsewhere that would lead the skilled person to solving this problem as claimed.

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4.9 An analogous reasoning applies in respect of each of claims 62, 71, 75 and 81 (assuming it can be clarified as per 4.1 above), each of which is therefore also held to meet the requirements of the PCT with respect to novelty and inventive step.

4.10 Claims 6-17 are dependent on claim 5 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4.11 Claims 42-60 are dependent on claim 41 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4.12 Claims 63 are dependent on claim 62 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4.13 Claims 82-92 are dependent on claim 81 and (assuming claim 81 can be clarified as per 4.1 above) as such also meet the requirements of the PCT with respect to novelty and inventive step.

5 **Re Item VII**

Certain defects in the international application

5.1 The features of claims 1-95 are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

5.2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D1 is not mentioned in the description, nor are these documents identified therein.

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO/ISA)

General information

For all international applications, the competent International Searching Authority **(ISA)** will establish an international search report **(ISR)** accompanied by a written opinion of the International Searching Authority **(WO/ISA)**. The **WO/ISA** may be responded to by

- filing informal comments with the **International Bureau of WIPO (IB)** (where no demand for international preliminary examination **(demand)** is filed)
- filing amendments under Art. 19 PCT (this can be done whether or not a **demand** is filed)
- filing amendments under Art. 34 PCT and/or formal observations in response to objections raised in the **WO/ISA** (where a **demand** *is* actually filed)

This document explains these possibilities.

Filing informal comments

After receipt of the **ISR and WO/ISA**, the applicant may file informal comments on the **WO/ISA, directly with the IB** (see International Search and Preliminary Examination Guidelines 2.15). These will be communicated to the designated/elected Offices, together with the International Preliminary Report on Patentability **(IPRP)** at 30 months from the priority date.

Amending claims under Art. 19 PCT

The applicant may file **amended claims** under Art. 19 PCT, **directly with the IB** by the later of the following dates:

- 2 months from the date of mailing of the **ISR** and the **WO/ISA**
- 16 months from the priority date

However, any such amendment received by the **IB** after the expiration of the applicable time limit shall be **considered to have been received on time** by the **IB**, if it reaches it **before** the technical preparations for international publication have been completed (the 15th day prior to the date of publication, see PCT Applicant's Guide, International Phase, 9.013).

For further information, please see Rule 46 PCT as well as form PCT/ISA/220.

Please also note that, when filing amended claims under Art. 19 PCT, such amendments shall be **accompanied by a letter** identifying the amendments made and also the basis for the amendments in the application as originally filed (Rule 46.5(b) PCT). Where a **demand** is filed, failure to comply with this requirement may result in the amendments being ignored in the International Preliminary Examination Report **(IPER)**, see Rule 70.2(c-*bis*) PCT.

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TISSUE CONTACT SENSING USING A MEDICAL DEVICE

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Applicant(s): BOSTON SCIENT SCIMED INC [US] ± (BOSTON SCIENTIFIC SCIMED INC)

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Abstract of WO2016134264 (A1)

Medical devices and methods for making and using medical devices are disclosed. An example system for sensing tissue contact is disclosed. The system comprises a catheter shaft including a distal end portion. The distal end portion includes a sensing assembly having a plurality of electrodes. The plurality of electrodes includes a current-carrying electrode, a first sensing electrode and a second sensing electrode. The first sensing electrode is positioned a first distance from the current-carrying electrode. The second sensing electrode is positioned a second distance from the current-carrying

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electrode and the first distance is different from the second distance. The system also includes a controller coupled to the plurality of mapping electrodes. The controller is capable of calculating a parameter based at least in part on the first and the second distances.

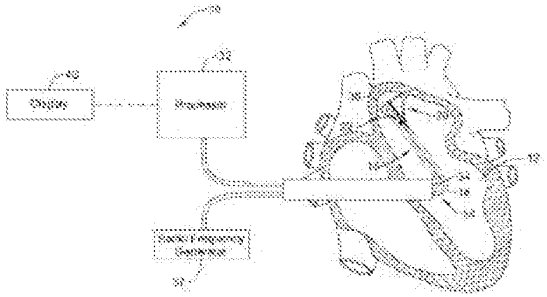


FIG. 1

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(54) **Title**: TISSUE CONTACT SENSING USING A MEDICAL DEVICE

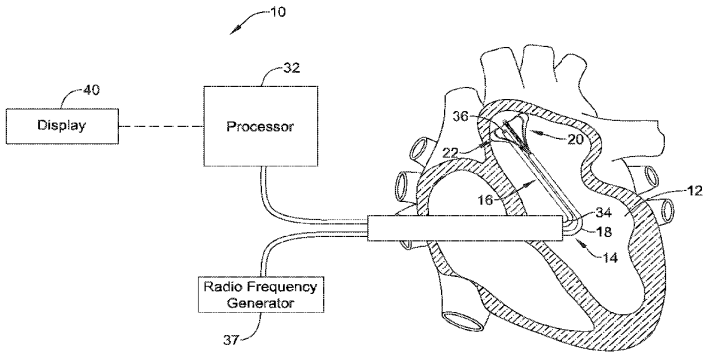


FIG. 1

(57) **Abstract**: Medical devices and methods for making and using medical devices are disclosed. An example system for sensing tissue contact is disclosed. The system comprises a catheter shaft including a distal end portion. The distal end portion includes a sensing assembly having a plurality of electrodes. The plurality of electrodes includes a current-carrying electrode, a first sensing electrode and a second sensing electrode. The first sensing electrode is positioned a first distance from the current-carrying electrode. The second sensing electrode is positioned a second distance from the current-carrying electrode and the first distance is different from the second distance. The system also includes a controller coupled to the plurality of mapping electrodes. The controller is capable of calculating a parameter based at least in part on the first and the second distances.

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TISSUE CONTACT SENSING USING A MEDICAL DEVICE

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application claims priority to Provisional Application No. 62/118,897, filed February 20, 2015, which is herein incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present disclosure pertains to medical devices, and methods for manufacturing medical devices. More particularly, the present disclosure pertains to tissue diagnosis and/or ablation.

BACKGROUND

[0003] A wide variety of intracorporeal medical devices have been developed for medical use, for example, intravascular use. Some of these devices include guidewires, catheters, and the like. These devices are manufactured by any one of a variety of different manufacturing methods and may be used according to any one of a variety of methods. Of the known medical devices and methods, each has certain advantages and disadvantages. There is an ongoing need to provide alternative medical devices as well as alternative methods for manufacturing and using medical devices.

SUMMARY

[0004] This disclosure provides design, material, manufacturing method, and use alternatives for medical devices. An example electrophysiology medical device is disclosed. The medical device comprises:

a catheter shaft including a distal end portion, wherein the distal end portion includes a sensing assembly having a plurality of mapping electrodes;

wherein the plurality of mapping electrodes includes at least one current-carrying electrode, a first sensing electrode and a second sensing electrode;

wherein the first sensing electrode is spaced from the current-carrying electrode a first distance;

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wherein the second sensing electrode is spaced from the current-carrying electrode a second distance;

wherein the first distance is different from the second distance; and

a controller coupled to the plurality of mapping electrodes;

wherein the controller is capable of calculating a parameter based at least in part on the first and the second distances.

[0005] Alternatively or additionally, the parameter indicates the proximity of the medical device to tissue.

[0006] Alternatively or additionally, calculating the parameter includes sensing a first voltage potential between the first electrode and one or more return electrodes, and sensing a second voltage potential between the second electrode and one or more return electrodes.

[0007] Alternatively or additionally, calculating the parameter includes solving at least one linear equation, and wherein the at least one linear equation includes the first distance, the second distance, the first voltage and the second voltage.

[0008] Alternatively or additionally, the sensing assembly includes a plurality of splines, and wherein the plurality of electrodes are disposed on the plurality of splines.

[0009] Alternatively or additionally, the sensing assembly includes a plurality of splines, and wherein the plurality of splines includes an outwardly facing surface, and wherein the plurality of electrodes are disposed on the outwardly facing surface.

[0010] Alternatively or additionally, the sensing assembly includes a plurality of splines, and wherein the plurality of splines are arranged in a basket.

[0011] Alternatively or additionally, the plurality of electrodes are each designed to sequentially and/or simultaneously operate in a sensing configuration and a current-carrying configuration.

[0012] Alternatively or additionally, further comprising displaying the parameter on a display.

[0013] Alternatively or additionally, displaying the parameter includes displaying a confidence value corresponding to the parameter.

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[0014] Alternatively or additionally, the displaying the parameter on a display further includes displaying an anatomical shell and/or an electroanatomical map that indicates the proximity of one or more of the plurality of electrodes to tissue.

[0015] Another example system for sensing tissue contact comprises:

a catheter shaft including a distal end portion, wherein the distal end portion includes a sensing assembly having a plurality of electrodes;

wherein the plurality of electrodes includes a current-carrying electrode, a first sensing electrode and a second sensing electrode;

wherein the first sensing electrode is positioned a first distance from the current-carrying electrode;

wherein the second sensing electrode is positioned a second distance from the current-carrying electrode;

wherein the first distance is different from the second distance;

a processor, wherein the processor is designed to:

simultaneously detect:

(a) a first parameter based at least in part on the first and second distances, and

(b) an impedance increase across at least one of the plurality of electrodes.

[0016] Alternatively or additionally, wherein the impedance increase is defined by a change in impedance by at least 100%.

[0017] Alternatively or additionally, wherein simultaneously detecting an impedance increase indicates that at least one of the plurality of electrodes is embedded in tissue.

[0018] Alternatively or additionally, wherein simultaneously detecting a first parameter based at least in part on the first and second distances includes sensing a first voltage potential between the first electrode and one or more return electrodes, and sensing a second voltage potential between the second electrode and the one or more return electrodes.

[0019] Alternatively or additionally, wherein simultaneously detecting a first parameter includes solving at least one linear equation, and wherein the at least one

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linear equation includes the first distance, the second distance, the first voltage and the second voltage.

[0020] Alternatively or additionally, wherein simultaneously detecting an impedance increase includes measuring an impedance between a current-carrying electrode and one or more return electrodes

[0021] Another example electrophysiology medical device comprises:

a catheter shaft including a distal end portion;

a sensing assembly having a plurality of electrodes, wherein the plurality of electrodes includes four or more terminals;

wherein the four or more terminals includes one or more current-carrying electrodes and one or more sensing electrodes;

wherein the one or more current- carrying electrodes, the one or more sensing electrodes, or both includes a mapping electrode;

wherein the four or more terminals are designed to measure an electrical characteristic; and

a processor coupled to the sensing assembly.

[0022] Alternatively or additionally, wherein the electrical characteristic is a voltage, an impedance, or both.

[0023] Alternatively or additionally, wherein the electrical characteristic indicates the proximity of the medical device to tissue.

[0024] Another medical device for sensing contact with tissue comprises:

a catheter shaft, wherein the shaft includes a distal portion;

a sensing assembly coupled to the distal portion of the catheter shaft, wherein the sensing assembly includes a plurality of electrodes; and

wherein the plurality of electrodes includes at least a first mapping electrode, and wherein the first mapping electrode is designed to detect an impedance increase, and wherein the impedance increase is defined by an increase of an impedance by 100% or more.

[0025] The above summary of some embodiments is not intended to describe each disclosed embodiment or every implementation of the present disclosure. The

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Figures, and Detailed Description, which follow, more particularly exemplify these embodiments.

[0026] While multiple embodiments are disclosed, still other embodiments of the present invention will become apparent to those skilled in the art from the following detailed description, which shows and describes illustrative embodiments of the invention. Accordingly, the drawings and detailed description are to be regarded as illustrative in nature and not restrictive.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] The disclosure may be more completely understood in consideration of the following detailed description in connection with the accompanying drawings, in which:

[0028] FIG. 1 is a plan view of an example tissue diagnosis and/or ablation system;

[0029] FIG. 2 illustrates an example medical device including an electrode structure, a catheter shaft and a handle;

[0030] FIG. 3 illustrates an example basket electrode structure including sensing electrodes;

[0031] FIG. 4 illustrates an example electrode having multiple layers;

[0032] FIG. 5 illustrates an example electrode having multiple layers;

[0033] FIGS. 6-8 illustrate an example electrode structure utilized with the system of FIG. 1 moving between blood and tissue;

[0034] FIG. 9 illustrates an example electrode structure having multiple sensing electrodes spaced different distances away from a tip electrode.

[0035] While the disclosure is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the invention to the particular embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the disclosure.

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DETAILED DESCRIPTION

[0036] For the following defined terms, these definitions shall be applied, unless a different definition is given in the claims or elsewhere in this specification.

[0037] All numeric values are herein assumed to be modified by the term "about", whether or not explicitly indicated. The term "about" generally refers to a range of numbers that one of skill in the art would consider equivalent to the recited value (e.g., having the same function or result). In many instances, the terms "about" may include numbers that are rounded to the nearest significant figure.

[0038] The recitation of numerical ranges by endpoints includes all numbers within that range (e.g. 1 to 5 includes 1, 1.5, 2, 2.75, 3, 3.80, 4, and 5).

[0039] As used in this specification and the appended claims, the singular forms "a", "an", and "the" include plural referents unless the content clearly dictates otherwise. As used in this specification and the appended claims, the term "or" is generally employed in its sense including "and/or" unless the content clearly dictates otherwise.

[0040] It is noted that references in the specification to "an embodiment", "some embodiments", "other embodiments", etc., indicate that the embodiment described may include one or more particular features, structures, and/or characteristics. However, such recitations do not necessarily mean that all embodiments include the particular features, structures, and/or characteristics. Additionally, when particular features, structures, and/or characteristics are described in connection with one embodiment, it should be understood that such features, structures, and/or characteristics may also be used connection with other embodiments whether or not explicitly described unless clearly stated to the contrary.

[0041] 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.

[0042] Cardiac arrhythmia and/or other cardiac pathology contributing to abnormal heart function may originate in cardiac cellular tissue. One technique that may be utilized to treat the arrhythmia and/or cardiac pathology may include ablation of tissue substrates

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contributing to the arrhythmia and/or cardiac pathology. Ablation by heat, chemicals or other means of creating a lesion in the tissue substrate may isolate diseased tissue from normal heart circuits. In some instances, electrophysiology therapy may involve locating tissue contributing to the arrhythmia and/or cardiac pathology using a mapping and/or diagnosing catheter and then using an ablation electrode to destroy and/or isolate the diseased tissue.

[0043] Prior to performing an ablation procedure, a physician and/or clinician may utilize specialized mapping and/or diagnostic catheters to precisely locate tissue contributing and/or causing an arrhythmia or other cardiac pathology. It is often desirable to precisely locate the targeted tissue prior to performing an ablation procedure in order to effectively alleviate and/or eliminate the arrhythmia and/or cardiac pathology. Further, precise targeting of the tissue may prevent or reduce the likelihood that healthy tissue (located proximate the targeted tissue) is damaged.

[0044] Several methods and/or techniques may be employed to precisely locate targeted tissue where an ablation or other therapeutic procedure may be performed. An example method may include utilizing an ablation, mapping and/or diagnostic catheter to determine how close the catheter is to targeted tissue. Further, the ablation, mapping and/or diagnostic catheter may include one or more sensing electrodes located on a distal portion of the catheter. The electrodes may sense, measure and/or provide a processor with information relating to electrical characteristics of the cardiac tissue and surrounding media. Using the sensed and/or measured information, the processor may be able to correlate the spatial location of the distal portion of the catheter to the cardiac tissue. For example, electrodes may sense the impedance, resistance, voltage potential, etc. of the cardiac tissue and/or surrounding media and determine how far a distal portion of a diagnostic and/or ablation catheter is to cardiac tissue.

[0045] In general, the size, shape and spacing of electrodes on a diagnostic (e.g. mapping) catheter may contribute to the accuracy to which a diagnostic catheter may sense and/or measure electrical characteristics. For example, some methods and/or techniques disclosed herein may emit a current from a first electrode and measure a voltage, impedance or other electrical characteristic of local tissue using other electrodes. Further, in some instances the size of an electrode may directly influence

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the magnitude of the measured response by a processor. For example, as will be discussed in detail later, impedance measurements corresponding to tissue contact may be magnified by using small, flat electrodes as compared to other sensing electrode configurations. Small, flat electrodes may increase the likelihood that a given electrode may become fully embedded and/or surrounded in cardiac tissue. Fully embedding a sensing electrode within cardiac tissue may directly correspond to determining whether the electrode is in contact with the cardiac tissue.

[0046] In addition, larger electrodes may be more susceptible (as compared to smaller electrodes) to detecting far field electrical activity. Detection of far field electrical activity may negatively affect the detection of local (e.g. targeted) electrical activity.

[0047] Therefore, in some instances it may be desirable to utilize and incorporate small, flat electrodes into the distal portion of a mapping and/or a diagnostic catheter. For example, some of the medical devices and methods disclosed herein may include sensing and measuring electrical activity using one or more relatively small, flat electrodes in conjunction with other sensing methods, electrodes, ablation electrodes, diagnostic catheters and/or other medical devices. Further, some of the medical devices and methods disclosed herein may utilize electrical characteristics collected from small, flat electrodes to assess tissue proximity and/or contact. Other methods and medical devices are also disclosed.

[0048] FIG. 1 is a schematic view of a system 10 for accessing a targeted tissue region in the body of a patient for diagnostic and/or therapeutic purposes. FIG. 1 generally shows the system 10 deployed in a region of the heart. For example, system 10 may be deployed in any chamber of the heart, such as the left atrium, left ventricle, right atrium, or right ventricle, another region of the cardiovascular system, or other anatomical region. While the illustrated embodiment shows the system 10 being used for sensing contact and/or proximity to myocardial tissue, the system 10 (and the methods described herein) may alternatively be configured for use in other tissue applications, such as procedures for sensing tissue in the prostate, brain, gall bladder, uterus, nerves, blood vessels and other regions of the body, including body regions not typically accessed by a catheter.

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[0049] System 10 includes a mapping catheter or probe 14. In some instances, system 10 may also include an ablation catheter or probe 16. Each probe 14/16 may be separately introduced into the selected heart region 12 through a vein or artery (e.g., the femoral vein or artery) using a suitable percutaneous access technique. Alternatively, mapping probe 14 and ablation probe 16 can be assembled in an integrated structure for simultaneous introduction and deployment in the heart region 12.

[0050] Mapping probe 14 may include flexible catheter body 18. The distal end of catheter body 18 carries three-dimensional multiple electrode structure 20. In the illustrated embodiment, structure 20 takes the form of a basket defining an open interior space 22 (see FIG. 2), although other multiple electrode structures could be used. Structure 20 carries a plurality of mapping electrodes 24 (not explicitly shown on FIG. 1, but shown on FIG. 2) each having an electrode location on structure 20 and a conductive member. Each mapping electrode 24 may be configured to sense electrical characteristics (e.g. voltage and/or impedance) in an adjacent anatomical region.

[0051] Electrodes 24 may be electrically coupled to processing system 32. A signal wire (not shown) may be electrically coupled to each electrode 24 on structure 20. The signal wires may extend through body 18 of probe 14 and electrically couple each electrode 24 to an input of processing system 32. Electrodes 24 may sense electrical characteristics correlated to an anatomical region adjacent to their physical location within the heart. The sensed cardiac electrical characteristic (e.g., voltage, impedance, etc.) may be processed by processing system 32 to assist a user, for example a physician, by generating processed output – e.g. an anatomical map (e.g., 3D map of heart chamber) – to identify one or more sites within the heart appropriate for a diagnostic and/or treatment procedure, such as an ablation procedure.

[0052] Processing system 32 may include dedicated circuitry (e.g., discrete logic elements and one or more microcontrollers; application-specific integrated circuits (ASICs); or specially configured programmable devices, such as, for example, programmable logic devices (PLDs) or field programmable gate arrays (FPGAs)) for receiving and/or processing the acquired physiological activity. In some examples, processing system 32 may include a general purpose microprocessor and/or a

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specialized microprocessor (e.g., a digital signal processor, or DSP, which may be optimized for processing activation signals) that executes instructions to receive, analyze and display information associated with the received physiological activity. In such examples, processing system 32 can include program instructions, which when executed, perform part of the signal processing. Program instructions can include, for example, firmware, microcode or application code that is executed by microprocessors or microcontrollers. The above-mentioned implementations are merely exemplary, and the reader will appreciate that processing system 32 can take any suitable form for receiving electrical signals and processing the received electrical signals.

[0053] Ablation probe 16 may include flexible catheter body 34 that carries one or more ablation electrodes 36. The one or more ablation electrodes 36 may be electrically connected to radio frequency (RF) generator 37 that is configured to deliver ablation energy to the one or more ablation electrodes 36. Ablation probe 16 may be movable with respect to the anatomical feature to be treated, as well as structure 20. Ablation probe 16 may be positionable between or adjacent to mapping electrodes 24 of structure 20 as the one or more ablation electrodes 36 are positioned with respect to the tissue to be treated.

[0054] Processing system 32 may output data to a suitable device, for example display device 40, which may display relevant information for a user. In some examples, device 40 is a display (e.g. a CRT, LED), or other type of display, or a printer. Device 40 may present the relevant characteristics in a format useful to the user. In addition, processing system 32 may generate position-identifying output for display on device 40 that aids the user in guiding an ablation electrode into contact with tissue at the site identified for ablation.

[0055] FIG. 2 illustrates mapping catheter 14 and shows mapping electrodes 24 at the distal end suitable for use in system 10 shown in FIG. 1. Mapping catheter 14 may include flexible catheter body 18, the distal end of which may carry three-dimensional multiple electrode structure 20 with mapping electrodes or sensors 24. Mapping electrodes 24 may sense electrical characteristics (e.g. voltage, impedance) in the myocardial tissue. The sensed cardiac electrical activity may be processed by the processing system 32 to assist a user in identifying the site or sites having a heart

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rhythm disorder or other myocardial pathology via generated and displayed relevant characteristics. This information can then be used to determine an appropriate location for applying appropriate therapy, such as ablation, to the identified sites, and to navigate the one or more ablation electrodes 36 to the identified sites.

[0056] Multiple electrode structure 20 may include base member 41 and distal tip 42 between which flexible splines 44 generally extend in a circumferentially spaced relationship. As discussed herein, structure 20 may take the form of a basket defining an open interior space 22. Structure 20 may flare distally from a constrained configuration to a more open configuration. In some examples, the splines 44 are made of a resilient inert material, such as Nitinol, other metals, silicone rubber, suitable polymers, or the like and are connected between base member 41 and distal tip 42. In some instances, splines 44 may be made of parylene. As shown in FIG. 2, splines 44 may include a substantially flat outwardly facing surface 21 and may resemble strips having a substantially reduced thickness and extending from distal tip 42 to catheter body 18. In some instances, splines 44 may have a rectangular and/or ovular cross-section. These are just examples; other cross-sectional shapes are contemplated. Other shapes, configurations and arrangements are contemplated including arrangements disclosed in U.S. Patent 8103327, the entire disclosure of which is herein incorporated by reference.

[0057] In some embodiments described herein, distal tip 42 may include an ablation electrode. Further, in some instances distal tip 42 may include an ablation electrode coupled to RF generator 37. Distal tip 42 may emit ablative energy and/or an electrical current.

[0058] In some instances, splines 44 are positioned in a resilient, pretensioned condition, to bend and conform to the tissue surface they contact. In the example illustrated in FIG. 2, eight splines 44 form three-dimensional multiple electrode structure 20. Additional or fewer splines 44 could be used in other examples. As illustrated, each spline 44 carries eight mapping electrodes 24. Additional or fewer mapping electrodes 24 could be disposed on each spline 44 in other examples of three dimensional multiple electrode structure 20. Slidable sheath 50 may be movable along the major axis of catheter body 18. Moving sheath 50 distally relative to catheter body 18 may cause

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sheath 50 to move over structure 20, thereby collapsing structure 20 into a compact, low profile condition suitable for introduction into and/or removal from an interior space of an anatomical structure, such as, for example, the heart. In contrast, moving sheath 50 proximally relative to the catheter body may expose structure 20, allowing structure 20 to elastically expand and assume the pre-tensioned position illustrated in FIG. 2.

[0059] In other examples, slidable sheath 50 (or other deployment shaft) may be connected to distal tip 42. Further, deployment of structure 20 may include manipulating a slidable sheath 50 (or other deployment shaft) coupled to distal tip 42. For example, deployment of structure 20 may be accomplished by pulling slidable sheath 50 (or other deployment shaft) in a proximal direction. The proximal movement of slidable sheath 50 (or other deployment shaft) may result in distal tip 42 moving in a proximal direction. As distal tip 42 moves proximally, it may force splines 44 to flare out and assume the shape of structure 20 shown in Fig. 2, for example.

[0060] A signal wire (not shown) may be electrically coupled to each mapping electrode 24. The signal wires may extend through body 18 of mapping catheter 14 (or otherwise through and/or along body 18) into handle 54, in which they are coupled to external connector 56, which may be a multiple pin connector. Connector 56 may electrically couple mapping electrodes 24 to processing system 32. It should be understood that these descriptions are just examples. Some addition details regarding these and other example mapping systems and methods for processing signals generated by a mapping catheter can be found in U.S. Patent Nos. 6,070,094, 6,233,491, and 6,735,465, the disclosures of which are hereby expressly incorporated herein by reference.

[0061] To illustrate the operation of system 10, FIG. 3 is a schematic side view of example basket structure 20 including a plurality of mapping electrodes 24. In the illustrated example, the basket structure includes 64 mapping electrodes 24. Mapping electrodes 24 are disposed in groups of eight electrodes (labeled 1, 2, 3, 4, 5, 6, 7, and 8) on each of eight splines (labeled A, B, C, D, E, F, G, and H). While an arrangement of sixty-four mapping electrodes 24 is shown disposed on basket structure 20, mapping electrodes 24 may alternatively be arranged in different numbers (more or fewer splines and/or electrodes), on different structures, and/or in different positions. In addition,

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multiple basket structures can be deployed in the same or different anatomical structures to simultaneously obtain signals from different anatomical structures.

[0062] FIG. 4 shows example electrode 60 disposed along spline 44. Electrode 60 may be one of the plurality of mapping electrodes 24. In some instances, such as that shown in FIG. 4, electrode 60 may be affixed along a surface of spline 44. However, it is contemplated that electrode 60 may be coupled to spline 44 using a variety of methodologies. As discussed herein, electrode 60 may be described as being "affixed," "on" and/or otherwise embedded and/or encased on any structure contemplated herein. This is not intended to be limiting. Positioning/locating electrode 60 along spline 44 may include embedding, partially embedding, encasing, partially encasing, isolating, attaching, affixing, fastening, bonding to the outer surface, embedding within the wall, or the like. Additionally, as shown and described with respect to FIGS. 1-3, it is contemplated that more than one electrode 60 may be affixed to spline 44.

[0063] In some instances, electrode 60 may include base layer 62 and top layer 64. Top layer 64 may be a layer of material applied over base layer 62. For example, in some instances base layer 62 may be made from gold, while top layer 64 may be made of iridium oxide. A masked layer of parylene may be applied over base layer 62 such that only top layer 64 is exposed. In some applications, base layer 62 may be applied as a plated layer. For example, electrode structure 20 may be constructed from a method of manufacturing that may bear some resemblance to an analogous processes utilized in the manufacturing of semiconductors. In other words, the manufacturing process may include "printing" or "layering" top layer 64 along, atop, within, embedded with, etc. bottom layer 62. Further, the example method of manufacturing may include forming bottom layer 62 of material (e.g. gold) upon which top layer 64 (e.g. iridium oxide) may be "printed," "layered," "plated," "sputtered," or the like. The manufacturing method may further include layering one or more additional layers on top and/or within the either top layer 64 and/or bottom layer 62. Additional layers of material may include traces, circuit components, or the like. In some instances, a portion of a layer may be removed to expose an underlying layer. These are just examples, other materials and manufacturing techniques are contemplated.

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Further, while the following discussion is directed toward the electrode structure previously described, it is contemplated that a variety of electrode designs, including those without multiple layers, may be utilized with any of the medical devices, systems or methodologies disclosed herein.

[0064] FIG. 5 shows a plan view of electrode 60 including spline 44, bottom layer 62 and top layer 64. FIG. 5 shows bottom layer 62 beneath top layer 64 and having a length substantially aligned with the length of spline 44. The length of top layer 64 is depicted by the letter "X." Further, FIG. 5 shows top layer 64 having a width perpendicular to the longitudinal axis of spline 44 and depicted by the letter "Y." In some instances, top layer 64 may have an exposed length of .25 – 1.5 mm, .5 – 1.25 mm, .75 – 1.0 mm, or the like. In some instances, the length of top layer 64 may be .95 mm.

[0065] As shown in FIGS. 4 & 5, electrode 60 may have a substantially low profile. This reduced profile may allow electrode 60 to be embedded within spline 44, set "flush" with the exterior surface 21 of spline 44, sit slightly "proud" of the top surface of spline 44 or sit significantly proud of spline 44. In instances where electrode 60 is embedded within spline 44, surfaces of electrode 60 other than top layer 64 may not be exposed to surfaces in contact with the outermost surface of spline 44. In other words, in some cases the only exposed surfaces of electrode 60 include top layer 64.

[0066] FIGS. 4 & 5 depict electrode 60 (including bottom layer 62 and top layer 64) as having generally rectangular shapes. This is merely an example. It is contemplated that electrode 60 (and any portion thereof) may be circular, trapezoidal, square, oval, triangular, or the like.

[0067] As stated above, basket structure 20 may be advanced into an anatomical structure and positioned adjacent to the anatomical structure to be treated (e.g. left atrium, left ventricle, right atrium, or right ventricle of the heart). Additionally, processing system 32 may be configured to record selected electrical characteristics (e.g. voltage, impedance, etc.) from each mapping electrode 24. In some instances, these electrical characteristics may provide diagnostic information corresponding to the relationship between the basket structure 20 and the anatomical structure.

[0068] An example method for assessing tissue contact may include determining a parameter of a model and observing changes in the parameter as the distal end of

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catheter 14 moves between different mediums (e.g. as between blood and tissue). It can be appreciated that catheter 14 may move between blood and tissue as catheter 14 is manipulated within a cardiac chamber.

[0069] A scaling factor may be a parameter in a model used for this purpose. The model may relate to one or more potential differences between one or more sensing electrodes and a reference electrode. A reference electrode may be an electrode placed a distance away from the potential measuring electrodes. For example, a reference electrode may be placed on the back of a patient. Sensing electrodes may be one of several combinations of electrodes 24 on basket structure 20.

[0070] Additionally or alternatively, the model may also relate to the distance in space between a current–carrying electrode and one or more sensing electrodes. The current–carrying electrode may take a variety of forms. For example, the current–carrying electrode may be any one of mapping electrodes 24 on basket structure 20 and/or a distal ablation tip electrode located on distal tip 42.

[0071] In some configurations, the potential measurement between a sensing electrode and a reference electrode may be modeled as being inversely proportional to the distance between a current–carrying electrode and a sensing electrode. For example, the relationship may be modeled as:

$$\varphi_{SEi} = \frac{K}{\|r_{CCE1} - r_{SEi}\|} + C$$

[0072] In this example, the parameter K may be used to assess tissue contact. The above equation is just an example. Other models and parameters are contemplated. In some instances, the parameter K may be referred to as a "K-factor."

[0073] As stated above, the model may relate to both the potential differences between one or more sensing electrodes and the distance between a current-carrying electrode and sensing electrodes. For example, FIG. 9 illustrates an example distal tip 42 including a current-carrying electrode 70 and four sensing electrodes 63, 65, 67 and 68. FIG. 9 is just an example. It is understood that combinations and configurations of any

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of mapping electrodes 24 on electrode structure 20 may be utilized for any embodiment described herein. For example, any one of mapping electrodes 24 may be configured as either a sensing and/or current-carrying electrode.

[0074] In some instances, the relationship between the above electrodes and potential values may be represented by the following equation:

$$\begin{bmatrix} \varphi_{SE1} \\ \varphi_{SE2} \\ \varphi_{SE3} \\ \varphi_{SE4} \end{bmatrix} = \begin{bmatrix} \frac{1}{\|r_{CCE1} - r_{SE1}\|} & 1 \\ \frac{1}{\|r_{CCE1} - r_{SE2}\|} & 1 \\ \frac{1}{\|r_{CCE1} - r_{SE3}\|} & 1 \\ \frac{1}{\|r_{CCE1} - r_{SE4}\|} & 1 \end{bmatrix} [K\ C]$$

[0075] It can be appreciated that the variables $\begin{bmatrix} \varphi_{SE1} \\ \varphi_{SE2} \\ \varphi_{SE3} \\ \varphi_{SE4} \end{bmatrix}$ represent the measured potential difference between the four sensing electrodes (e.g. 63, 65, 67, 68 in FIG. 9) and a reference electrode (not shown in FIG. 9). Additionally, the potential differences may be determined by system 10. Further, it can be appreciated that $\|r_{CCE1} - r_{SE1}\|, \|r_{CCE1} - r_{SE2}\|, \|r_{CCE1} - r_{SE3}\|$ and $\|r_{CCE1} - r_{SE4}\|$ represent the absolute value of the distance (in space) between the current-carrying electrode (e.g. 70 in FIG. 9) and the four sensing electrodes (e.g. 63, 65, 67, 68 in FIG. 9), respectively. It is further understood that these distances may be determined as the position (and distance) for every sensing electrode in relation to the current-carrying electrode is known. For example, because the electrodes are fixed along the spline, the distance between electrodes on the spline is known. Furthermore, it is contemplated that when the spline is in a non-linear configuration (e.g. expanded), the distance between electrodes can be determined using curvilinear and/or straight line calculation. In other

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words, the position, and therefore, the distances, between example sensing electrodes 63, 65, 67, 68 and current-carrying electrode 70 are known on electrode structure 20.

[0076] The parameters K and C in the above system of linear equations can be estimated using a number of well-known techniques for optimization or linear regression. For example, least squares can be used to estimate K and C. Other methods are contemplated. Furthermore, it can be appreciated that the above system of linear equations may be arranged in other ways. For example, the linear equations may be combined such that the parameter C vanishes and only K remains to be estimated.

[0077] Scaling factor K may be inversely proportional to the conductivity of a given medium. In other words, the scaling factor K will be different for two mediums having different conductivities. For example, the conductivity of blood is greater than that of cardiac tissue, and therefore, the scaling factor K will be lower for blood as compared to cardiac tissue.

[0078] Knowing the potential differences and absolute distance values, it may be possible to solve the linear equation set (above) for the scaling factor, K. Is should be noted that in order to solve the disclosed linear equation set, sensing electrodes must be located at different distances away from the current injecting electrode. If, for example, the distances were all identical, then the matrix on the right-hand side of the equation would be singular and result in an infinite number of equally valid solutions. Referring to Fig. 9, it can be seen that sensing electrodes 63, 65, 67, 68 are located at different distances from current injecting electrode 70.

[0079] Fig. 9 illustrates the sensing electrodes 63, 65, 67, 68 positioned longitudinally along spline 44. However, it is contemplated that the sensing electrodes 63, 65, 67, 68 may be positioned in a configuration other than along the longitudinal axis and yet still maintain variable distances between the sensing electrodes and the current-carrying electrode 70. Additionally, in some instances it may be possible to reduce the number of sensing electrodes to two or three and solve the corresponding linear equation set for scaling factor K. In other instances, it may be desirable to increase the number of sensing electrodes; the parameter K can still be estimated using well-known techniques such as least squares.

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[0080] It can be appreciated from the above discussion that it may be possible to utilize known variables to solve the disclosed linear equation for the scaling factor K. Therefore, system 10 may determine and compare different scaling factor values as the distal end portion of catheter 14 is moved between different mediums (e.g. blood, tissue). The difference in the scaling factors may be utilized as a diagnostic indicator of tissue contact.

[0081] Furthermore, because each individual mapping electrode 24 may be configured as either a sensing and/or current-carrying electrode, more than one electrode may be utilized to indicate tissue contact through the use of multiplexed measurements. Multiplexing may include any of a number of known techniques such as time-division, frequency-division, or code-division multiplexing. For example, in one frequency or time "slot", electrode 63 may be the current-carrying electrode, while electrodes 65, 67, and 68 may be sensing electrodes. In a second frequency or time slot, electrode 65 may be the current-carrying electrode, while electrodes 63, 67, and 68 may be sensing electrodes. It is understood than any combination of electrodes on structure 20 may be current-carrying and/or the sensing electrodes. Further, because most of the impedance "seen" by the current-carrying electrode is due to the conductive medium nearest the electrode, any given electrode may be indicative of the contact of a different part of the electrode structure 20 with tissue. Multiple electrodes may therefore be combined to provide two or more spatially-distinct contact indicators.

[0082] It can be appreciated from the above discussion that the size and arrangement of the mapping electrodes 24 disclosed herein may be more desirable for detecting a localized scaling factor K as compared to other electrode structures. The small, flat electrode geometry may make the applied current distribution more localized to nearby tissue than would be achieved with a larger, non-flat electrode. The close spacing of the mapping electrodes 24 may result in a more localized estimate of the scaling factor than would be achieved with larger electrode spacing.

[0083] Using the scaling factor K to assess tissue contact may be highly reliable. However, in some instances, the positioning and/or configuration of system 10 may alter the scaling K-factor results. In these instances, it may be desirable to utilize a supplemental method for assessing tissue contact. A variety of supplemental methods

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for assessing tissue contact are contemplated. For example, a supplemental method for assessing tissue contact may include comparing the amplitude of measured cardiac activation, or a spatial or temporal derivative thereof, to a threshold value. Another example supplemental method for assessing tissue contact may include determining a threshold impedance value that positively identifies tissue contact. More specifically, in some instances system 10 may be capable of sensing and/or measuring an impedance increase and correlating the impedance increase to a visual, audible, etc. indication of tissue contact.

[0084] For example, system 10 may be capable of utilizing threshold impedance measurements to sense contact between mapping electrodes 24 and adjacent tissue. In general, the impedance of a given medium may be measured by applying a known voltage or current to a given medium and measuring the resulting voltage or current. In other words, impedance measurements of a given medium can be obtained by injecting current between two electrodes and measuring the resulting voltage between the same electrodes through which the current was injected. The ratio of the voltage potential provides an indication of the impedance of the medium through which the current traveled.

[0085] For example, in some instances a current may be injected between an electrode 24 and one or more return electrodes (e.g. patch electrode, mini-electrode, measuring electrode, sensing electrode, or the like). Impedance of the medium (e.g. tissue, blood) adjacent to a current-carrying electrode 24 may be measured according to the methodology disclosed above. For example, if electrode 24 is adjacent to or embedded in cardiac tissue, the impedance of the cardiac tissue may be determined by measuring the ratio of the voltage potential between electrode 24 and the one or more return electrodes. While the above discussion generally describes utilizing the current carrying electrodes and the return electrode(s) in unipolar mode, it is contemplated that electrodes 24 may be capable of operating, or configured to operate, in bipolar sensing modes.

[0086] The size and shape of electrodes 24 may influence the ability (or inability) of electrodes 24 to measure the electrical characteristics (e.g. impedance) of cellular tissue and/or a surrounding medium (e.g. blood). In some instances, the degree of

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contact that an electrode 24 maintains with the cardiac tissue may influence the magnitude of a sensed electrical response. For example, an exaggerated impedance value may be sensed when electrode 24 is completely covered and/or embedded in tissue. In some instances, this exaggerated impedance value may be described as an "impedance increase." This impedance increase may, therefore, directly correspond to tissue contact. It can be appreciated that the substantially flat, reduced-profile and relatively smaller shape of electrode 60 shown in FIG. 4 may increase the likelihood that as electrode 60 is positioned adjacent tissue it will be completely covered by tissue and thereby trigger an impedance increase. Further, this impedance increase may be sensed by processing system 32, and in some instances, output a signal to display 40 indicating that electrode 60 has made contact with tissue. The impedance increase may be 100%, 150%, 200%, 250%, 300%, 350%, 400%, 500%, 600%, 700%, 800%, 900%, 1000%, 2000%, 50,000% or more of the magnitude of a measured baseline impedance value.

[0087] FIGS. 6-8 are a series of drawings that illustrate electrode structure 20 being manipulated within an example cardiac chamber. More specifically, FIGS. 6-8 depict electrode structure 20 advancing through blood toward cardiac tissue. For example, FIG. 6 shows electrode structure 20, including mapping electrode 24, surrounded entirely by blood. FIG. 7 shows mapping electrode 24 positioned at a blood/tissue interface, while FIG. 8 shows electrode structure 20 embedded within cardiac tissue. In these examples, one or more of the plurality of mapping electrodes 24 may be continuously sensing impedance values adjacent to their respective outer surfaces as electrode structure 20 is manipulated within the cardiac chamber. Additionally, processing system 32 may be continuously operating to "sense" an impedance increase from any one of electrodes 24. For example, as mapping electrode 24 moves from a position illustrated in FIG. 6 to an embedded positioned illustrated in FIG. 8, processing system 32 may sense an impedance increase and output a corresponding indication of tissue contact to display 40.

[0088] It can be appreciated from the above discussion that the size and shape of the electrodes disclosed herein may be more desirable for detecting an impedance increase as compared to relatively larger, non-flat electrodes. In other words, the

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electrode size and shape disclosed herein may be more easily covered and/or embedded in adjacent tissue, thereby leading to a greater number of sensed impedance increases and correspondingly positive indications of tissue contact.

[0089] In addition or alternatively to any of the embodiments disclosed herein, in some instances it may be desirable to sense tissue contact by simultaneously using two or more methods discussed herein. As stated above, in some instances processing system 32 may have difficulty sensing and comparing a change in K-factor values while being manipulated in an anatomical structure (e.g. cardiac chamber). Therefore, it may be desirable for processing system 32 to sense an impedance increase while simultaneously monitoring and determining changes in the K-factor. However, in some instances processing system 32 may detect an impedance increase correlating to positive tissue contact despite not having sensed tissue contact utilizing the K-factor method. Having detected an impedance increase (in the absence of a positive tissue contact via the K-factor method), system 10 may be designed such that a positive indication of tissue contact is output to a display and/or a clinician. Likewise, processing system 10 may, at times, sense a change in the K-factor corresponding to positive tissue contact despite not having sensed an impedance increase. Furthermore, it is contemplated that in some instances system 10 may simultaneously sense a change in the K-factor and an impedance increase, both of which provide a positive indication of tissue contact.

[0090] In addition or alternatively to any of the embodiments disclosed herein, improvements in the measurements of any electrical characteristic disclosed herein (e.g. impedance) may be achieved by utilizing a four-terminal sensing configuration among any of mapping electrodes 24 on electrode structure 20 (of which any number may be operated as sensing and/or current-carrying electrodes). In general, a four-terminal sensing configuration drives current through a pair of “current-carrying” electrodes and measures the voltage across a different pair of “sensing” electrodes.

[0091] One advantage of a four-terminal sensing configuration is that the measured impedance may not be sensitive to the impedance of the electrodes themselves. In a two-terminal sensing configuration, the measured impedance includes the surrounding medium and both electrodes. In contrast, a four-terminal sensing

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configuration measures voltage across electrodes through which the current is negligible. As a result, the measured impedance is that of the surrounding medium and is largely independent of the impedance of the electrode and its interface with the surrounding medium.

[0092] Additionally, in some instances, improvements in the measurements of any electrical characteristic disclosed herein (e.g. impedance) may be improved by utilizing a three-terminal sensing configuration among any of mapping electrodes 24 on electrode structure 20 (of which any number may be operated as sensing and/or current-carrying electrodes). Some examples of three-terminal sensing may be found in U.S. Patent Application 8,449,535, the entirety of which is incorporated herein by reference. Further, in at least some instances, three-terminal sensing may be used instead of the four-terminal sensing configurations described herein, to the extent applicable.

[0093] It can be appreciated that four-terminal sensing may be incorporated and/or utilized by any combination of mapping electrodes 24 on electrode structure 20. Additionally, it is contemplated that any individual mapping electrode 24 on electrode structure 20 may operate as a sensing electrode or a current-carrying electrode. Additionally, as described above, system 10 may multiplex sensing configurations such that mapping electrodes 24 are both sensing and current carrying electrodes.

[0094] Furthermore, it is contemplated that sensing tissue contact utilizing the K-factor method, the impedance method or a combination of both can further incorporate four-terminal sensing as desired. For example, voltage values for the K-factor method may be obtained using four-terminal sensing. Likewise, impedance increase values for the impedance increase method may be obtained using four-terminal sensing. Additionally, either method may utilize four-terminal sensing in combination with any other method. For example, a “K-factor four terminal” method may be utilized simultaneously with the impedance increase method, which, in turn, may or may not incorporate four-terminal sensing. Additionally, an “impedance increase four terminal” method may be utilized simultaneously with the K-factor method, which, in turn, may or may not incorporate four-terminal sensing.

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[0095] In some examples, mapping electrodes 24 may be operatively coupled to processor 32. Further, generated output from mapping electrodes 24 may be sent to processor 32 of system 10 for processing in one or more manners discussed herein and/or for processing in other manners. As stated, an electrical characteristic (e.g. impedance) and/or an output signal from an electrode pair may at least partially form the basis of a contact assessment.

[0096] Further, system 10 may be capable of processing or may be configured to process the electrical signals from mapping electrodes 24. Based, at least in part, on the processed output from mapping electrodes 24 processor 32 may generate an output to a display (not shown) for use by a physician or other user. In instances where an output is generated to a display and/or other instances, processor 32 may be operatively coupled to or otherwise in communication with the display. Illustratively, the display may include various static and/or dynamic information related to the use of system 10. In one example, the display may include one or more of an image of the target area, an anatomical shell, a map conveying tissue proximity achieved at locations on the anatomical shell, an electroanatomical map that incorporates tissue proximity information, an image of structure 20, and/or indicators conveying information corresponding to tissue proximity, which may be analyzed by the user and/or by a processor of system 10 to determine the existence and/or location of arrhythmia substrates within the heart, to determine the location of catheter 18 within the heart, and/or to make other determinations relating to use of catheter 18 and/or other elongated members.

[0097] System 10 may include an indicator in communication with processor 32. The indicator may be capable of providing an indication related to a feature of the output signals received from one or more of the electrodes of structure 20. In one example, an indication to the clinician about a characteristic of structure 20 and/or the myocardial tissue interacted with and/or being mapped may be provided on the display. In some cases, the indicator may provide a visual and/or audible indication to provide information concerning the characteristic of structure 20 and/or the myocardial tissue interacted with and/or being mapped. For example, system 10 may determine that a measured impedance corresponds to an impedance value of cardiac tissue and

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therefore may output a color indicator (e.g. green) to a display. The color indicator may allow a physician to more easily determine whether to apply ablative therapy to a given cardiac location. This is just an example. It is contemplated that a variety of indicators may be utilized by system 10.

[0098] In some embodiments, the processed output from mapping electrodes 24 may be used by processor 32 in ways that are not directly visible to the clinician. For example, processed information for contact assessment may be incorporated into algorithms for catheter localization, generation of anatomical shells and electroanatomical maps, or registration of images.

[0099] In some embodiments, the display may include an anatomical shell or an electroanatomical map that incorporates tissue proximity information. For example, regions of an anatomical shell where impedance values of cardiac tissue are measured may be more opaque than regions where impedance values of blood are measured. In other examples, an electroanatomical map displaying features such as voltage, activation time, dominant frequency, or the like may display an indicator (e.g. color, texture, pattern, etc.) in regions where impedance values of blood are measured. In both cases, the indication of regions where tissue contact may have occurred (or has likely occurred above a given probability or acceptability threshold) may guide the physician in moving the catheter and collecting measurements. Examples of anatomical shells and electroanatomical maps may be found in U.S. Patent Application Publication 20120184863, U.S. Patent Application Publication 20120184864 and U.S. Patent Application Publication 20120184865, the entirety of which is incorporated herein by reference.

[00100] In some examples, tissue proximity data may be collected for one or more mapping electrodes 24 on the structure 20 according to any of the processes and/or methods disclosed herein. Further, the collected parameter and/or tissue proximity values may be displayed on an anatomical shell and/or electroanatomical map as discussed above.

[00101] In other examples, tissue contact information may be used to mask portions of an anatomical shell and/or an electroanatomical map. Further, displayed (or masked) portions of the shell or map may correspond to a threshold confidence levelof

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tissue contact. For example, masked portions may correspond to parameter values that are below a threshold confidence value.

[00102] As discussed above, the anatomical and/or electroanatomical map displaying (or masking) tissue contact locations may be manipulated by a clinician in order to generate more accurate diagnostic representations of an anatomical region (e.g. heart chamber).

[00103] The following documents are herein incorporated by reference: U.S. Patent Application Pub. US2008/0243214, U.S. Patent Application Pub. US2014/0058375, U.S. Patent Application Pub. US2013/0190747, U.S. Patent Application Pub. US2013/0060245, and U.S. Patent Application Pub. US2009/0171345.

[00104] Various modifications and additions can be made to the exemplary embodiments discussed without departing from the scope of the present invention. For example, while the embodiments described above refer to particular features, the scope of this invention also includes embodiments having different combinations of features and embodiments that do not include all of the described features. Accordingly, the scope of the present invention is intended to embrace all such alternatives, modifications, and variations as fall within the scope of the claims, together with all equivalents thereof.

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CLAIMS

We claim:

1. An electrophysiology medical device, comprising:
a catheter shaft including a distal end portion, wherein the distal end portion includes a sensing assembly having a plurality of mapping electrodes;
wherein the plurality of mapping electrodes includes at least one current-carrying electrode, a first sensing electrode and a second sensing electrode;
wherein the first sensing electrode is spaced from the current-carrying electrode a first distance;
wherein the second sensing electrode is spaced from the current-carrying electrode a second distance;
wherein the first distance is different from the second distance; and
a controller coupled to the plurality of mapping electrodes;
wherein the controller is capable of calculating a parameter based at least in part on the first and the second distances.

2. The medical device of claim 1, wherein the parameter indicates the proximity of the medical device to tissue.

3. The medical device of any one of claims 1-2, wherein calculating the parameter includes sensing a first voltage potential between the first electrode and one or more return electrodes, and sensing a second voltage potential between the second electrode and one or more return electrodes.

4. The medical device of claim 3, wherein calculating the parameter includes solving at least one linear equation, and wherein the at least one linear equation includes the first distance, the second distance, the first voltage and the second voltage.

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5. The medical device of any one of claims 1-4, wherein the sensing assembly includes a plurality of splines, and wherein the plurality of electrodes are disposed on the plurality of splines.

6. The medical device of any one of claims 1-4, wherein the sensing assembly includes a plurality of splines, and wherein the plurality of splines includes an outwardly facing surface, and wherein the plurality of electrodes are disposed on the outwardly facing surface.

7. The medical device of any one of claims 5-6, wherein the sensing assembly includes a plurality of splines, and wherein the plurality of splines are arranged in a basket.

8. The medical device of any one of claims 1-7, wherein the plurality of electrodes are each designed to sequentially and/or simultaneously operate in a sensing configuration and a current-carrying configuration.

9. The medical device of any one of claims 1-8, further comprising displaying the parameter on a display.

10. The medical device of claim 9, wherein displaying the parameter includes displaying a confidence value corresponding to the parameter.

11. The medical device of any one of claims 1-10, wherein the displaying the parameter on a display further includes displaying an anatomical shell and/or an electroanatomical map.

12. The medical device of claim 11, wherein the anatomical shell and/or electroanatomical map correspond to one or more parameter values, and wherein the one or more parameter values indicates the proximity of one or more electrodes to tissue.

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13. The medical device of any one of claims 11-12, further comprising masking a portion of the anatomical shell and/or the electroanatomical map.

14. The medical device of claim 13, wherein the masked portion corresponds to one or more parameter values that are below a threshold confidence value.

15. The medical device of claim 12, wherein the parameter values correspond to a color, texture, symbol and/or pattern.

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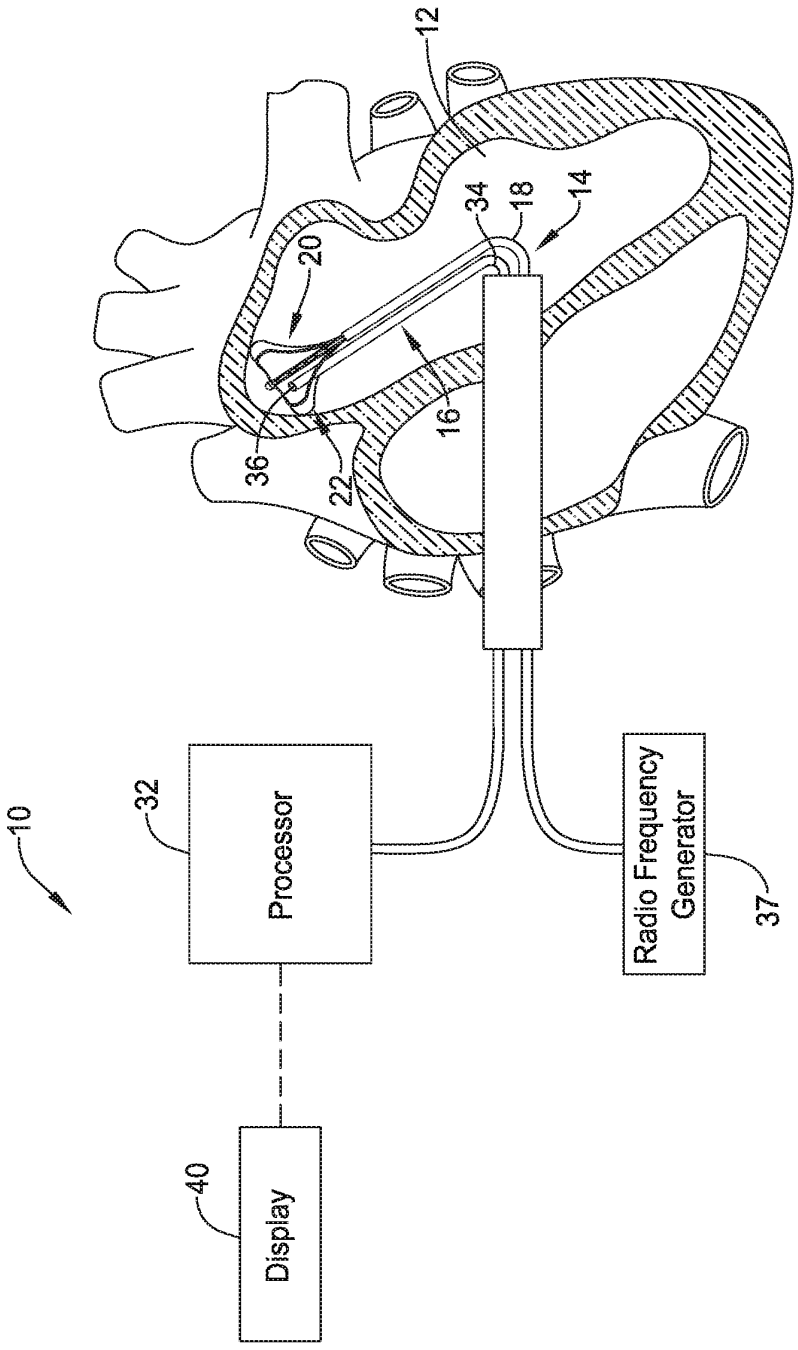

12
34
18
14
20
16
36
22
10
32
Processor
Radio Frequency Generator
37
40
Display

FIG. 1

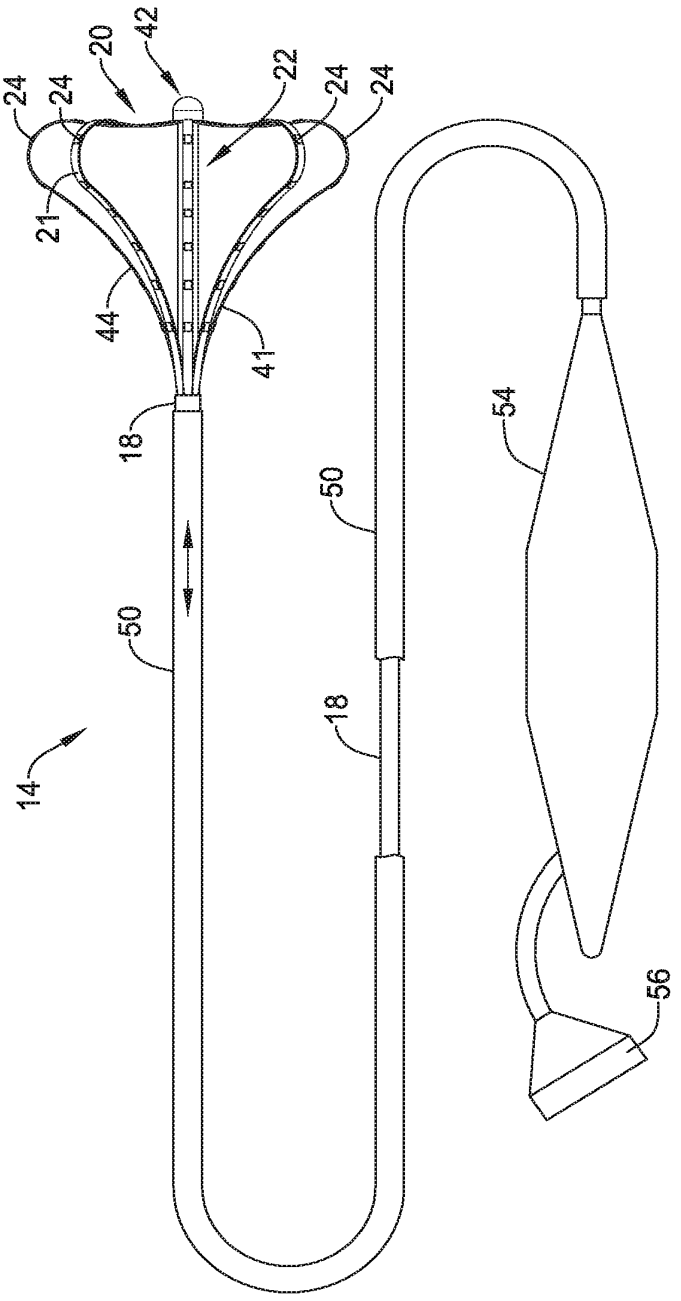


FIG. 2

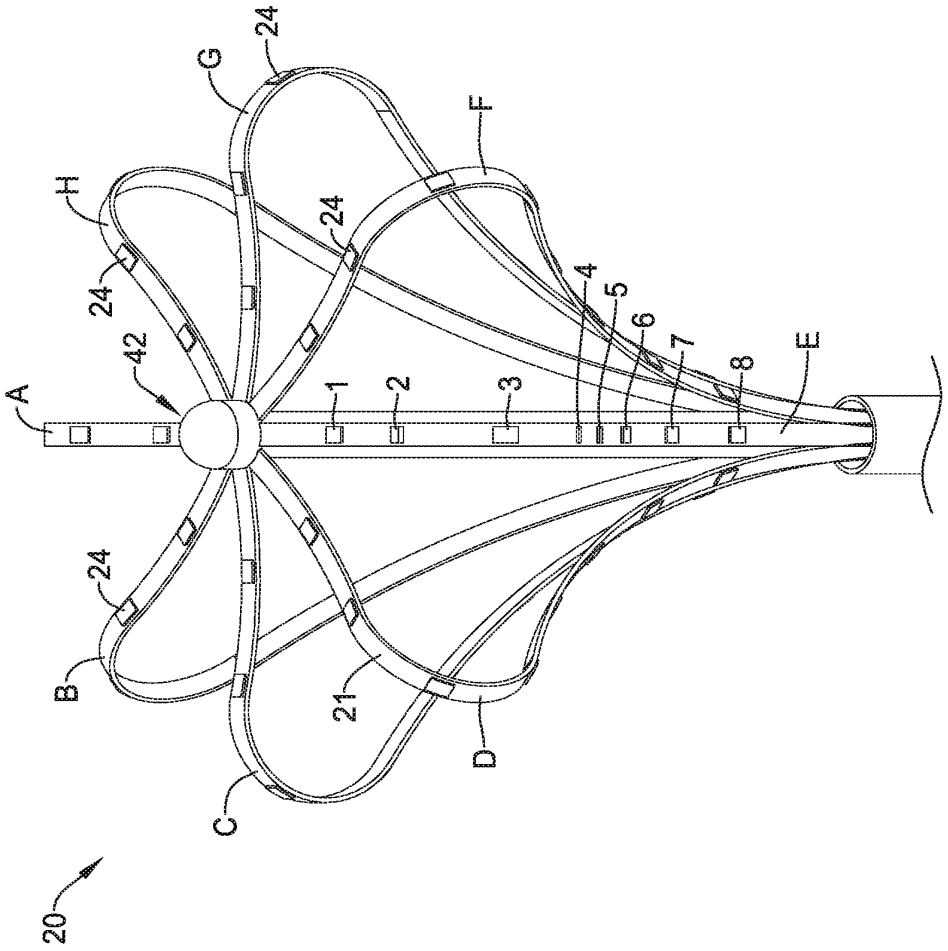


FIG. 3

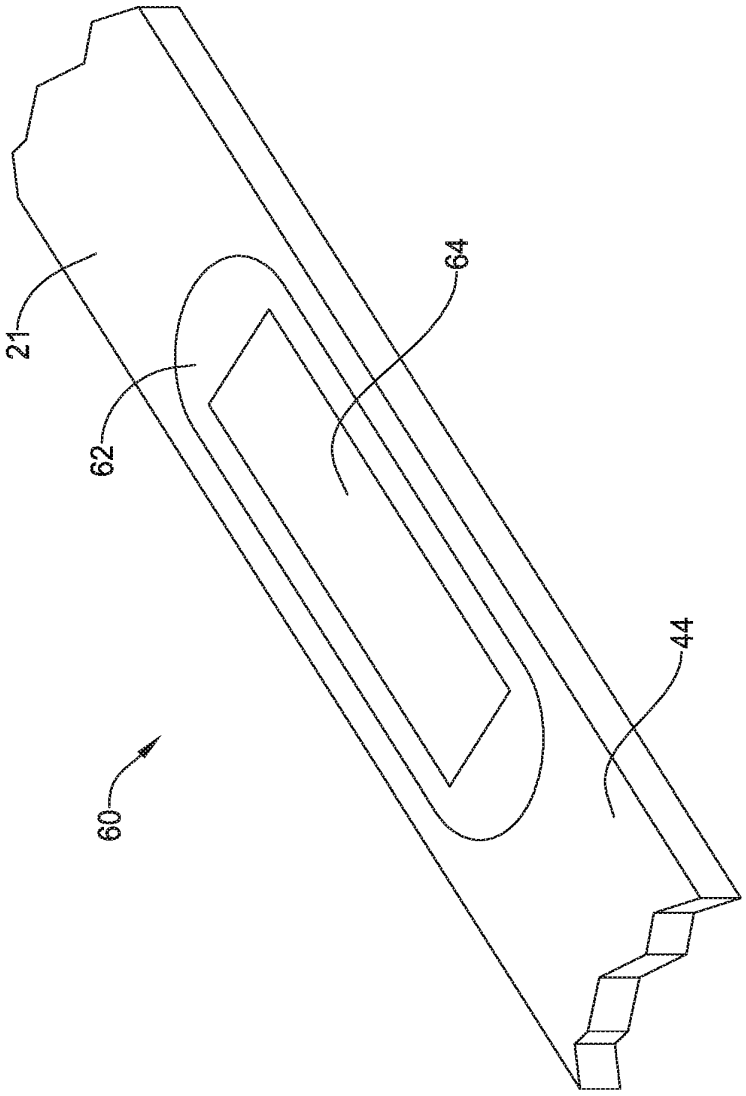


FIG. 4

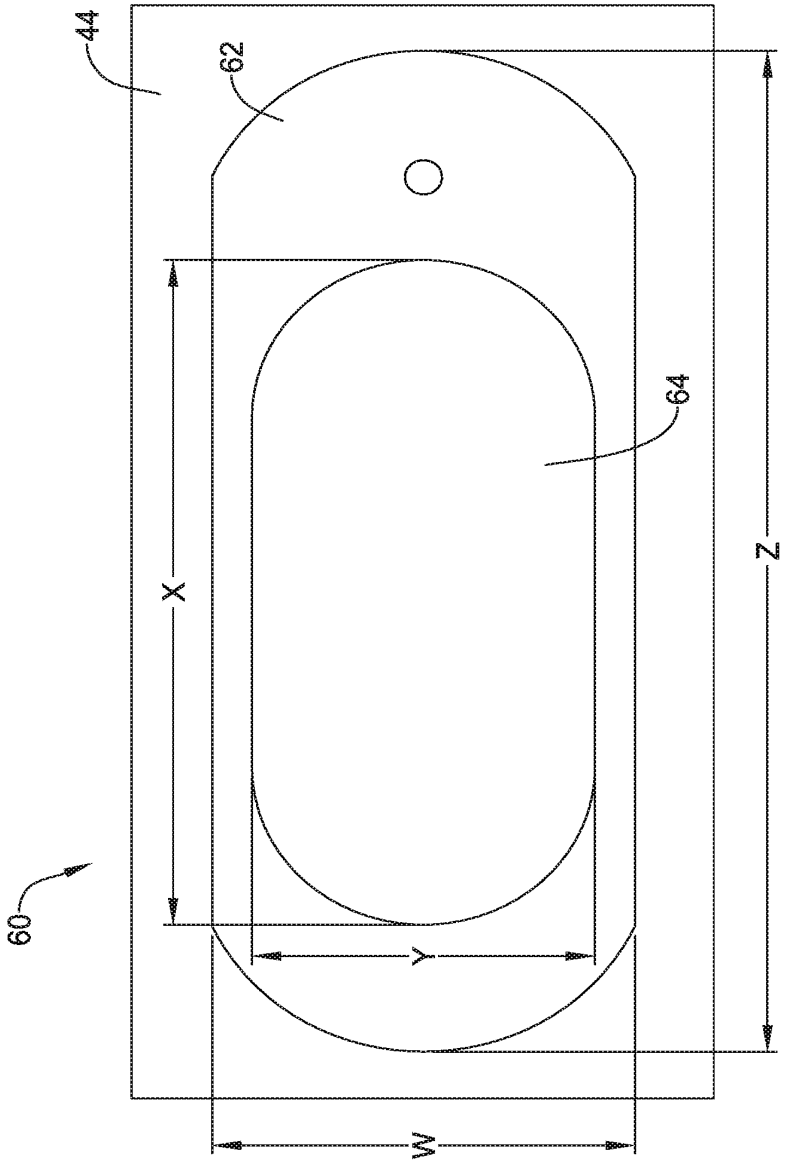


FIG. 5

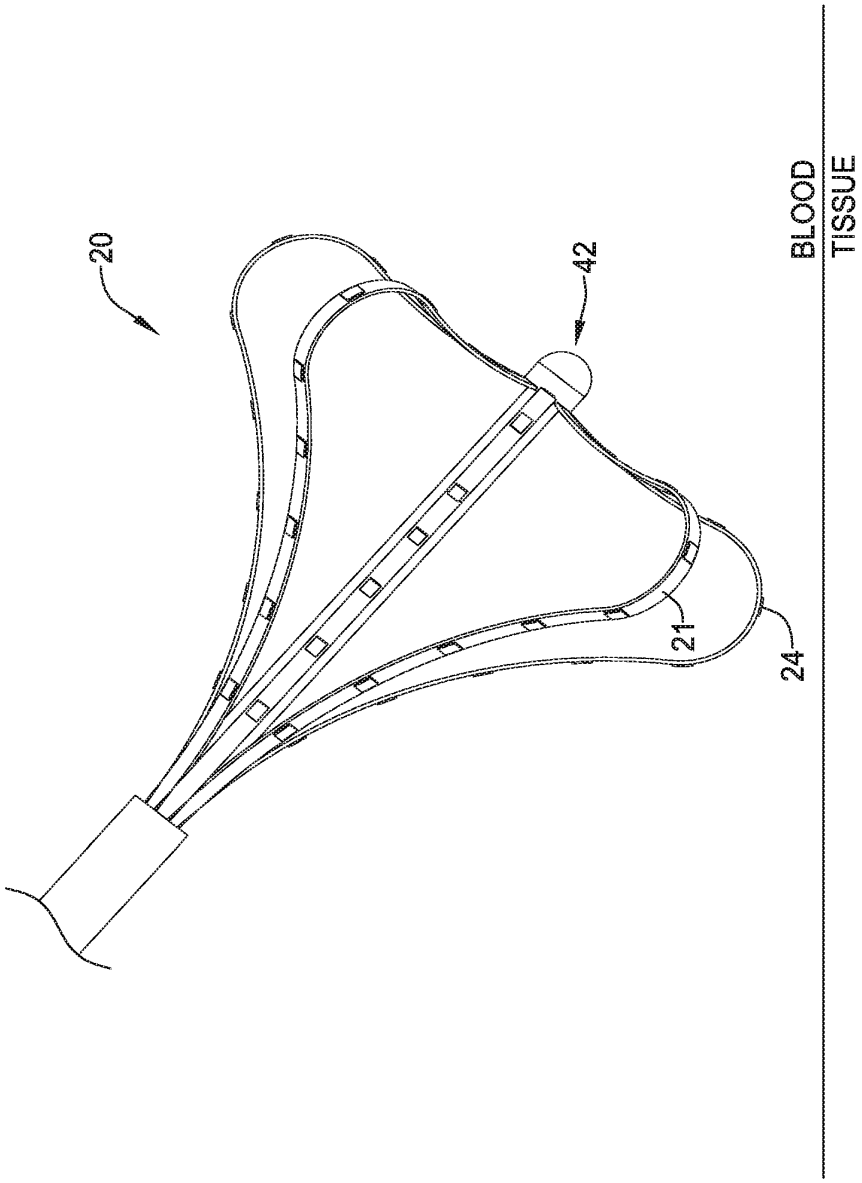


FIG. 6

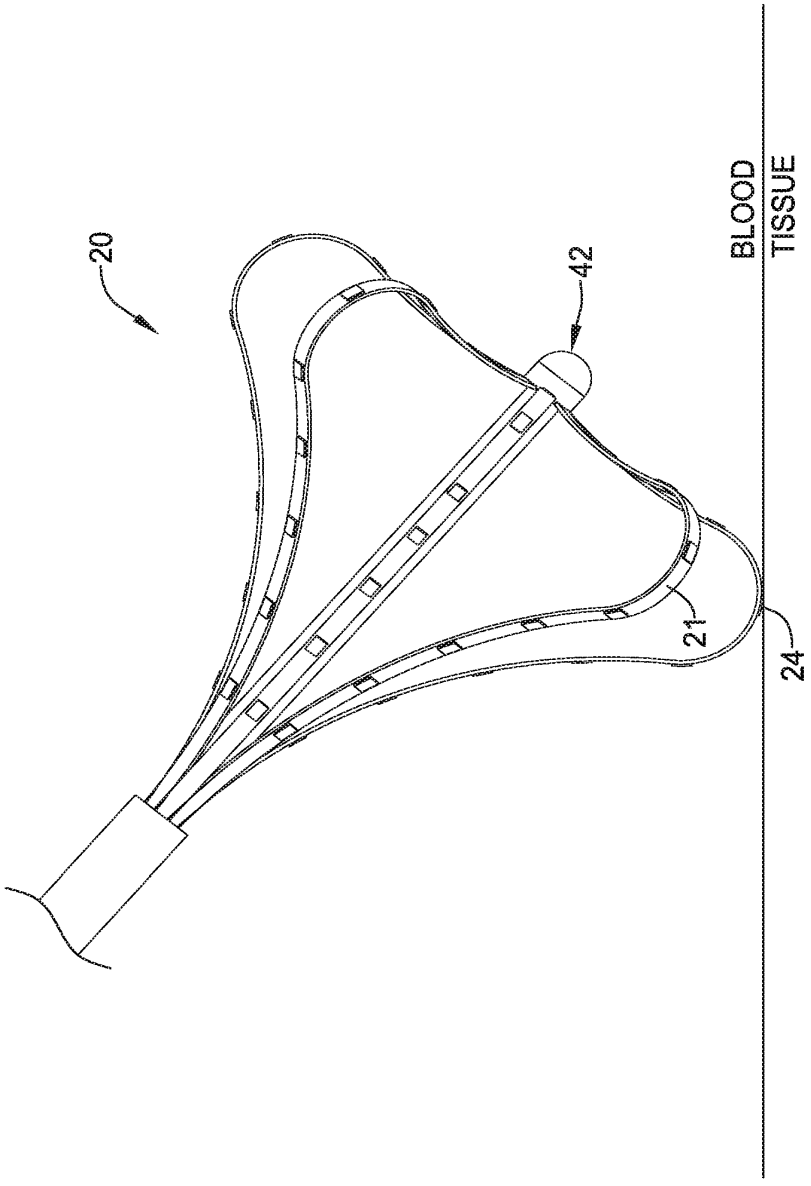


FIG. 7

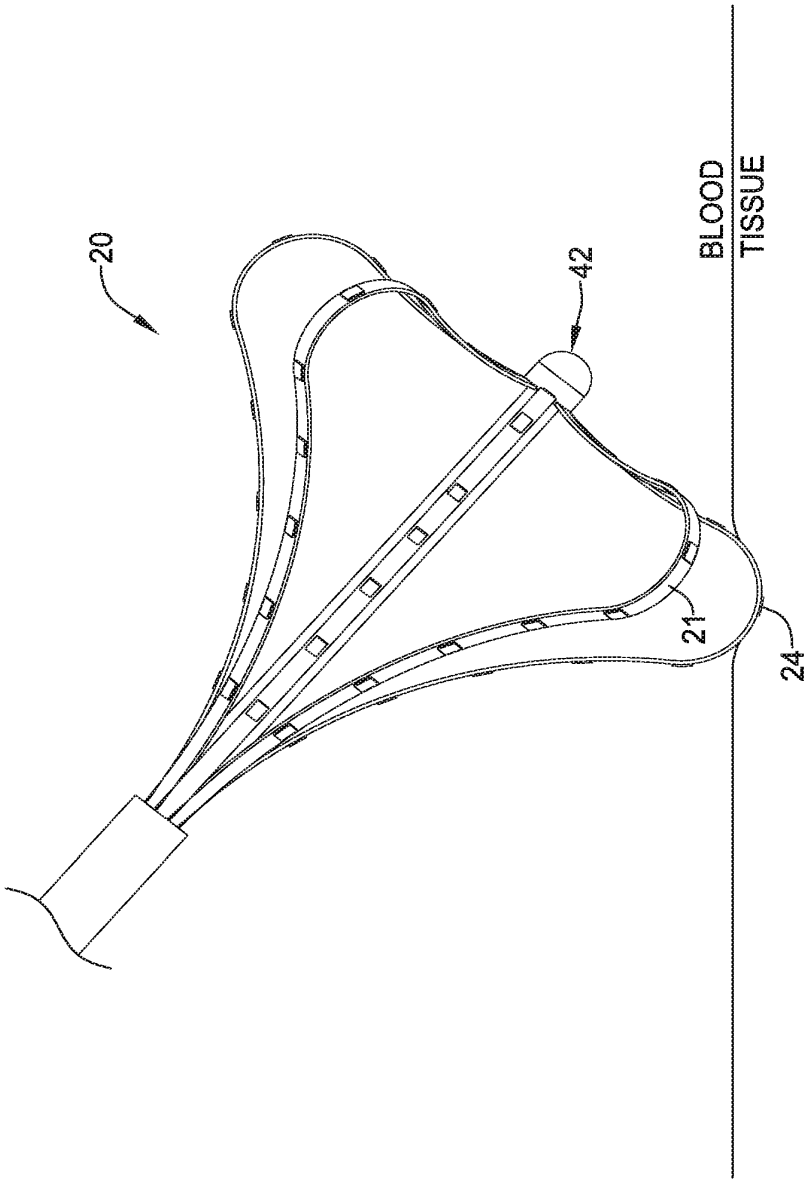


FIG. 8

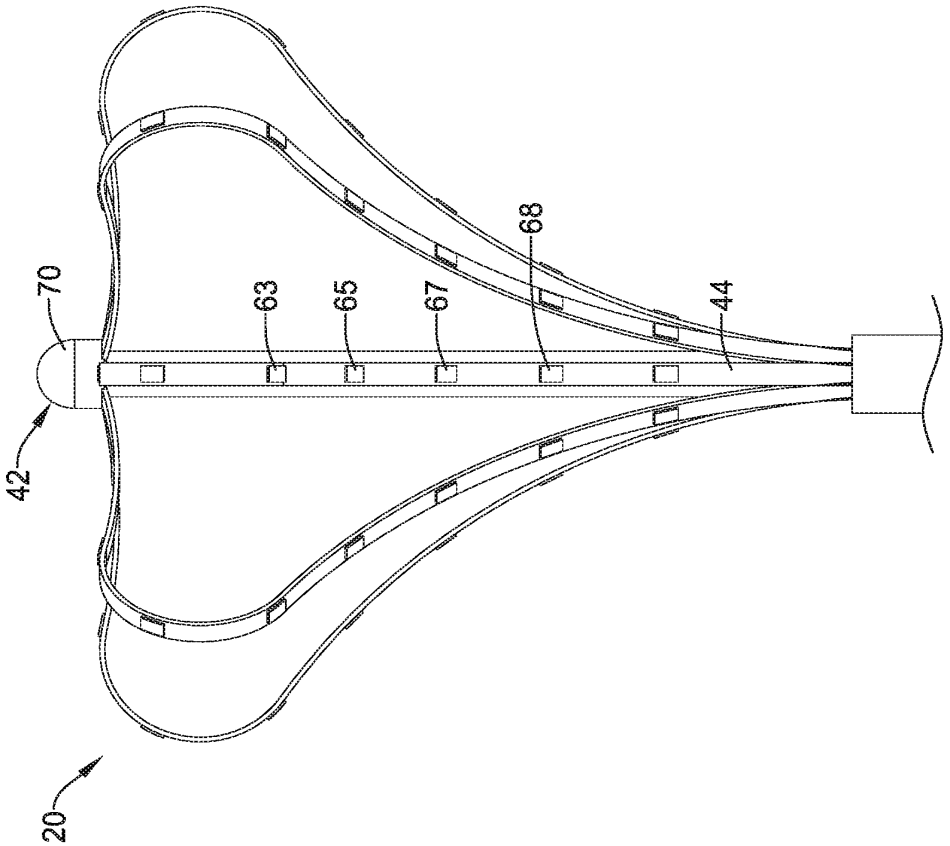


FIG. 9

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/018689

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00 A61B5/053 A61B5/06
ADD. A61B18/14 A61B18/00

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)
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	WO 2014/036439 A2 (ACUTUS MEDICAL INC [US]) 6 March 2014 (2014-03-06) abstract; figure 1A paragraphs [0036] - [0038], [0085] - [0094], [0103] - [0104], [0118] - [0120], [0138] the whole document	1-15
X	US 2014/364715 A1 (HAUCK JOHN A [US]) 11 December 2014 (2014-12-11) abstract; figure 3 paragraphs [0024] - [0027] the whole document	1-15

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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 :

"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

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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
20 April 2016	28/04/2016

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	Furlan, Stéphane

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/018689

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 6 391 024 B1 (SUN WEIMIN [US] ET AL) 21 May 2002 (2002-05-21) abstract; figures 8a-8c column 4, line 6 - line 42 the whole document -----	1-15
A	US 2009/275827 A1 (AIKEN ROBERT D [US] ET AL) 5 November 2009 (2009-11-05) abstract paragraphs [0057] - [0064]; figure 6 the whole document -----	1-15

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/018689

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(71) Applicant: **NEURENT MEDICAL LIMITED** [IE/IE]; No. 1 Ocean Point, Main Street, Oranmor, Galway (IE).

(72) Inventor: **TOWNLEY, David**; Latoon North, Newmarket-on-fergus, County Clare (IE).

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(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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

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: SYSTEMS AND METHODS FOR THERAPEUTIC NASAL TREATMENT

(57) Abstract: The invention generally relates to systems and methods for treating at least one of rhinitis, congestion, and/or rhinorrhea to thereby reduce or eliminate symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

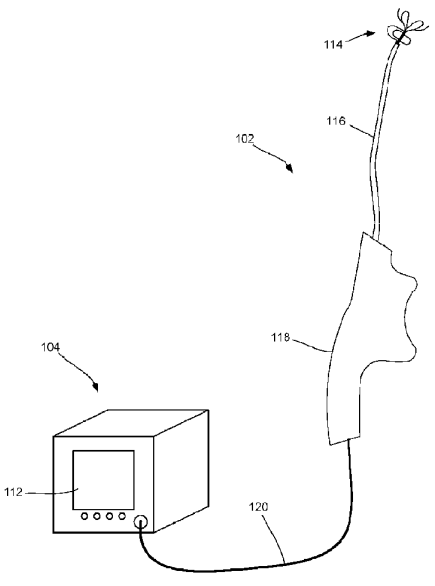


FIG. 2

WO 2021/205230 A1

SYSTEMS AND METHODS FOR THERAPEUTIC NASAL TREATMENT

Cross-reference to Related Applications

This application claims the benefit of, and priority to, U.S. Provisional Patent Application No. 63/007,575, filed April 9, 2020, the contents of which are incorporated by reference.

Field of the Invention

The invention generally relates to systems and methods for treating medical conditions, and, more particularly, systems and methods for treating at least one of rhinitis, congestion, and/or rhinorrhea to thereby reduce or eliminate symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

Background

Rhinitis is an inflammatory disease of the nose and is reported to affect up to 40% of the population. It is the fifth most common chronic disease in the United States. The most common and impactful symptoms of rhinitis are congestion and rhinorrhea. Allergic rhinitis accounts for up to 65% of all rhinitis patients. Allergic rhinitis is an immune response to an exposure to allergens, such as airborne plant pollens, pet dander or dust. Non-allergic rhinitis is the occurrence of common rhinitis symptoms of congestion and rhinorrhea. As non-allergic rhinitis is not an immune response, its symptoms are not normally seasonal and are often more persistent. The symptoms of rhinitis include a runny nose, coughing, sneezing, nasal and/or throat irritation and itching, and general congestion, all of which commonly leads to difficulty sleeping.

Allergen avoidance and pharmacotherapy are relatively effective in the majority of mild cases, but these medications need to be taken on a long-term basis, incurring costs and side effects and often have suboptimal efficacy. For example, pharmaceutical agents prescribed for rhinosinusitis have limited efficacy and undesirable side effects, such as sedation, irritation, impairment to taste, sore throat, dry nose, and other side effects.

There are two modern surgical options: the delivery of thermal energy to the inflamed soft tissue, resulting in scarring and temporary volumetric reduction of the tissue to improve nasal airflow; and microdebrider resection of the inflamed soft tissue, resulting in the removal of

tissue to improve nasal airflow. Both options address congestion as opposed to rhinorrhea and have risks ranging from bleeding and scarring to the use of general anesthetic.

Summary

The invention recognizes that a problem with current surgical procedures is that such procedures are not accurate and cause significant collateral damage in order to treat rhinitis and further fail to adequately treat the underlying symptoms.

The invention solves that problem by providing treatment devices having a combination of unique components, including an elongate body (which may be in the form of a shaft or sheath, or other elongate body), a retractable and expandable multi-segment end effector, and handle, that, as a whole, provide a high level of precise control and feedback to an operator during a procedure. In particular, the elongate body is configured to not only aid an operator in the positioning and delivery of the multi-segment end effector to a desired target site within the sino-nasal cavity, but further includes an electrode array provided along a length thereof that is configured to deliver energy to specific target sites within the nasal passage and nasal cavity, in conjunction with neuromodulation provided by the multi-segment end effector. The multi-segment end effector is configured to complement anatomy at multiple different locations within the nasal cavity. The handle is configured with multiple ergonomic and functional features that improve device use and feedback, such as independent control of deployment of the end effector and energy delivery and a shape associated with the architecture of the end effector in the deployed configuration. The handle may also include one or more markings that provide a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

In that manner, the present invention provides devices that are capable of highly conforming to anatomical variations within a nasal passage and nasal cavity while providing unprecedented control and guidance to an operator so that an operator can perform an accurate, minimally invasive, and localized application of energy to one or more target sites within the nasal passage and nasal cavity to cause multi-point interruption of neural signal without causing collateral damage or disruption to other neural structures.

Unlike other surgical treatments for rhinitis, the devices of the invention are minimally invasive. Accordingly, a procedure can be performed in an office environment under local

anesthetic. The multi-segment end-effector allows for targeting the autonomic supply to the nasal turbinates and will have a positive impact on both allergic and non-allergic rhinitis. Using this approach, it is expected that devices of the invention will be able to provide long-term symptom relief (e.g., years instead of months). Since the treatment is accurate with minimal collateral damage to the surrounding tissue, patients will begin to feel symptom relief immediately following the treatment. It is fully expected that patients will be removed from their pharmacotherapies following this therapy.

The systems and methods of the present invention include a handheld device comprising a retractable and expandable multi-segment end effector that, once delivered to the one more target sites within the nasal cavity, can expand to a specific shape and/or size corresponding to anatomical structures within the nasal cavity and associated with the target sites. In particular, the end effector includes at least a first flexible segment and a second flexible segment, each of which includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

The handheld device further includes an elongate body operably associated with the end effector and a handle operably associated with the elongate body. The elongate body may be in the form of a shaft or sheath (or other elongate body operably associated with or coupled to the end effector). The elongate body may include a pre-defined shape (i.e., bent or angled at a specific orientation) so as to assist the surgeon (or other medical professional) for placement of the end effector at the target sites. The elongate body further includes one or more electrodes provided on one or respective portions along a length thereof and can be used to deliver energy

to tissue adjacent to, or in contact with, such portions of the elongate body. For example, in some embodiments, the elongate body may reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes of the multi-segment end effector, the surgeon may also activate and deliver energy from electrodes associated with the elongate body to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

The handle includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. The handle further includes multiple user-operated mechanisms, including at least a

first mechanism for deployment of the end effector from the retracted configuration to the expanded deployed configuration and a second mechanism for controlling of energy output by the end effector. The user inputs for the first and second mechanisms are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome. Furthermore, the handle and/or the elongate body may include markings (e.g., text, symbols, color-coding insignia, etc.) that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. In particular, multiple markings may be provided on the handle and/or elongate body and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the elongate body, a surgeon can rely on the markings on the handle and/or elongate body as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

Accordingly, the handheld device of the present invention provides a user-friendly, non-invasive means of treating rhinosinusitis conditions, including precise and focused application of energy to the intended target sites for therapeutic modulation of the intended structures, including, but not limited to, engorged sub-mucosal tissue as well as neural structures without causing collateral and unintended damage or disruption to other structures. Thus, the efficacy of a vidian neurectomy procedure can be achieved with the systems and methods of the present invention without the drawbacks discussed above. Most notably, the handheld device provides a surgeon with a user-friendly, non-invasive, and precise means for treating rhinorrhea and other symptoms of rhinosinusitis, notably congestion, coughing, sneezing, nasal and throat irritation, to thereby improve sleep, by targeting only those specific structures associated with such conditions, notably tissue responsible for providing engorgement of certain structures (i.e., inferior turbinates) and postganglionic parasympathetic nerves innervating nasal mucosa, thereby reducing engorgement of inferior turbinate tissue to thereby increase volumetric flow through a nasal passage of the patient as well as disrupting the parasympathetic nerve supply and

interrupting parasympathetic tone. The device further allows for treatment of multiple areas within the nasal passage and/or nasal cavity that would normally require repositioning of an end effector due to their separated locations. In particular, inclusion of an elongate body with a dedicated set of electrodes, in addition to the multi-segment end effector with its own set of electrodes, allows for two separate target sites to receive treatment simultaneously, thereby reducing the need to reposition the end effector. Accordingly, such treatment is effective at treating rhinosinusitis conditions while greatly reducing the risk of causing lateral damage or disruption to other tissues, including other nerve fibers, thereby reducing the likelihood of unintended complications and side effects.

One aspect of the invention provides a device for treating a condition within a nasal cavity of a patient. The device includes an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon.

In some embodiments, the elongate body generally includes a shaft to which the end effector is coupled. For example, the shaft may include an outer sheath surrounding a hypotube or metallic member, such that at least one of the outer sheath, the hypotube, and the metallic member includes one or more of the first set of electrodes provided thereon. In other embodiments, the elongate body includes one or more of a plurality of support elements forming at least a portion of the end effector.

In some embodiments, each of the first set of electrodes is positioned on separate respective portion of the elongate body. In some embodiments, one or more of the separate respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

Each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of a patient. The energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or

result in local hypoxia or coagulation necrosis of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

In some embodiments, each of the one or more of the first set of electrodes is configured to be independently activated and controlled to thereby deliver energy independent of one another. Accordingly, in some embodiments, an operator (i.e., surgeon) may selectively activate one or more of the first set of electrodes as desired to treat specific sites of inferior turbinate tissue.

In some embodiments, the end effector is multi-segmented and includes a proximal segment that is spaced apart from a separate distal segment. The proximal segment may include a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate. The distal segment may include a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Each of the second set of electrodes may be configured to deliver energy to a second target site associated with a sphenopalatine foramen within the sino-nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina or microforamina of a palatine bone of the patient.

In some embodiments, each of the one or more of the second set of electrodes is configured to be independently activated and controlled to thereby deliver energy independent of one another. Accordingly, in some embodiments, an operator (i.e., surgeon) may selectively activate one or more of the second set of electrodes as desired to treat specific sites associated with the sphenopalatine foramen.

Another aspect of the invention provides a method for treating a condition within a sino-nasal cavity of a patient. The method includes providing a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon. The method further

includes advancing the elongate body and end effector through a nasal passage and into a nasal cavity of a patient until a length of the elongate body is positioned at a first target site and the end effector is positioned at a separate second target site. The method further includes delivering energy, via the first and second sets of electrodes, to tissue at the respective first and second target sites.

In some embodiments, the elongate body generally includes a shaft to which the end effector is coupled. For example, the shaft may include an outer sheath surrounding a hypotube or metallic member, such that at least one of the outer sheath, the hypotube, and the metallic member includes one or more of the first set of electrodes provided thereon. In other embodiments, the elongate body includes one or more of a plurality of support elements forming at least a portion of the end effector.

In some embodiments, each of the first set of electrodes is positioned on separate respective portion of the elongate body. In some embodiments, one or more of the separate respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

Each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of a patient. The energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or result in local hypoxia of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

In some embodiments, the end effector is multi-segmented and includes a proximal segment that is spaced apart from a separate distal segment. The proximal segment may include a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate. The distal segment may include a second set of

flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Each of the second set of electrodes may be configured to deliver energy to a second target site associated with a sphenopalatine foramen within the nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina or microforamina of a palatine bone of the patient.

Brief Description of the Drawings

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic neuromodulation system for treating a condition within a nasal cavity using a handheld device according to some embodiments of the present disclosure.

FIG. 2 is a diagrammatic illustration of the console coupled to the handheld neuromodulation device consistent with the present disclosure, further illustrating a multi-segment end effector of the handheld device for delivering energy, via proximal and distal segments, to tissue at the one or more target sites within the nasal cavity.

FIG. 3A is a cut-away side view illustrating the anatomy of a lateral nasal wall.

FIG. 3B is an enlarged side view of the nerves of the lateral nasal wall of FIG. 1A.

FIG. 3C is a front view of a left palatine bone illustrating geometry of microforamina in the left palatine bone.

FIG. 4 is a side view of one embodiment of a handheld device for providing therapeutic nasal neuromodulation consistent with the present disclosure.

FIG. 5A is an enlarged, perspective view of the multi-segment end effector illustrating the first (proximal) segment and second (distal) segment.

FIG. 5B is an exploded, perspective view of the multi-segment end effector.

FIG. 5C is an enlarged, top view of the multi-segment end effector.

FIG. 5D is an enlarged, side view of the multi-segment end effector.

FIG. 5E is an enlarged, front (proximal facing) view of the first (proximal) segment of the multi-segment end effector.

FIG. 5F is an enlarged, front (proximal facing) view of the second (distal) segment of the multi-segment end effector.

FIG. 6 is a perspective view, partly in section, of a portion of a support element illustrating an exposed conductive wire serving as an energy delivery element or electrode element.

FIG. 7 is a cross-sectional view of a portion of the shaft of the handheld device taken along lines 7-7 of FIG. 4.

FIG. 7A is a side view of the shaft and multi-segment end effector extending from a distal end thereof, further illustrating a plurality of electrodes provided on separate respective portions of the shaft.

FIG. 7B is a sectional view of the shaft illustrating one embodiment in which a plurality of electrodes are embedded within the outer sheath of the shaft.

FIG. 7C is a sectional view of the shaft illustrating another embodiment in which a plurality of electrodes are provided on the hypotube and associated portions of the outer sheath are absent or removed to thereby expose the underlying electrodes on the hypotube.

FIG. 7D is a perspective view of a length of the shaft illustrating exposed portions of the outer sheath to reveal the underlying electrodes provided on the hypotube.

FIG. 7E is a sectional view of the shaft illustrating another embodiment in which a plurality of electrodes are provided on one or more support elements extending through the hypotube, portions of which form the end effector.

FIG. 7F is an enlarged, perspective view of the multi-segment end effector extending from the shaft and illustrating the plurality of electrodes provided on the support elements.

FIG. 7G is a cross-sectional view of the shaft illustrating exemplary portions of the shaft that are retractable and expandable.

FIG. 8 is a side view of the handle of the handheld device.

FIG. 9 is a side view of the handle illustrating internal components enclosed within.

FIG. 10 is a side view of the handle illustrating multiple markings on a portion of the handle for providing a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

FIG. 11 is a perspective view of the shaft illustrating multiple markings on a distal portion thereof for providing a user with a spatial orientation of the end effector while the end effector is in a nasal cavity.

FIG. 12 is a partial cut-away side views illustrating one approach for delivering a shaft and an associated end effector to respective target sites within a nasal region in accordance with embodiments of the present disclosure.

FIG. 13 is a flow diagram illustrating one embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 14 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 15 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

FIG. 16 is a flow diagram illustrating another embodiment of a method for treating a condition within a nasal cavity of a patient.

Detailed Description

There are various conditions related to the nasal cavity which may impact breathing and other functions of the nose. One of the more common conditions is rhinitis, which is defined as inflammation of the membranes lining the nose. The symptoms of rhinitis include nasal blockage, obstruction, congestion, nasal discharge (e.g., rhinorrhea and/or posterior nasal drip), facial pain, facial pressure, and/or reduction or complete loss of smell and/or taste. Sinusitis is another common condition, which involves an inflammation or swelling of the tissue lining the sinuses, and results in similar symptoms as rhinitis, and may further lead to infection if left untreated or if it persists for prolonged periods of time. As a result of such symptoms, many individuals have sleeping difficulties (i.e., difficulty falling asleep and/or remaining asleep). Rhinitis and sinusitis are frequently associated with one another, as sinusitis is often preceded by rhinitis. Accordingly, the term rhinosinusitis is often used to describe both conditions.

Depending on the duration and type of systems, rhinosinusitis can fall within different subtypes, including allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, recurrent rhinitis, chronic sinusitis, acute sinusitis, recurrent sinusitis, and medical resistant rhinitis and/or sinusitis, in addition to combinations of one or more of the preceding conditions. It should be noted that an acute rhinosinusitis condition is one in which symptoms last for less than twelve weeks, whereas a chronic rhinosinusitis condition refers to symptoms lasting longer than twelve weeks.

A recurrent rhinosinusitis condition refers to four or more episodes of an acute rhinosinusitis condition within a twelve-month period, with resolution of symptoms between each episode. There are numerous environmental and biological causes of rhinosinusitis. Non-allergic rhinosinusitis, for example, can be caused by environmental irritants, medications, foods, hormonal changes, and/or nasal septum deviation. Triggers of allergic rhinitis can include exposure to seasonal allergens, perennial allergens that occur any time of year, and/or occupational allergens. Accordingly, rhinosinusitis affects millions of people and is a leading cause for patients to seek medical care.

The invention recognizes that a problem with current surgical procedures is that such procedures are not accurate and cause significant collateral damage in order to treat rhinitis and further fail to adequately treat the underlying symptoms.

The invention solves that problem by providing treatment devices having a combination of unique components, including an elongate body (which may be in the form of a shaft or sheath, or other elongate body), a retractable and expandable multi-segment end effector, and handle, that, as a whole, provide a high level of precise control and feedback to an operator during a procedure. In particular, the elongate body is configured to not only aid an operator in the positioning and delivery of the multi-segment end effector to a desired target site within the sino-nasal cavity, but further includes an electrode array provided along a length thereof that is configured to deliver energy to specific target sites within the nasal passage and sino-nasal cavity, in conjunction with neuromodulation provided by the multi-segment end effector. The multi-segment end effector is configured to complement anatomy at multiple different locations within the sino-nasal cavity. The handle is configured with multiple ergonomic and functional features that improve device use and feedback, such as independent control of deployment of the end effector and energy delivery and a shape associated with the architecture of the end effector in the deployed configuration. The handle may also include one or more markings that provide a user with a spatial orientation of the end effector while the end effector is in a sino-nasal cavity.

In that manner, the present invention provides devices that are capable of highly conforming to anatomical variations within a nasal passage and sino-nasal cavity while providing unprecedented control and guidance to an operator so that an operator can perform an accurate, minimally invasive, and localized application of energy to one or more target sites within the nasal passage and nasal cavity to cause multi-point interruption of neural signal without causing

collateral damage or disruption to other neural structures.

Unlike other surgical treatments for rhinitis, the devices of the invention are minimally invasive. Accordingly, a procedure can be performed in an office environment under local anesthetic. The multi-segment end-effector allows for targeting the autonomic supply to the nasal turbinates and will have a positive impact on both allergic and non-allergic rhinitis. Using this approach, it is expected that devices of the invention will be able to provide long-term symptom relief (e.g., years instead of months). Since the treatment is accurate with minimal collateral damage to the surrounding tissue, patients will begin to feel symptom relief immediately following the treatment. It is fully expected that patients will be removed from their pharmacotherapies following this therapy.

The systems and methods of the present invention include a handheld device comprising a retractable and expandable multi-segment end effector that, once delivered to the one more target sites within the sino-nasal cavity, can expand to a specific shape and/or size corresponding to anatomical structures within the sino-nasal cavity and associated with the target sites. In particular, the end effector includes at least a first flexible segment and a second flexible segment, each of which includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments become accurately positioned within the sino-nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

The handheld device further includes an elongate body operably associated with the end effector and a handle operably associated with the elongate body. The elongate body may be in the form of a shaft or sheath (or other elongate body operably associated with or coupled to the end effector). The elongate body may include a pre-defined shape (i.e., bent or angled at a

specific orientation) so as to assist the surgeon (or other medical professional) for placement of the end effector at the target sites. The elongate body further includes one or more electrodes provided on one or respective portions along a length thereof and can be used to deliver energy to tissue adjacent to, or in contact with, such portions of the elongate body. For example, in some embodiments, the elongate body may reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes of the multi-segment end effector, the surgeon may also activate and deliver energy from electrodes associated with the elongate body to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

It should be noted that, although many of the embodiments are described with respect to

devices, systems, and methods for therapeutically modulating tissue (neural and/or non-neural tissue) in the nasal region for the treatment of rhinitis, congestion, and/or rhinorrhea, other applications and other embodiments in addition to those described herein are within the scope of the present disclosure. For example, at least some embodiments of the present disclosure may be useful for the treatment of other indications, such as the treatment of chronic sinusitis and epistaxis. In particular, the embodiments described herein may be configured to treat allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, chronic sinusitis, acute sinusitis, chronic rhinosinusitis, acute rhinosinusitis, and/or medical resistant rhinitis.

It should further be noted that the devices described herein, most notably the elongate body (which may be in the form of a shaft, outer sheath, hypotube, metallic member, or other elongate body that is operably associated with the end effector) may be included and incorporated in any of the treatment devices, systems, and methods illustrated and described in U.S. Publication Nos.: 2016/0331459; 2018/0133460; 2017/0231651; 2017/0252089; 2018/0177542; 2018/0177546; 2018/0185085; 2018/0228533; 2018/0317997; 2018/0344378; 2019/0076185; 2019/0175242; 2019/0201069; 2019/0231409; 2019/0282289; 2016/0354136; 2017/0231474; 2018/0078327; 2018/0103994; 2018/0125560; 2018/0153375; 2018/0317993; 2018/0344411; and 2019/0083157, as well as U.S. Patent Nos.: 8,936,594; 8,986,301; 9,072,597; 9,179,964; 9,179,967; 9,237,924; 9,415,194; 9,433,463; 9,452,010; 9,486,278; 9,526,571; 9,687,296; 9,788,886; 9,801,752; 9,888,957; 9,913,682; 9,943,361; 10,028,780; 10,265,115; 10,335,221; 10,376,300; 10,398,489; 10,456,185; 10,456,186; 10,485,603; 7,758,571; 9,687,288; 9,763,723; 9,763,743; 10,028,781; 10,159,538; 10,201,687; 10,307,200; and 10,448,985, the contents of each of which are incorporated by reference herein in their entireties.

FIGS. 1A and 1B are diagrammatic illustrations of a therapeutic neuromodulation system 100 for treating a condition within a nasal cavity using a handheld device 102 according to some embodiments of the present disclosure. The system 100 generally includes a neuromodulation device 102 and a neuromodulation console 104 to which the device 102 is to be connected. FIG. 2 is a diagrammatic illustration of the console 104 coupled to the handheld neuromodulation device 102. As illustrated, the neuromodulation device 102 is a handheld device, which includes a retractable and expandable multi-segment end effector 114, a shaft 116 operably associated with the end effector 114 and a handle 118 operably associated with the shaft 116. The end effector 114 is configured to be advanced into the nasal cavity of a patient 12 and positioned at a

location associated with one or more target sites to undergo therapeutic neuromodulation treatment. It should be noted that the terms "end effector" and "therapeutic assembly" may be used interchangeably throughout this disclosure.

For example, a surgeon or other medical professional performing a procedure can utilize the handle 118 to manipulate and advance the shaft 116 within the nasal cavity, wherein the shaft 116 is configured to locate at least a distal portion thereof intraluminally at a treatment or target site within a nasal region. The one or more target sites may generally be associated with postganglionic parasympathetic fibers that innervate the nasal mucosa. The target site may be a region, volume, or area in which the target nerves are located and may differ in size and shape depending upon the anatomy of the patient. Once positioned, the end effector 114 may be deployed and subsequently deliver energy to the one or more target sites to thereby therapeutically modulating nerves of interest, particularly nerves associated with a rhinosinusitis condition so as to treat such condition. For example, the end effector 114 may include at least one energy delivery element, such as an electrode, configured to therapeutically modulate the postganglionic parasympathetic nerves. For example, one or more electrodes may be provided by one or more portions of the end-effector 114, wherein the electrodes may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the end effector 114 may include other energy delivery elements configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power.

In some embodiments, the end effector 114 may include one or more sensors (not shown), such as one or more temperature sensors (e.g., thermocouples, thermistors, etc.), impedance sensors, and/or other sensors. The sensors and/or the electrodes may be connected to one or more wires extending through the shaft 116 and configured to transmit signals to and from the sensors and/or convey energy to the electrodes.

As shown, the device 102 is operatively coupled to the console 104 via a wired connection, such as cable 120. It should be noted, however, that the device 102 and console 104 may be operatively coupled to one another via a wireless connection. The console 104 is configured to provide various functions for the neuromodulation device 102, which may include,

but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the neuromodulation device 102. For example, when the neuromodulation device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 may include an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the neuromodulation device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the neuromodulation device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via evaluation/feedback algorithms 110. For example, the evaluation/feedback algorithms 110 can be configured to provide information associated with the temperature of the tissue at the treatment site, the location of nerves at the treatment site, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In

certain embodiments, the evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to monitor temperature at the treatment site during therapy and automatically shut off the energy delivery when the temperature reaches a predetermined maximum (e.g., when applying RF energy) or predetermined minimum (e.g., when applying cryotherapy). In other embodiments, the evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a graphical user interface (GUI) 112 provided via a display on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104, such as a tablet or monitor. The GUI 112 may generally provide operational instructions for the procedure, such as directing the operator to select which nasal cavity to treat, indicating when the device 102 is primed and ready to perform treatment, and further providing status of therapy during the procedure, including indicating when the treatment is complete.

For example, in some embodiments, the end effector 114and/or other portions of the system 100 can be configured to detect various parameters of the heterogeneous tissue at the target site to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate nerves and/or other structures, and allow for neural mapping. For example, the end effector 114 may be configured to detect impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers in the target region. As shown in FIG. 1, the console 104 may further include a monitoring system 108 configured to receive detected electrical and/or thermal measurements of tissue at the target site taken by the end effector 114, specifically sensed by appropriate sensors (e.g., temperature sensors and/or impedance sensors), and process this information to identify the presence of nerves, the location of nerves, and/or neural activity at the target site. The nerve monitoring system 108 can be operably coupled to the electrodes and/or other features of the end effector 102 via signal wires (e.g., copper wires) that extend through the cable 120 and through

the length of the shaft 116. In other embodiments, the end effector 114 can be communicatively coupled to the nerve monitoring system 108 using other suitable communication means.

The nerve monitoring system 108 can determine neural locations and activity before therapeutic neuromodulation to determine precise treatment regions corresponding to the positions of the desired nerves, during treatment to determine the effect of the therapeutic neuromodulation, and/or after treatment to evaluate whether the therapeutic neuromodulation treated the target nerves to a desired degree. This information can be used to make various determinations related to the nerves proximate to the target site, such as whether the target site is suitable for neuromodulation. In addition, the nerve monitoring system 108 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site. For example, the nerve monitoring system 108 can further determine electroneurogram (ENG) signals based on recordings of electrical activity of neurons taken by the end effector 114 before and after therapeutic neuromodulation. Statistically meaningful (e.g., measurable or noticeable) decreases in the ENG signal(s) taken after neuromodulation can serve as an indicator that the nerves were sufficiently ablated. Additional features and functions of the nerve monitoring system 108, as well as other functions of the various components of the console 104, including the evaluation/feedback algorithms 110 for providing real-time feedback capabilities for ensuring optimal therapy for a given treatment is administered, are described in at least U.S. Publication No. 2016/0331459 and U.S. Publication No. 2018/0133460, the contents of each of which are incorporated by reference herein in their entireties.

As will be described in greater detail herein, the neuromodulation device 102 provides access to target sites deep within the nasal region, such as at the immediate entrance of parasympathetic fibers into the nasal cavity to therapeutically modulate autonomic activity within the nasal cavity. In certain embodiments, for example, the neuromodulation device 102 can position the end effector 114 into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

FIG. 3A is a cut-away side view illustrating the anatomy of a lateral nasal wall and FIG. 3B is an enlarged side view of the nerves of the lateral nasal wall of FIG. 1A. The sphenopalatine foramen (SPF) is an opening or conduit defined by the palatine bone and the

sphenoid bone through which the sphenopalatine vessels and the posterior superior nasal nerves travel into the nasal cavity. More specifically, the orbital and sphenoidal processes of the perpendicular plate of the palatine bone define the sphenopalatine notch, which is converted into the SPF by the articulation with the surface of the body of the sphenoid bone.

The location of the SPF is highly variable within the posterior region of the lateral nasal cavity, which makes it difficult to visually locate the SPF. Typically, the SPF is located in the middle meatus (MM). However, anatomical variations also result in the SPF being located in the superior meatus (SM) or at the transition of the superior and middle meatuses. In certain individuals, for example, the inferior border of the SPF has been measured at about 19 mm above the horizontal plate of the palatine bone (i.e., the nasal sill), which is about 13 mm above the horizontal lamina of the inferior turbinate (IT) and the average distance from the nasal sill to the SPF is about 64.4 mm, resulting in an angle of approach from the nasal sill to the SPA of about 11.4°. However, studies to measure the precise location of the SPF are of limited practical application due to the wide variation of its location.

The anatomical variations of the SPF are expected to correspond to alterations of the autonomic and vascular pathways traversing into the nasal cavity. In general, it is thought that the posterior nasal nerves (also referred to as lateral posterior superior nasal nerves) branch from the pterygopalatine ganglion (PPG), which is also referred to as the sphenopalatine ganglion, through the SPF to enter the lateral nasal wall of the nasal cavity, and the sphenopalatine artery passes from the pterygopalatine fossa through the SPF on the lateral nasal wall. The sphenopalatine artery branches into two main portions: the posterior lateral nasal branch and the posterior septal branch. The main branch of the posterior lateral nasal artery travels inferiorly into the inferior turbinate IT (e.g., between about 1.0 mm and 1.5 mm from the posterior tip of the inferior turbinate IT), while another branch enters the middle turbinate MT and branches anteriorly and posteriorly.

Beyond the SPF, studies have shown that over 30% of human patients have one or more accessory foramen that also carries arteries and nerves into the nasal cavity. The accessory foramen are typically smaller than the SPF and positioned inferior to the SPF. For example, there can be one, two, three or more branches of the posterior nasal artery and posterior nasal nerves that extend through corresponding accessory foramen. The variability in location, size, and quantity associated with the accessory foramen and the associated branching arteries and

nerves that travel through the accessory foramen gives rise to a great deal of uncertainty regarding the positions of the vasculature and nerves of the sphenopalatine region. Furthermore, the natural anatomy extending from the SPF often includes deep inferior and/or superior grooves that carry neural and arterial pathways, which make it difficult to locate arterial and neural branches. For example the grooves can extend more than 5 mm long, more than 2 mm wide, and more than 1 mm deep, thereby creating a path significant enough to carry both arteries and nerves. The variations caused by the grooves and the accessory foramen in the sphenopalatine region make locating and accessing the arteries and nerves (positioned posterior to the arteries) extremely difficult for surgeons.

Recent microanatomic dissection of the pterygopalatine fossa (PPF) have further evidenced the highly variable anatomy of the region surrounding the SPF, showing that a multiplicity of efferent rami that project from the pterygopalatine ganglion (PPG) to innervate the orbit and nasal mucosa via numerous groups of small nerve fascicles, rather than an individual postganglionic autonomic nerves (e.g., the posterior nasal nerve). Studies have shown that at least 87% of humans have microforamina and micro rami in the palatine bone.

FIG. 3C, for example, is a front view of a left palatine bone illustrating geometry of microforamina and micro rami in a left palatine bone. In FIG. 3C, the solid regions represent nerves traversing directly through the palatine bone, and the open circles represent nerves that were associated with distinct microforamina. As such, FIG. 3C illustrates that a medial portion of the palatine bone can include at least 25 accessory posterolateral nerves.

The respiratory portion of the nasal cavity mucosa is composed of a type of ciliated pseudostratified columnar epithelium with a basement membrane. Nasal secretions (e.g., mucus) are secreted by goblet cells, submucosal glands, and transudate from plasma. Nasal seromucous glands and blood vessels are highly regulated by parasympathetic innervation deriving from the vidian and other nerves. Parasympathetic (cholinergic) stimulation through acetylcholine and vasoactive intestinal peptide generally results in mucus production. Accordingly, the parasympathetic innervation of the mucosa is primarily responsible submucosal gland activation/hyper activation, venous engorgement (e.g., congestion), and increased blood flow to the blood vessels lining the nose. Accordingly, severing or modulating the parasympathetic pathways that innervate the mucosa are expected to reduce or eliminate the hyper activation of

the submucosal glands and engorgement of vessels that cause symptoms associated with rhinosinusitis and other indications.

As previously described herein, postganglionic parasympathetic fibers that innervate the nasal mucosa (i.e., posterior superior nasal nerves) were thought to travel exclusively through the SPF as a sphenopalatine neurovascular bundle. The posterior nasal nerves are branches of the maxillary nerve that innervate the nasal cavity via a number of smaller medial and lateral branches extending through the mucosa of the superior and middle turbinates ST, MT (i.e., nasal conchae) and to the nasal septum. The nasopalatine nerve is generally the largest of the medial posterior superior nasal nerves, and it passes anteroinferiorly in a groove on the vomer to the floor of the nasal cavity. From here, the nasopalatine nerve passes through the incisive fossa of the hard palate and communicates with the greater palatine nerve to supply the mucosa of the hard palate. The posterior superior nasal nerves pass through the pterygopalatine ganglion PPG without synapsing and onto the maxillary nerve via its ganglionic branches.

Based on the understanding that the posterior nasal nerves exclusively traverse the SPF to innervate the nasal mucosa, surgeries have been performed to selectively sever the posterior nasal nerve as it exits the SPF. However, as discussed above, the sinonasal parasympathetic pathway actually comprises individual rami project from the pterygopalatine ganglion (PPG) to innervate the nasal mucosa via multiple small nerve fascicles (i.e., accessory posterolateral nerves), not a single branch extending through the SPF. These rami are transmitted through multiple fissures, accessory foramina, and microforamina throughout the palatine bone and may demonstrate anastomotic loops with both the SPF and other accessory nerves. Thus, if only the parasympathetic nerves traversing the SPF were severed, almost all patients (e.g., 90% of patients or more) would retain intact accessory secretomotor fibers to the posterolateral mucosa, which would result in the persistence of symptoms the neurectomy was meant to alieve.

Accordingly, embodiments of the present disclosure are configured to therapeutically modulate nerves at precise and focused treatment sites corresponding to the sites of rami extending through fissures, accessory foramina, and microforamina throughout the palatine bone (e.g., target region T shown in FIG. 3B). In certain embodiments, the targeted nerves are postganglionic parasympathetic nerves that go on to innervate the nasal mucosa. This selective neural treatment is also expected to decrease the rate of postoperative nasal crusting and dryness because it allows a clinician to titrate the degree of anterior denervation through judicious

sparing of the rami orbitonasal. Furthermore, embodiments of the present disclosure are also expected to maintain at least some sympathetic tone by preserving a portion of the sympathetic contributions from the deep petrosal nerve and internal maxillary periarterial plexus, leading to improved outcomes with respect to nasal obstruction. In addition, embodiments of the present disclosure are configured to target a multitude of parasympathetic neural entry locations (e.g., accessory foramen, fissures, and microforamina) to the nasal region to provide for a complete resection of all anastomotic loops, thereby reducing the rate of long-term re-innervation.

FIG. 4 is a side view of one embodiment of a handheld device 102 for providing therapeutic nasal neuromodulation consistent with the present disclosure. As illustrated, the device 102 includes a multi-segment end effector 114 transformable between a retracted configuration and an expanded deployed configuration, a shaft 116 operably associated with the end effector 114, and a handle 118 operably associated with the shaft 116. The multi-segment end effector 114 includes at least a first segment 122 and a second segment 124 spaced apart from one another. The first segment 122 is generally positioned closer to a distal end of the shaft 116, and is thus sometimes referred to herein as the proximal segment 122, while the second segment 124 is generally positioned further from the distal end of the shaft 116 and is thus sometimes referred to herein as the distal segment 124. Each of the first and second segments 122 and 124 is transformable between a retracted configuration, which includes a low-profile delivery state to facilitate intraluminal delivery of the end effector 114 to a treatment site within the nasal region, and a deployed configuration, which includes an expanded state, as shown in FIG. 4 and further illustrated in FIGS. 5A-5F. The handle 118 includes at least a first mechanism 126 for deployment of the multi-segment end effector 114, notably the first and second segments 122, 124, from the retracted configuration to the deployed configuration and a second mechanism 128, separate from the first mechanism 124, for control of energy output by either of the first and second segments 122, 124 of the end effector 114, specifically electrodes or other energy elements provided by first and/or second segments 122, 124. The handheld device 102 may further include an auxiliary line 121, which may provide a fluid connection between a fluid source, for example, and the shaft 116 such that fluid may be provided to a target site via the distal end of the shaft 116. In some embodiments, the auxiliary line 121 may provide a connection between a vacuum source and the shaft 116, such that the device 102 may include suction capabilities (via the distal end of the shaft 116).

FIGS. 5A, 5B, 5C, 5D, 5E, and 5F are enlarged views of the multi-segment end effector 114, illustrating various views of the first and second segments 122, 124 in greater detail. FIG. 5A is an enlarged, perspective view of the multi-segment end effector 114. FIG. 5B is an exploded, perspective view of the multi-segment end effector 114. FIGS. 5C and 5D are enlarged, top and side views, respectively, of the multi-segment end effector 114. FIG. 5E is an enlarged, front (proximal facing) view of the first segment 122 of the multi-segment end effector 114. FIG. 5F is an enlarged, front (proximal facing) view of the second segment 124 of the multi-segment end effector 114.

As illustrated, the first segment 122 includes at least a first set of flexible support elements, generally in the form of wires, arranged in a first configuration, and the second segment 124 includes a second set of flexible support elements, also in the form of wires, arranged in a second configuration. The first and second sets of flexible support elements include composite wires having conductive and elastic properties. For example, in some embodiments, the composite wires include a shape memory material, such as nitinol. The flexible support elements may further include a highly lubricious coating, which may allow for desirable electrical insulation properties as well as desirable low friction surface finish. Each of the first and second segments 122, 124 is transformable between a retracted configuration and an expanded deployed configuration such that the first and second sets of flexible support elements are configured to position one or more electrodes provided on the respective segments (see electrodes 136 in FIGS. 5E and 5F) into contact with one or more target sites when in the deployed configuration.

As shown, when in the expanded deployed configuration, the first set of support elements of the first segment 122 includes at least a first pair of struts 130a, 130b, each comprising a loop (or leaflet) shape and extending in an upward direction and a second pair of struts 132a, 132b, each comprising a loop (or leaflet) shape and extending in a downward direction, generally in an opposite direction relative to at least the first pair of struts 130a, 130b. It should be noted that the terms upward and downward are used to describe the orientation of the first and second segments 122, 124 relative to one another. More specifically, the first pair of struts 130a, 130b generally extend in an outward inclination in a first direction relative to a longitudinal axis of the multi-segment end effector 114 and are spaced apart from one another. Similarly, the second pair of struts 132a, 132b extend in an outward inclination in a second direction substantially

opposite the first direction relative to the longitudinal axis of the multi-segment end effector and spaced apart from one another.

The second set of support elements of the second segment 124, when in the expanded deployed configuration, includes a second set of struts 134(1), 134(2), 134(n) (approximately six struts), each comprising a loop shape extending outward to form an open-ended circumferential shape. As shown, the open-ended circumferential shape generally resembles a blooming flower, wherein each looped strut 134 may generally resemble a flower petal. It should be noted that the second set of struts 134 may include any number of individual struts and is not limited to six, as illustrated. For example, in some embodiments, the second segment 124 may include two, three, four, five, six, seven, eight, nine, ten, or more struts 134.

The first and second segments 122, 124, specifically struts 130, 132, and 134 include one or more energy delivery elements, such as a plurality of electrodes 136. It should be noted that any individual strut may include any number of electrodes 136 and is not limited to one electrode, as shown. In the expanded state, the struts 130, 132, and 134 can position any number of electrodes 136 against tissue at a target site within the nasal region (e.g., proximate to the palatine bone inferior to the SPF). The electrodes 136 can apply bipolar or multi-polar radiofrequency (RF) energy to the target site to therapeutically modulate postganglionic parasympathetic nerves that innervate the nasal mucosa proximate to the target site. In various embodiments, the electrodes 136 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

The first and second segments 122, 124 and the associated struts 130, 132, and 134 can have sufficient rigidity to support the electrodes 136 and position or press the electrodes 136 against tissue at the target site. In addition, each of the expanded first and second segments 122, 124 can press against surrounding anatomical structures proximate to the target site (e.g., the turbinates, the palatine bone, etc.) and the individual struts 130, 132, 134 can at least partially conform to the shape of the adjacent anatomical structures to anchor the end effector 114 In addition, the expansion and conformability of the struts 130, 132, 134 can facilitate placing the electrodes 136 in contact with the surrounding tissue at the target site. The electrodes 136 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene (PEDOT), titanium, titanium nitride, carbon, carbon

nanotubes, platinum grey, Drawn Filled Tubing (DFT) with a silver core, and/or other suitable materials for delivery RF energy to target tissue. In some embodiments, such as illustrated in FIG. 6, a strut may include an outer jacket surrounding a conductive wire, wherein portions of the outer jacket are selectively absent along a length of the strut, thereby exposing the underlying conductive wire so as to act as an energy delivering element (i.e., an electrode) and/or sensing element, as described in greater detail herein.

In certain embodiments, each electrode 136 can be operated independently of the other electrodes 136. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein. The selective independent control of the electrodes 136 allows the end effector 114 to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 136 can be activated to target neural fibers in a specific region while the other electrodes 136 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 124 that is adjacent to tissue at the target site, and the electrodes 136 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves on the lateral nasal wall within one nostril without applying energy to structures in other portions of the nasal cavity.

The electrodes 136 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1) via wires (not shown) that extend from the electrodes 136, through the shaft 116, and to the RF generator. When each of the electrodes 136 is independently controlled, each electrode 136 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 136 can be controlled together and, therefore, multiple electrodes 136 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 136. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 136, and do so while activating the electrodes 136 in a predetermined pattern selected based on the position of the end effector 114 relative to the treatment site and/or the identified locations of the target nerves. The RF generator is able to provide bipolar low power (10 watts with maximum

setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

Once deployed, the first and second segments 122, 124 contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. In turn, the first and second segments 122, 124 become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes 136, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. More specifically, the first and second segments 122, 124 have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments 122, 124, and thus one or more electrodes associated therewith 136, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

For example, the first set of flexible support elements of the first segment 122 conforms to and complements a shape of a first anatomical structure at the first location when the first segment 122 is in the deployed configuration and the second set of flexible support elements of the second segment 124 conforms to and complements a shape of a second anatomical structure at the second location when the second segment is in the deployed configuration. The first and second anatomical structures may include, but are not limited to, inferior turbinate, middle turbinate, superior turbinate, inferior meatus, middle meatus, superior meatus, pterygopalatine region, pterygopalatine fossa, sphenopalatine foramen, accessory sphenopalatine foramen(ae), and sphenopalatine micro-foramen(ae).

In some embodiments, the first segment 122 of the multi-segment end effector 114 is configured in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to the middle turbinate and the second segment 124 of the multi-segment end effector is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the middle turbinate.

For example, the first set of flexible support elements of the first segment (i.e., struts 130 and 132) conforms to and complements a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 122 is in the deployed configuration and the second set of flexible support elements (i.e., struts 134) of the second segment 124 contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment

and posterior-inferior edge of middle turbinate when the second segment 124 is in the deployed configuration. Accordingly, when in the deployed configuration, the first and second segments 122, 124 are configured to position one or more associated electrodes 136 at one or more target sites relative to either of the middle turbinate and the plurality of tissue locations in the cavity behind the middle turbinate. In turn, electrodes 136 are configured to deliver RF energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

As illustrated in FIG. 5E, the first segment 122 comprises a bilateral geometry. In particular, the first segment 122 includes two identical sides, including a first side formed of struts 130a, 132a and a second side formed of struts 130b, 132b. This bilateral geometry allows at least one of the two sides to conform to and accommodate an anatomical structure within the nasal cavity when the first segment 122 is in an expanded state. For example, when in the expanded state, the plurality of struts 130a, 132a contact multiple locations along multiple portions of the anatomical structure and electrodes provided by the struts are configured to emit energy at a level sufficient to create multiple micro-lesions in tissue of the anatomical structure that interrupt neural signals to mucus producing and/or mucosal engorgement elements. In particular, struts 130a, 132a conform to and complement a shape of a lateral attachment and posterior-inferior edge of the middle turbinate when the first segment 122 is in the deployed configuration, thereby allowing for both sides of the anatomical structure to receive energy from the electrodes. By having this independence between first and second side (i.e., right and left side) configurations, the first segment 122 is a true bilateral device. By providing a bilateral geometry, the multi-segment end effector 114 does not require a repeat use configuration to treat the other side of the anatomical structure, as both sides of the structure are accounted at the same time due to the bilateral geometry. The resultant micro-lesion pattern can be repeatable and is predictable in both macro element (depth, volume, shape parameter, surface area) and can be controlled to establish low to high effects of each, as well as micro elements (the thresholding of effects within the range of the macro envelope can be controlled), as well be described in greater detail herein. The systems of the present invention are further able to establish gradients within allowing for control over neural effects without having widespread effect to other cellular bodies, as will be described in greater detail herein.

FIG. 7 is a cross-sectional view of a portion of the shaft 116 of the handheld device taken along lines 7-7 of FIG. 4. As illustrated, the shaft 116 may be constructed from multiple components so as to have the ability to constrain the end effector 114 in the retracted configuration (i.e., the low-profile delivery state) when the end effector 114 is retracted within the shaft 116, and to further provide an atraumatic, low profile and durable means to deliver the end effector 114 to the target site. The shaft 116 includes coaxial tubes which travel from the handle 118 to a distal end of the shaft 116. The shaft 116 assembly is low profile to ensure trans-nasal delivery of therapy. The shaft 116 includes an outer sheath 138, surrounding a hypotube 140, which is further assembled over electrode wires 129 which surround an inner lumen 142. The outer sheath 138 serves as the interface between the anatomy and the device 102. The outer sheath 138 may generally include a low friction PTFE liner to minimize friction between the outer sheath 138 and the hypotube 140 during deployment and retraction. In particular, the outer sheath 138 may generally include an encapsulated braid along a length of the shaft 116 to provide flexibility while retaining kink resistance and further retaining column and/or tensile strength. For example, the outer sheath 138 may include a soft Pebax material, which is atraumatic and enables smooth delivery through the nasal passage. The outer sheath 138 may further include orientation/landmark markings on an exterior surface thereof, generally at the distal end, wherein the markings may provide a visual indication to an operator of the architecture and/or spatial orientation of first and/or second segments 122, 124 of the end effector 114 to assist in positioning and deployment of the end effector 114.

The hypotube 140 is assembled over the electrode wires starting within the handle 118 and travelling to the proximal end of the end effector 114. The hypotube 140 generally acts to protect the wires during delivery and is malleable to enable flexibility without kinking to thereby improve trackability. The hypotube 140 provides stiffness and enables torqueability of the device 102 to ensure accurate placement of the end effector 114. The hypotube 140 also provides a low friction exterior surface which enables low forces when the outer sheath 138 moves relative to the hypotube 140 during deployment and retraction or constraint. The shaft 116 may be pre-shaped in such a manner so as to complement the nasal cavity. For example, the hypotube 140 may be annealed to create a bent shaft 116 with a pre-set curve. The hypotube 140 may include a stainless-steel tubing, for example, which interfaces with a liner in the outer sheath 138 for low friction movement.

The inner lumen 142 may generally provide a channel for fluid extraction during a treatment procedure. For example, the inner lumen 142 extends from the distal end of the shaft 116 through the hypotube 140 and to atmosphere via a fluid line (line 121 of FIG. 4). The inner lumen 142 materials are chosen to resist forces of external components acting thereon during a procedure.

FIG. 7A is a side view of one embodiment of an elongate body and a multi-segment end effector extending from a distal end thereof, further illustrating a plurality of electrodes provided on separate respective portions of the elongate body. In the illustrated example, the elongate body may generally be in the form of the shaft 116, including one or more specific components of the shaft 116, as previously described herein. For example, the elongate body in the present example may include the outer sheath 138, such that one or more electrodes 137 are provided and positioned on separate respective portions of the outer sheath 138. FIG. 7B is a sectional view of the shaft 116 illustrating one embodiment in which a plurality of electrodes are embedded within the outer sheath 138. As further illustrated in FIG. 7B, the electrodes 137 may be provided along an entirety of the circumference of the outer sheath 138 (i.e., along substantially all sides of the outer sheath 138).

FIG. 7C is a sectional view of the shaft 116 illustrating another embodiment in which a plurality of electrodes 137 are provided on the hypotube 140 and associated portions of the outer sheath 138 are absent or removed to thereby expose the underlying electrodes 137 on the hypotube 140. FIG. 7D is a perspective view of a length of the shaft 116 illustrating exposed portions of the outer sheath 138 to reveal the underlying electrodes 137 provided on the hypotube 140. More specifically, portions of the outer sheath 138 may be selectively absent along a length thereof, thereby exposing any underlying electrodes 137 provided on the enclosed portion of the hypotube 140. Accordingly, in such an embodiment, the elongate body is in the form of the hypotube 140.

FIG. 7E is a sectional view of the shaft 116 illustrating another embodiment in which a plurality of electrodes 137 are provided on one or more support elements 129 extending through the hypotube 140, portions of which form the end effector 114. FIG. 7F is an enlarged, perspective view of the multi-segment end effector 114 extending from the shaft 116, specifically the hypotube 140 and illustrating the plurality of electrodes 137 provided on the support elements 129. For example, during deployment of the end effector 114 from the

retracted to expanded configurations, proximal portions of the support elements 129 that form the proximal and distal segments 122 and 124 may be further exposed to thereby further expose the electrodes 137 provided thereon. Accordingly, in such an embodiment, the elongate body is in the form of the assembly of support elements 129.

In some embodiments, respective portions of the elongate body may be transformable between a retracted configuration and an expanded configuration. For example, FIG. 7G is a cross-sectional view of the shaft 116, specifically the outer sheath 138, illustrating exemplary portions of the sheath 138 that may be retractable and expandable. When in the expanded configuration, each separate respective portion of the outer sheath 138 may be configured to position a separate associated one of the electrodes 137 into contact with a target tissue.

Similar to electrodes 136, the electrodes 137 may be configured to apply electromagnetic neuromodulation energy (e.g., radiofrequency (RF) energy) to target sites. In other embodiments, the electrodes 137 may be configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power. Yet still, in other embodiments, the electrodes can apply bipolar or multi-polar radiofrequency (RF) energy to a target site to therapeutically modulate tissue at the target site, which may include ablation of the tissue. For example, in various embodiments, the electrodes 136 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

In certain embodiments, each electrode 137 can be operated independently of the other electrodes 137. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 107 previously described herein. The selective independent control of the electrodes 137 allows respective portions of the shaft to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 137 can be activated to target tissue in a specific portion of the inferior turbinate while the other electrodes 137 remain inactive.

The electrodes 137 are electrically coupled to an RF generator (e.g., the generator 106 of FIG. 1) via wires (not shown) that extend from the electrodes 137, through the shaft 116, and to the RF generator. When each of the electrodes 137 is independently controlled, each electrode

137 couples to a corresponding wire that extends through the shaft 116. In other embodiments, multiple electrodes 137 can be controlled together and, therefore, multiple electrodes 137 can be electrically coupled to the same wire extending through the shaft 116. As previously described, the RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 137. For example, the RF generator can deliver RF power at about 460-480 kHz (+ or - 5 kHz) to the electrodes 137, and do so while activating the electrodes 137 in a predetermined pattern selected based on the position of the shaft 116 relative to the treatment site and/or the identified locations of the target tissue. The RF generator is able to provide bipolar low power (10 watts with maximum setting of 50 watts) RF energy delivery, and further provide multiplexing capabilities (across a maximum of 30 channels).

The electrodes 137 may be used to deliver energy to tissue adjacent to, or in contact with, such the respective portions of the shaft 116. For example, in some embodiments, the shaft 116 may generally reside with a portion of the nasal cavity proximate to the inferior turbinate upon advancing and deploying the multi-segment end effector 114 in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes 136 of the multi-segment end effector 114, the surgeon may also activate and deliver energy from electrodes 137 associated with a given component of the shaft 116 (i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to tissue associated with the inferior turbinate. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient and improve a patient's ability to breathe. For example, the energy may be delivered at a level sufficient to disrupt multiple neural signals to, or result in local hypoxia of, mucus producing and/or mucosal engorgement elements associated with the inferior turbinate. For example, delivery of energy may result in ablation of targeted tissue of the inferior turbinate. The ablation may be thermal ablation. The ablation may be caused by delivery of radiofrequency (RF) energy, for example.

Accordingly, in a given procedure, the surgeon may utilize the multi-segment end effector 114 to deliver energy (via electrodes 136) at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a

palatine bone of the patient and further utilize a component of the shaft 116 or other elongate body operably associated with the end effector 114 (i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to deliver energy (via electrodes 137) at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient. Such a combination of energy delivery to two specific targeted sites improves the manner in which at least one of rhinitis, congestion, and rhinorrhea are treated, thereby increasing the potential for reducing or completely eliminating symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

FIG. 8 is a side view of the handle 118. FIG. 9 is a side view of the handle 118 illustrating internal components enclosed within. The handle 118 generally includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure. For example, the handle 118 may include specific contours, including recesses 144, 146, and 148 which are designed to naturally receive one or more of an operator's fingers in either of an overhand grip or underhand grip style and provide a comfortable feel for the operator. For example, in an underhand grip, recess 144 may naturally receive an operator's index finger, recess 146 may naturally receive an operator's middle finger, and recess 148 may naturally receive an operator's ring and little (pinkie or pinky) fingers which wrap around the proximal protrusion 150 and the operator's thumb naturally rests on a top portion of the handle 118 in a location adjacent to the first mechanism 126. In an overhand grip, the operator's index finger may naturally rest on the top portion of the handle 118, adjacent to the first mechanism 126, while recess 144 may naturally receive the operator's middle finger, recess 146 may naturally receive a portion of the operator's middle and/or ring fingers, and recess 148 may naturally receive and rest within the space (sometimes referred to as the purlicue) between the operator's thumb and index finger.

As previously described, the handle includes multiple user-operated mechanisms, including at least a first mechanism 126 for deployment of the end effector 114 from the retracted configuration to the expanded deployed configuration and a second mechanism 128 for controlling of energy output by the end effector, notably energy delivery from one or more electrodes 136. As shown, the user inputs for the first and second mechanisms 126, 128 are

positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. For example, user input for the first mechanism 126 is positioned on a top portion of the handle 118 adjacent the grip portion and user input for the second mechanism 128 is positioned on side portions of the handle 118 adjacent the grip portion. As such, in an underhand grip style, the operator's thumb rests on the top portion of the handle adjacent to the first mechanism 126 and at least their middle finger is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. In an overhand grip system, the operator's index finger rests on the top portion of the handle adjacent to the first mechanism 126 and at least their thumb is positioned adjacent to the second mechanism 128, each of the first and second mechanisms 126, 128 accessible and able to be actuated. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

Referring to FIG. 9, the various components provided within the handle 118 are illustrated. As shown, the first mechanism 126 may generally include a rack and pinion assembly providing movement of the end effector 114 between the retracted and deployed configurations in response to input from a user-operated controller. The rack and pinion assembly generally includes a set of gears 152 for receiving input from the user-operated controller and converting the input to linear motion of a rack member 154 operably associated with at least one of the shaft 116 and the end effector 114. The rack and pinion assembly comprises a gearing ratio sufficient to balance a stroke length and retraction and deployment forces, thereby improving control over the deployment of the end effector. As shown, the rack member 154 may be coupled to a portion of the shaft 116, for example, such that movement of the rack member 154 in a direction towards a proximal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector 114 remains stationary, thereby exposing the end effector 114 and allowing the end effector 114 to transition from the constrained, retracted configuration to the expanded, deployed configuration. Similarly, upon movement of the rack member 154 in a direction towards a distal end of the handle 118 results in corresponding movement of the shaft 116 while the end effector 114 remains stationary, thereby enclosing the end effector 114 within the shaft 116. It should be noted that, in other embodiments, the rack member 154 may be directly coupled to a portion of the end effector 114

such that movement of the rack member 154 results in corresponding movement of the end effector 114 while the shaft 116 remains stationary, thereby transitioning the end effector 114 between the retracted and deployed configurations.

The user-operated controller associated with the first mechanism 126 may include a slider mechanism operably associated with the rack and pinion rail assembly. Movement of the slider mechanism in a rearward direction towards a proximal end of the handle results in transitioning of the end effector 114 to the deployed configuration and movement of the slider mechanism in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration. In other embodiment, the user-operated controller associated with the first mechanism 126 may include a scroll wheel mechanism operably associated with the rack and pinion rail assembly. Rotation of the wheel in a rearward direction towards a proximal end of the handle results in transitioning of the end effector to the deployed configuration and rotation of the wheel in a forward direction towards a distal end of the handle results in transitioning of the end effector to the retracted configuration.

The user-operated controller associated with the first mechanism 126 may generally provide a high degree of precision and control over the deployment (and retraction) of the first and second segments 122, 124. For example, in some instances, the operator may wish to only deploy the second segment 124 during the procedure, while the first segment 122 remains in the retracted configuration. The user-operated controller allows for an operator to provide a sufficient degree of input (i.e., slide the slider mechanism or scroll the scroll wheel to a specific position) which results in only the second segment 124 transitioning from the retracted configuration to the deployed configuration (while the first segment 122 remains enclosed within the shaft 116 and in the retracted configuration). For example, in some embodiments, the end effector 114 may further include a detent feature, such as a catch or similar element, positioned between the first and second segments 122, 124 and configured to provide a surgeon with feedback, such as haptic or tactile feedback, during deployment of the end effector segments, alerting the surgeon when at least the second segment 124 is fully deployed. In particular, as the surgeon slides the slider mechanism or scrolls the scroll wheel during deployment of the second segment 124, the detect feature (provided between the first and second segments 122, 124) may then reach a portion of the shaft 116 and cause an increase in resistance on the slider mechanism or scroll wheel, thereby indicating to the surgeon that the second segment 124 has been deployed

and the first segment 122 remains in the retracted configuration. Accordingly, the surgeon can position and orient the second segment 124 as they desire without concern over the first segment 122 as it remains in the retracted configuration. In turn, one the second segment 124 is positioned at the desired target site, the surgeon may then deploy the first segment 122 to perform the procedure. Yet still, in some instances, only the second segment 124 may be used to perform a procedure (i.e., deliver energy to one or more target sites in contact with the second segment 124) and, as such, the first segment 122 may never be deployed.

The second mechanism 128 may generally include a user-operated controller configured to be actuated between at least an active position and an inactive position to thereby control delivery of energy from the end effector 114, notable delivery of energy from the electrodes 136. The user-operated controller may be multi-modal in that the user-operated controller may be actuated between multiple positions providing different functions/modes. For example, upon a single user input (i.e., single press of button associated within controller), the second mechanism may provide a baseline apposition / sensing check function prior to modulation. Upon pressing and holding the controller button for a pre-defined period of time, the energy output from the end effector may be activated. Further, upon double-tapping the controller button, energy output is deactivated.

Furthermore, the handle and/or the shaft may include markings that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. FIG. 10 is a side view of the handle 118 illustrating multiple markings on a distal end of the handle 118 and FIG. 11 is a perspective view of a portion of the shaft 116 illustrating multiple markings on a distal end thereof. In particular, multiple markings may be provided on the handle and/or shaft and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. The markings may include, for example, text, symbols, color-coding insignia, or the like. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the shaft, a surgeon can rely on the markings on the handle and/or shaft as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

For example, the handle and/or shaft may include markings associated with each of the first pair of struts 130a, 130b and each of the second pair of struts 132a, 132b, so as to provide an operator with a visual indication as to the resulting spatial orientation and architecture of at least the first segment 122 when initially navigating the nasal cavity and delivering the distal end of the shaft 116 to a target site, prior to deployment of the end effector 114. In other words, the markings provide an operator with an indication of the orientation of at least the first segment 122 of the end effector 114 prior to deploying the end effector 114, thereby ensuring accurate positioning at the desired location.

FIG. 12 is a partial cut-away side view illustrating one approach for delivering an end effector 114 a target site within a nasal region in accordance with embodiments of the present disclosure. As shown, the distal portion of the shaft 116 extends into the nasal passage (NP), through the inferior meatus (IM) between the inferior turbinate (IT) and the nasal sill (NS), and around the posterior portion of the inferior turbinate (IT) where the end effector 114 is deployed at a treatment site. The treatment site can be located proximate to the access point or points of postganglionic parasympathetic nerves (e.g., branches of the posterior nasal nerve and/or other parasympathetic neural fibers that innervate the nasal mucosa) into the nasal cavity. In other embodiments, the target site can be elsewhere within the nasal cavity depending on the location of the target nerves.

In various embodiments, the distal portion of the shaft 116 may be guided into position at the target site via a guidewire (not shown) using an over-the-wire (OTW) or a rapid exchange (RX) technique. For example, the end effector 114 can include a channel for engaging the guidewire. Intraluminal delivery of the end effector 114 can include inserting the guide wire into an orifice in communication with the nasal cavity (e.g., the nasal passage or mouth), and moving the shaft 116 and/or the end effector 114 along the guide wire until the end effector 114 reaches a target site (e.g., inferior to the SPF).

Yet still, in further embodiments, the neuromodulation device 102 can be configured for delivery via a guide catheter or introducer sheath (not shown) with or without using a guide wire. The introducer sheath can first be inserted intraluminally to the target site in the nasal region, and the distal portion of the shaft 116 can then be inserted through the introducer sheath. At the target site, the end effector 114 can be deployed through a distal end opening of the introducer sheath or a side port of the introducer sheath. In certain embodiments, the introducer sheath can

include a straight portion and a pre-shaped portion with a fixed curve (e.g., a 5 mm curve, a 4 mm curve, a 3 mm curve, etc.) that can be deployed intraluminally to access the target site. In this embodiment, the introducer sheath may have a side port proximal to or along the pre-shaped curved portion through which the end effector 114 can be deployed. In other embodiments, the introducer sheath may be made from a rigid material, such as a metal material coated with an insulative or dielectric material. In this embodiment, the introducer sheath may be substantially straight and used to deliver the end effector 114 to the target site via a substantially straight pathway, such as through the middle meatus (MM) (FIG. 3A).

Image guidance may be used to aid the surgeon's positioning and manipulation of the distal portion of the shaft 116, as well as the deployment and manipulation of the end effector 114, specifically the first and second segments 122 thereof. For example, an endoscope 100 and/or other visualization device can be positioned to visualize the target site, the positioning of the end effector 114 at the target site, and/or the end effector 114 during therapeutic neuromodulation. The endoscope 100 may be delivered proximate to the target site by extending through the nasal passage NP and through the middle meatus MM between the inferior and middle turbinates IT and MT. From the visualization location within the middle meatus MM, the endoscope 100 can be used to visualize the treatment site, surrounding regions of the nasal anatomy, and the end effector 114.

In some embodiments, the distal portion of the shaft 116 may be delivered via a working channel extending through an endoscope, and therefore the endoscope can provide direct in-line visualization of the target site and the end effector 114. In other embodiments, an endoscope is incorporated with the end effector 114 and/or the distal portion of the shaft 116 to provide in-line visualization of the end effector 114 and/or the surrounding nasal anatomy. In other embodiments, image guidance can be provided with various other guidance modalities, such as image filtering in the infrared (IR) spectrum to visualize the vasculature and/or other anatomical structures, computed tomography (CT), fluoroscopy, ultrasound, optical coherence tomography (OCT), and/or combinations thereof. Yet still, in some embodiments, image guidance components may be integrated with the neuromodulation device 102 to provide image guidance during positioning of the end effector 114.

Once positioned at the target site, the therapeutic modulation may be applied via the one or more electrodes 136 and/or other features of the end effector 114 to precise, localized regions

of tissue to induce one or more desired therapeutic neuromodulating effects to disrupt parasympathetic motor sensory function. The end effector 114 can selectively target postganglionic parasympathetic fibers that innervate the nasal mucosa at a target or treatment site proximate to or at their entrance into the nasal region. For example, the end effector 114 can be positioned to apply therapeutic neuromodulation at least proximate to the SPF (FIG. 3A) to therapeutically modulate nerves entering the nasal region via the SPF. The end effector 114 can also be positioned to inferior to the SPF to apply therapeutic neuromodulation energy across accessory foramen and microforamina (e.g., in the palatine bone) through which smaller medial and lateral branches of the posterior superior lateral nasal nerve enter the nasal region. The purposeful application of the energy at the target site may achieve therapeutic neuromodulation along all or at least a portion of posterior nasal neural fibers entering the nasal region. The therapeutic neuromodulating effects are generally a function of, at least in part, power, time, and contact between the energy delivery elements and the adjacent tissue. For example, in certain embodiments therapeutic neuromodulation of autonomic neural fibers are produced by applying RF energy at a power of about 2-20 W (e.g., 5 W, 7 W, 10 W, etc.) for a time period of about 1-20 sections (e.g., 5-10 seconds, 8-10 seconds, 10-12 seconds, etc.).

The therapeutic neuromodulating effects may include partial or complete denervation via thermal ablation and/or non-ablative thermal alteration or damage (e.g., via sustained heating and/or resistive heating). Desired thermal heating effects may include raising the temperature of target neural fibers above a desired threshold to achieve non-ablative thermal alteration, or above a higher temperature to achieve ablative thermal alteration. For example, the target temperature may be above body temperature (e.g., approximately 37° C.) but less than about 90° C. (e.g., 70-75° C.) for non-ablative thermal alteration, or the target temperature may be about 100° C. or higher (e.g., 110° C., 120° C., etc.) for the ablative thermal alteration. Desired non-thermal neuromodulation effects may include altering the electrical signals transmitted in a nerve.

Sufficiently modulating at least a portion of the parasympathetic nerves is expected to slow or potentially block conduction of autonomic neural signals to the nasal mucosa to produce a prolonged or permanent reduction in nasal parasympathetic activity. This is expected to reduce or eliminate activation or hyperactivation of the submucosal glands and venous engorgement and, thereby, reduce or eliminate the symptoms of rhinosinusitis. Further, because the device 102 applies therapeutic neuromodulation to the multitude of branches of the posterior nasal

nerves rather than a single large branch of the posterior nasal nerve branch entering the nasal cavity at the SPF, the device 102 provides a more complete disruption of the parasympathetic neural pathway that affects the nasal mucosa and results in rhinosinusitis. Accordingly, the device 102 is expected to have enhanced therapeutic effects for the treatment of rhinosinusitis and reduced re-innervation of the treated mucosa.

In other embodiments, the device 102 can be configured to therapeutically modulate nerves and/or other structures to treat different indications. For example, the device 102 can be used to therapeutically modulate nerves that innervate the para-nasal sinuses to treat chronic sinusitis. In further embodiments, the system 100 and the device 102 disclosed herein can be configured therapeutically modulate the vasculature within the nasal anatomy to treat other indications, such as epistaxis (i.e., excessive bleeding from the nose). For example, the system 100 and the device 102 devices described herein can be used to apply therapeutically effective energy to arteries (e.g., the sphenopalatine artery and its branches) as they enter the nasal cavity (e.g., via the SPF, accessory foramen, etc.) to partially or completely coagulate or ligate the arteries. In other embodiments, the system 100 and the device 102 can be configured to partially or completely coagulate or ligate veins and/or other vessels. For such embodiments in which the end effector 114 ligates or coagulates the vasculature, the system 100 and device 102 would be modified to deliver energy at significantly higher power (e.g., about 100 W) and/or longer times (e.g., 1 minute or longer) than would be required for therapeutic neuromodulation.

As further illustrated in FIG. 12, the shaft 116 may reside with a portion of the nasal cavity proximate to the IT upon advancing and deploying the multi-segment end effector 114 in the desired location (i.e., a target site associated with a sphenopalatine foramen within the nasal cavity of the patient). Accordingly, in addition to delivering energy from the electrodes 136 of the multi-segment end effector 114, the surgeon may also activate and deliver energy from electrodes 137 associated with the shaft 116 ((i.e., outer sheath 138, hypotube 140, or assembly of support elements 129) to tissue associated with the IT. Such energy may be delivered at a level sufficient to reduce engorgement of tissue associated with the IT to thereby increase volumetric flow through a nasal passage of the patient and improve a patient's ability to breathe.

FIG. 13 is a flow diagram illustrating one embodiment of a method 400 for treating a condition within a nasal cavity of a patient. The method 400 includes advancing a multi-segment end effector within the nasal cavity of the patient (operation 410) wherein the multi-segment end

effector includes a first segment spaced apart from a second segment. The multi-segment end effector is retractable and expandable such that, once delivered to the one more target sites within the nasal cavity, the first and second segments can expand to a specific shape and/or size corresponding to anatomical structures within the nasal cavity and associated with the target sites. The method 400 further includes deploying the first and second segments at respective first and second locations within the nasal cavity (operation 420). In particular, each of the first and second flexible segments includes a specific geometry when in a deployed configuration to complement anatomy of respective locations within the nasal cavity. Accordingly, once deployed, the first and second segments contact and conform to a shape of the respective locations, including conforming to and complementing shapes of one or more anatomical structures at the respective locations. The method 400 further includes delivering energy, via the first and second segments, to tissue at one or more target sites with respect to the first and second locations (operation 430). In particular, the first and second segments become accurately positioned within the nasal cavity to subsequently deliver, via one or more electrodes, precise and focused application of RF thermal energy to the one or more target sites to thereby therapeutically modulate associated neural structures. The first and second segments have shapes and sizes when in the expanded configuration that are specifically designed to place portions of the first and second segments, and thus one or more electrodes associated therewith, into contact with target sites within nasal cavity associated with postganglionic parasympathetic fibers that innervate the nasal mucosa.

FIG. 14 is a flow diagram illustrating another embodiment of a method 500 for treating a condition within a nasal cavity of a patient. The method 500 includes providing a treatment device comprising an end effector transformable between a retracted configuration and an expanded deployed configuration, a shaft operably associated with the end effector, and a handle operably associated with the shaft (operation 510). The method 500 further includes advancing the end effector to one or more target sites within the nasal cavity of the patient (operation 520). The shaft may include a pre-defined shape (i.e., bent or angled at a specific orientation) so as to assist the operation for placement of the end effector at the target sites. The handle includes an ergonomically-designed grip portion which provides ambidextrous use for both left and right handed use and conforms to hand anthropometrics to allow for at least one of an overhand grip style and an underhand grip style during use in a procedure.

The handle and/or the shaft may include markings (e.g., text, symbols, color-coding insignia, etc.) that provide a surgeon with a spatial orientation of the end effector while the end effector is in a nasal cavity. In particular, multiple markings may be provided on the handle and/or shaft and provide a visual indication of the spatial orientation of one or more portions of the first segment and second segment of the end effector when in the deployed configurations. Thus, during initial placement of the end effector, when in a retracted configuration and enclosed within the shaft, a surgeon can rely on the markings on the handle and/or shaft as a visual indication of the spatial orientation of the end effector (e.g., linear, axial, and/or depth position) prior to deployment to thereby ensure that, once deployed, the end effector, including both the first and second segments, are positioned in the intended locations within the nasal cavity.

The method 500 further includes deploying the end effector at the one or more target sites (operation 530) and delivering energy from the end effector to tissue at the one or more target sites (operation 540). The handle includes multiple user-operated mechanisms, including at least a first mechanism for deployment of the end effector from the retracted configuration to the expanded deployed configuration and a second mechanism for controlling of energy output by the end effector. The user inputs for the first and second mechanisms are positioned a sufficient distance to one another to allow for simultaneous one-handed operation of both user inputs during a procedure. Accordingly, the handle accommodates various styles of grip and provides a degree of comfort for the surgeon, thereby further improving execution of the procedure and overall outcome.

FIG. 15 is a flow diagram illustrating another embodiment of a method 600 for treating a condition within a nasal cavity of a patient. The method 600 includes providing a treatment device comprising a multi-segment end effector, including a proximal segment that is spaced apart from a distal segment, and a visual marker (operation 610). As previously described herein, the visual marker may be provided by a shaft, for example, operably associated with the multi-segment end effector. The visual marker may be in the form of text, symbols, color-coding insignia, or the like, that generally provides a user (i.e., a surgeon or other medical professional) with a visual indication of a spatial orientation of one or more portions of the proximal segment while the multi-segment end effector is in a nasal cavity.

The method 600 further includes advancing, under image guidance, the proximal segment and the distal segment through a nasal cavity of a patient and past a middle turbinate (operation

620) and deploying the distal segment from a retracted configuration to an expanded configuration (operation 630). The image guidance may be in the form of an endoscope and/or other visualization device that can be positioned to so as to provide visualization to the user of one or more locations within the nasal cavity and to further provide visualization of the multi-segment end effector and other portions of the treatment device (i.e., at least a distal portion of the shaft with a visual marker) during advancement into the nasal cavity to assist the user in placement of the multi-segment end effector.

Upon deploying the distal segment to an expanded configuration, the method 600 further includes aligning, under the image guidance and with reference to the visual marker, the proximal segment with respect to the middle turbinate (operation 640). The visual marker may be provided on the shaft, for example, and provide a visual indication of the spatial orientation of one or more portions of the proximal segment when in the deployed configuration. For example, the deployed proximal segment may include a geometry to complement a shape of the middle turbinate. More specifically, the proximal segment may include a set of flexible support elements that conform to and complement a shape of the middle turbinate when the proximal segment is in the deployed expanded configuration. The visual marker, provided by the shaft, provides a visual indication of the spatial orientation of one or more portions of the proximal segment, including, for example, a spatial orientation of the set of flexible support elements when in a deployed expanded configuration. Accordingly, aligning the proximal segment with respect to the middle turbinate includes the user positioning, under the image guidance, the shaft and associated visual marker relative to the middle turbinate.

Thus, during initial placement of at least the proximal segment when it is in a retracted configuration, a surgeon can rely on the markings on the shaft as a visual indication of the spatial orientation (e.g., linear, axial, and/or depth position) of one or more portions of the proximal segment prior to its deployment, thereby ensuring that, once deployed, the proximal segment is positioned in the intended location within the nasal cavity.

The method 600 further includes deploying the proximal segment around the middle turbinate and advancing the deployed proximal segment toward the middle turbinate to establish contact and secure the proximal segment to the middle turbinate (operation 650). Again, the set of flexible support elements of the proximal segment are able to conform to and complement a shape of the middle turbinate when the proximal segment is in the deployed expanded

configuration, thereby ensuring that the deployed proximal segment is secured to the middle turbinate.

It should be noted that the treatment device further includes a handle operably associated with the multi-segment end effector and the shaft. The handle generally includes a controller mechanism for providing independent, controlled deployment of each of the proximal and distal segments from a retracted configuration to an expanded configuration within the nasal cavity. In particular, in some embodiments, the controller mechanism includes a rack and pinion assembly providing movement of the at least one of the proximal and distal segments between the retracted configuration and expanded configuration in response to user input from an associated user-operated controller. The rack and pinion assembly may include, for example, a set of gears for receiving user input from the user-operated controller and converting the user input to linear motion of a rack member operably associated with the multi-segment end effector.

The controller mechanism may further include a detent feature positioned relative to the proximal and distal segments and configured to provide active feedback to a user indicative of deployment of at least one of the proximal and distal segments. The active feedback may be in the form haptic feedback provided by the controller mechanism. For example, the haptic feedback may include an increase or decrease in resistance associated with user input with the controller mechanism for corresponding movement of the at least one of the proximal and distal segments between retracted and expanded configurations, and/or configurations therebetween (i.e., a plurality of configurations between a fully retracted configuration and a fully expanded configuration). For example, upon deploying the distal segment, the controller mechanism, as a result of interaction with the detent, may provide haptic feedback, in the form of a vibration or other motion (e.g., click(s) or change in resistance), to the user via the user-operated controller. The haptic feedback may indicate to the user that the distal segment is fully deployed and any further input with the user-operated controller will result in deployment of the proximal segment. The controller mechanism may further provide specific haptic feedback during deployment of a given segment, such as deployment of the proximal segment. For example, the haptic feedback may be in the form of an increase or decrease in resistance upon the user-operated controller, for example, which corresponds to the degree to which the proximal segment is deployed.

In some embodiments, the controller mechanism may further include a friction-based feature configured to provide stable movement of at least one of the proximal and distal

segments between the retracted and expanded configurations and further provide active feedback to a user indicative of deployment of at least one of the proximal and distal segments. The friction-based feature may include, for example, a lock mechanism configured to provide constant friction between one or more portions of the rack and pinion assembly sufficient to maintain a position of at least one of the proximal and distal segments during deployment thereof.

For example, the constant friction may be sufficient to hold either of the proximal or distal segments in a certain position as the segment transitions between retracted and expanded configurations regardless of whether the user maintains contact with the user-operated controller. In other words, a user does not need to maintain contact with the user-operated controller in order to ensure that the proximal or distal segment holds a certain position during deployment thereof. Rather, a user can simply interact with the user-operated controller to transition one of the proximal and distal segments to a desired configuration and the constant friction provided by the locking mechanism is sufficient to maintain the configuration of proximal or distal segment in the event that the user goes hands free (i.e., removes any contact with the user-operated controller). The constant friction is of a level sufficient to prevent undesired movement of the proximal or distal segments (i.e., unintended collapsing or expanding), while still allowing for a user to overcome such friction to move the proximal or distal segment to a desired configuration upon user input with the user-operated controller.

In some embodiments, the user-operated controller includes a slider mechanism operably associated with the rack and pinion rail assembly, wherein movement of the slider mechanism in a first direction results in transitioning of at least one of the proximal and distal segments to an expanded configuration and movement of the slider mechanism in a second opposite direction results in transitioning of at least one of the proximal and distal segments to the retracted configuration. In other embodiments, the user-operated controller includes a scroll wheel mechanism operably associated with the rack and pinion rail assembly, wherein rotation of the wheel in a first direction results in transitioning of at least one of the proximal and distal segments to an expanded configuration and rotation of the wheel in a second opposite direction results in transitioning of at least one of the proximal and distal segments to the retracted configuration. As such, during deployment of the proximal segment, the slider mechanism or

scroll wheel may provide increased resistance to a user as the user transitions the proximal segment from a fully retracted configuration to a fully deployed configuration.

Accordingly, during deployment of either of the distal and proximal segments, the controller mechanism provides active feedback to the user, wherein such active feedback can be indicative of which segment is being actively controlled and/or the extent of deployment of either of the distal or proximal segments, thereby improving user control over the deployment of either of the distal and proximal segments.

Upon securing the proximal segment to the middle turbinate, the method 600 further includes delivering energy, via the proximal segment, to the middle turbinate to treat a condition (operation 660). The condition may include, but is not limited to, allergic rhinitis, non-allergic rhinitis, chronic rhinitis, acute rhinitis, chronic sinusitis, acute sinusitis, chronic rhinosinusitis, acute rhinosinusitis, and medical resistant rhinitis, and a combination thereof. In some embodiments, delivering energy from the proximal segment includes delivering radiofrequency (RF) energy, via one or more electrodes provided by the proximal segment, to tissue of the middle turbinate at one or more target sites, wherein the one or more target sites are associated with parasympathetic nerve supply. In some embodiments, RF energy is delivered, via the one or more electrodes provided by the proximal segment, at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at an innervation pathway within the nasal cavity of the patient.

FIG. 16 is a flow diagram illustrating another embodiment of a method 700 for treating a condition within a nasal cavity of a patient. The method 700 includes providing a treatment device comprising an elongate body including one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and including one or more of a second set of electrodes provided thereon (operation 710).

The method 700 further includes advancing the shaft and end effector through a nasal passage and into a nasal cavity of a patient (operation 720) at which point a length of the elongate body is positioned at a first target site and the end effector is positioned at a second target site separate from the first target site (operation 730). For example, in some embodiments, the procedure may involve extending the elongate body into the nasal passage (NP), through the inferior meatus (IM) between the inferior turbinate (IT) and the nasal sill (NS). In other

embodiments, the procedure may involve extending the elongate body into the nasal passage (NP), through the middle meatus (MM) between the inferior turbinate (IT) and the middle turbinate (MT). In each instance, a proximal segment (of the end effector) is arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate and a separate distal segment (of the end effector) is configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate. Additionally, the elongate body resides in a location adjacent to the inferior turbinate (IT).

The method 700 further includes delivering energy from the first and second sets of electrodes (associated with elongate body and end effector, respectively) to tissue at the first and second target sites, respectively (operation 740). In particular, a given procedure, the surgeon may utilize the multi-segment end effector to deliver energy (via electrodes) at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the patient and further utilize the elongate body to deliver energy (via electrodes) at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through the nasal passage of the patient. Such a combination of energy delivery to two specific targeted sites improves the manner in which at least one of rhinitis, congestion, and rhinorrhea are treated, thereby increasing the potential for reducing or completely eliminating symptoms associated therewith, including, but not limited to, coughing, sneezing, nasal or throat irritation and itching, and difficulty sleeping.

Accordingly, the treatment device of the present invention recognizes the desire or need to treat larger areas within the nasal cavity or passage that are located outside of a treatment zone associated with the end effector. For example, when performing surgical procedures using current rhinitis treatment devices, the surgeon must reposition an end effector when attempting to treat multiple areas within the nasal cavity, particularly those areas that are located outside of any given treatment zone. The need to reposition the end effector multiple times during a given procedure can lead to inaccuracy when delivering energy, resulting in unintended collateral damage, and further increases the time in which it takes to complete a given procedure. The treatment device of the present invention recognizes and addresses this problem by providing an elongate body including one or more electrodes thereon, in addition to a multi-segment end

effector operably associated with the elongate body and including separate electrodes thereon. Accordingly, the elongate body serves to not only aid in positioning and delivering the end effector to a desired target site (to which the end effector may deliver energy), but the elongate body can also deliver energy to a target site that is separate and remote from the end effector. Such a design improves the efficiency with which a given procedure can be accomplished, particularly those procedures requiring treatment to multiple, separate areas within the nasal cavity or passage.

Neuromodulation Monitoring, Feedback, and Mapping Capabilities

As previously described, the system 100 includes a console 104 to which the device 102 is to be connected. The console 104 is configured to provide various functions for the neuromodulation device 102, which may include, but is not limited to, controlling, monitoring, supplying, and/or otherwise supporting operation of the neuromodulation device 102. The console 104 can further be configured to generate a selected form and/or magnitude of energy for delivery to tissue or nerves at the target site via the end effector 114, and therefore the console 104 may have different configurations depending on the treatment modality of the device 102. For example, when device 102 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 104 includes an energy generator 106 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally-delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy. When the device 102 is configured for cryotherapeutic treatment, the console 104 can include a refrigerant reservoir (not shown), and can be configured to supply the device 102 with refrigerant. Similarly, when the device 102 is configured for chemical-based treatment (e.g., drug infusion), the console 104 can include a chemical reservoir (not shown) and can be configured to supply the device 102 with one or more chemicals.

In some embodiments, the console 104 may include a controller 107 communicatively coupled to the neuromodulation device 102. However, in the embodiments described herein, the controller 107 may generally be carried by and provided within the handle 118 of the

neuromodulation device 102. The controller 107 is configured to initiate, terminate, and/or adjust operation of one or more electrodes provided by the end effector 114 directly and/or via the console 104. For example, the controller 107 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., surgeon or other medical professional or clinician). For example, the controller 107 and/or other components of the console 104 (e.g., processors, memory, etc.) can include a computer-readable medium carrying instructions, which when executed by the controller 107, causes the device 102 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, perform nerve mapping, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

The console 104 may further be configured to provide feedback to an operator before, during, and/or after a treatment procedure via mapping/evaluation/feedback algorithms 110. For example, the mapping/evaluation/feedback algorithms 110 can be configured to provide information associated with the location of nerves at the treatment site, the location of other anatomical structures (e.g., vessels) at the treatment site, the temperature at the treatment site during monitoring and modulation, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the mapping/evaluation/feedback algorithm 110 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 100. For example, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107 and the end effector 114, can be configured to monitor neural activity and/or temperature at the treatment site during therapy and automatically shut off the energy delivery when the neural activity and/or temperature reaches a predetermined threshold (e.g., a threshold reduction in neural activity, a threshold maximum temperature when applying RF energy, or a threshold minimum temperature when applying cryotherapy). In other embodiments, the mapping/evaluation/feedback algorithm 110, in conjunction with the controller 107, can be configured to automatically terminate treatment after a predetermined maximum

time, a predetermined maximum impedance or resistance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 100 can be communicated to the operator via a display 112 (e.g., a monitor, touchscreen, user interface, etc.) on the console 104 and/or a separate display (not shown) communicatively coupled to the console 104.

In various embodiments, the end effector 114 and/or other portions of the system 100 can be configured to detect various bioelectric-parameters of the tissue at the target site, and this information can be used by the mapping/evaluation/feedback algorithms 110 to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate neural structures, differentiate between different types of neural structures, map the anatomical and/or neural structure at the target site, and/or identify neuromodulation patterns of the end effector 114 with respect to the patient's anatomy. For example, the end effector 114 can be used to detect resistance, complex electrical impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers and/or other anatomical structures in the target region. In certain embodiments, the end effector 114, together with the mapping/evaluation/feedback algorithms 110, can be used to determine resistance (rather than impedance) of the tissue (i.e., the load) to more accurately identify the characteristics of the tissue. The mapping/evaluation/feedback algorithms 110 can determine resistance of the tissue by detecting the actual power and current of the load (e.g., via the electrodes 136).

In some embodiments, the system 100 provides resistance measurements with a high degree of accuracy and a very high degree of precision, such as precision measurements to the hundredths of an Ohm (e.g., 0.01Ω) for the range of 1-50Ω. The high degree of resistance detection accuracy provided by the system 100 allows for the detection sub-microscale structures, including the firing of neural structures, differences between neural structures and other anatomical structures (e.g., blood vessels), and event different types of neural structures. This information can be analyzed by the mapping/evaluation/feedback algorithms and/or the controller 107 and communicated to the operator via a high resolution spatial grid (e.g., on the display 112) and/or other type of display to identify neural structures and other anatomy at the

treatment site and/or indicate predicted neuromodulation regions based on the ablation pattern with respect to the mapped anatomy.

As previously described, in certain embodiments, each electrode 136 can be operated independently of the other electrodes 136. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm executed by the controller 107. The selective independent control of the electrodes 136 allows the end effector 114 to detect information and deliver RF energy to highly customized regions. For example, a select portion of the electrodes 136 can be activated to target specific neural fibers in a specific region while the other electrodes 136 remain inactive. In certain embodiments, for example, electrodes 136 may be activated across the portion of the second segment 124 that is adjacent to tissue at the target site, and the electrodes 136 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. In addition, the electrodes 136 can be individually activated to stimulate or therapeutically modulate certain regions in a specific pattern at different times (e.g., via multiplexing), which facilitates detection of anatomical parameters across a zone of interest and/or regulated therapeutic neuromodulation.

The electrodes 136 can be electrically coupled to the energy generator 106 via wires (not shown) that extend from the electrodes 136, through the shaft 116, and to the energy generator 106. When each of the electrodes 136 is independently controlled, each electrode 136 couples to a corresponding wire that extends through the shaft 116. This allows each electrode 136 to be independently activated for stimulation or neuromodulation to provide precise ablation patterns and/or individually detected via the console 104 to provide information specific to each electrode 136 for neural or anatomical detection and mapping. In other embodiments, multiple electrodes 136 can be controlled together and, therefore, multiple electrodes 136 can be electrically coupled to the same wire extending through the shaft 116. The energy generator 16 and/or components (e.g., a control module) operably coupled thereto can include custom algorithms to control the activation of the electrodes 136. For example, the RF generator can deliver RF power at about 200-100 W to the electrodes 136, and do so while activating the electrodes 136 in a predetermined pattern selected based on the position of the end effector 114 relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the energy generator 106 delivers power at lower levels (e.g., less than 1 W, 1-5 W, 5-15 W, 15-50

W, 50-150 W, etc.) for stimulation and/or higher power levels. For example, the energy generator 106 can be configured to delivery stimulating energy pulses of 1-3 W via the electrodes 136 to stimulate specific targets in the tissue.

As previously described, the end effector 114 can further include one or more temperature sensors disposed on the flexible first and second segments 122, 124 and/or other portions of the end effector 114 and electrically coupled to the console 104 via wires (not shown) that extend through the shaft 116. In various embodiments, the temperature sensors can be positioned proximate to the electrodes 136 to detect the temperature at the interface between tissue at the target site and the electrodes 136. In other embodiments, the temperature sensors can penetrate the tissue at the target site (e.g., a penetrating thermocouple) to detect the temperature at a depth within the tissue. The temperature measurements can provide the operator or the system with feedback regarding the effect of the therapeutic neuromodulation on the tissue. For example, in certain embodiments the operator may wish to prevent or reduce damage to the tissue at the treatment site (e.g., the nasal mucosa), and therefore the temperature sensors can be used to determine if the tissue temperature reaches a predetermined threshold for irreversible tissue damage. Once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact and avoid significant tissue sloughing during wound healing. In certain embodiments, the energy delivery can automatically terminate based on the mapping/evaluation/feedback algorithm 110 stored on the console 104 operably coupled to the temperature sensors.

In certain embodiments, the system 100 can determine the locations and/or morphology of neural structures and/or other anatomical structures before therapy such that the therapeutic neuromodulation can be applied to precise regions including target neural structures, while avoiding negative effects on non-target structures, such as blood vessels. As described in further detail below, the system 100 can detect various bioelectrical parameters in an interest zone (e.g., within in the nasal cavity) to determine the location and morphology of various neural structures (e.g., different types of neural structures, neuronal directionality, etc.) and/or other tissue (e.g., glandular structures, vessels, bony regions, etc.). In some embodiments, the system 100 is configured to measure bioelectric potential. To do so, one or more of the electrodes 136 is placed in contact with an epithelial surface at a region of interest (e.g., a treatment site). Electrical stimuli (e.g., constant or pulsed currents at one or more frequencies) are applied to the

tissue by one or more electrodes 136 at or near the treatment site, and the voltage and/or current differences at various different frequencies between various pairs of electrodes 136 of the end effector 114 may be measured to produce a spectral profile or map of the detected bioelectric potential, which can be used to identify different types of tissues (e.g., vessels, neural structures, and/or other types of tissue) in the region of interest. For example, current (i.e., direct or alternating current) can be applied to a pair of electrodes 136 adjacent to each other and the resultant voltages and/or currents between other pairs of adjacent electrodes 136 are measured. It will be appreciated that the current injection electrodes 136 and measurement electrodes 136 need not be adjacent, and that modifying the spacing between the two current injection electrodes 136 can affect the depth of the recorded signals. For example, closely-spaced current injection electrodes 136 provided recorded signals associated with tissue deeper from the surface of the tissue than further spaced apart current injection electrodes 136 that provide recorded signals associated with tissue at shallower depths. Recordings from electrode pairs with different spacings may be merged to provide additional information on depth and localization of anatomical structures.

Further, complex impedance and/or resistance measurements of the tissue at the region of interest can be detected directly from current-voltage data provided by the bioelectric potential measurements while differing levels of frequency currents are applied to the tissue (e.g., via the end effector 114), and this information can be used to map the neural and anatomical structures by the use of frequency differentiation reconstruction. Applying the stimuli at different frequencies will target different stratified layers or cellular bodies or clusters. At high signal frequencies (e.g., electrical injection or stimulation), for example, cell membranes of the neural structures do not impede current flow, and the current passes directly through the cell membranes. In this case, the resultant measurement (e.g., impedance, resistance, capacitance, and/or induction) is a function of the intracellular and extracellular tissue and liquids. At low signal frequencies, the membranes impede current flow to provide different defining characteristics of the tissues, such as the shapes of the cells or cell spacing. The stimulation frequencies can be in the megahertz range, in the kilohertz range (e.g., 400-500 kHz, 450-480 kHz, etc.), and/or other frequencies attuned to the tissue being stimulated and the characteristics of the device being used. The detected complex impedance or resistances levels from the zone

of interest can be displayed to the user (e.g., via the display 112) to visualize certain structures based on the stimulus frequency.

Further, the inherent morphology and composition of the anatomical structures in the nasal region react differently to different frequencies and, therefore, specific frequencies can be selected to identify very specific structures. For example, the morphology or composition of targeted structures for anatomical mapping may depend on whether the cells of tissue or other structure are membranonic, stratified, and/or annular. In various embodiments, the applied stimulation signals can have predetermined frequencies attuned to specific neural structures, such as the level of myelination and/or morphology of the myelination. For example, second axonal parasympathetic structures are poorly myelinated than sympathetic nerves or other structures and, therefore, will have a distinguishable response (e.g., complex impedance, resistance, etc.) with respect to a selected frequency than sympathetic nerves. Accordingly, applying signals with different frequencies to the target site can distinguish the targeted parasympathetic nerves from the non-targeted sensory nerves, and therefore provide highly specific target sites for neural mapping before or after therapy and/or neural evaluation post-therapy. In some embodiments, the neural and/or anatomical mapping includes measuring data at a region of interest with at least two different frequencies to identify certain anatomical structures such that the measurements are taken first based on a response to an injection signal having a first frequency and then again based on an injection signal having a second frequency different from the first. For example, there are two frequencies at which hypertrophied (i.e., disease-state characteristics) sub-mucosal targets have a different electrical conductivity or permittivity compared to "normal" (i.e., healthy) tissue. Complex conductivity may be determined based on one or more measured physiological parameters (e.g., complex impedance, resistance, dielectric measurements, dipole measurements, etc.) and/or observance of one or more confidently known attributes or signatures. Furthermore, the system 100 can also apply neuromodulation energy via the electrodes 136 at one or more predetermined frequencies attuned to a target neural structure to provide highly targeted ablation of the selected neural structure associated with the frequency(ies). This highly targeted neuromodulation also reduces the collateral effects of neuromodulation therapy to non-target sites/structures (e.g., blood vessels) because the targeted signal (having a frequency tuned to a target neural structure) will not have the same modulating effects on the non-target structures.

Accordingly, bioelectric properties, such as complex impedance and resistance, can be used by the system 100 before, during, and/or after neuromodulation therapy to guide one or more treatment parameters. For example, before, during, and/or after treatment, impedance or resistance measurements may be used to confirm and/or detect contact between one or more electrodes 136 and the adjacent tissue. The impedance or resistance measurements can also be used to detect whether the electrodes 136 are placed appropriately with respect to the targeted tissue type by determining whether the recorded spectra have a shape consistent with the expected tissue types and/or whether serially collected spectra were reproducible. In some embodiments, impedance or resistance measurements may be used to identify a boundary for the treatment zone (e.g., specific neural structures that are to be disrupted), anatomical landmarks, anatomical structures to avoid (e.g., vascular structures or neural structures that should not be disrupted), and other aspects of delivering energy to tissue.

The bioelectric information can be used to produce a spectral profile or map of the different anatomical features tissues at the target site, and the anatomical mapping can be visualized in a 3D or 2D image via the display 112 and/or other user interface to guide the selection of a suitable treatment site. This neural and anatomical mapping allows the system 100 to accurately detect and therapeutically modulate the postganglionic parasympathetic neural fibers that innervate the mucosa at the numerous neural entrance points into the nasal cavity. Further, because there are not any clear anatomical markers denoting the location of the SPF, accessory foramen, and microforamina, the neural mapping allows the operator to identify and therapeutically modulate nerves that would otherwise be unidentifiable without intricate dissection of the mucosa. In addition, anatomical mapping also allows the clinician to identify certain structures that the clinician may wish to avoid during therapeutic neural modulation (e.g., certain arteries). The neural and anatomical bioelectric properties detected by the system 100 can also be used during and after treatment to determine the real-time effect of the therapeutic neuromodulation on the treatment site. For example, the mapping/evaluation/feedback algorithms 110 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to assess whether the application of therapeutic neuromodulation was effective across the treatment site.

In various embodiments, the system 100 can also be configured to map the expected therapeutic modulation patterns of the electrodes 136 at specific temperatures and, in certain embodiments, take into account tissue properties based on the anatomical mapping of the target site. For example, the system 100 can be configured to map the ablation pattern of a specific electrode ablation pattern at the 45° C. isotherm, the 55° C. isotherm, the 65° C. isotherm, and/or other temperature/ranges (e.g., temperatures ranging from 45° C. to 70° C. or higher) depending on the target site and/or structure.

The system 100 may provide, via the display 112, three-dimensional views of such projected ablation patterns of the electrodes 136 of the end effector 114. The ablation pattern mapping may define a region of influence that each electrode 136 has on the surrounding tissue. The region of influence may correspond to the region of tissue that would be exposed to therapeutically modulating energy based on a defined electrode activation pattern (i.e., one, two, three, four, or more electrodes on any given strut of the first and second segments 122, 124). In other words, the ablation pattern mapping can be used to illustrate the ablation pattern of any number of electrodes 136, any geometry of the electrode layout, and/or any ablation activation protocol (e.g., pulsed activation, multi-polar/sequential activation, etc.).

In some embodiments, the ablation pattern may be configured such that each electrode 136 has a region of influence surrounding only the individual electrode 136 (i.e., a "dot" pattern). In other embodiments, the ablation pattern may be such that two or more electrodes 136 may link together to form a sub-grouped regions of influence that define peanut-like or linear shapes between two or more electrodes 136. In further embodiments, the ablation pattern can result in a more expansive or contiguous pattern in which the region of influence extends along multiple electrodes 136 (e.g., along each strut). In still further embodiments, the ablation pattern may result in different regions of influence depending upon the electrode activation pattern, phase angle, target temperature, pulse duration, device structure, and/or other treatment parameters. The three-dimensional views of the ablation patterns can be output to the display 112 and/or other user interfaces to allow the clinician to visualize the changing regions of influence based on different durations of energy application, different electrode activation sequences (e.g., multiplexing), different pulse sequences, different temperature isotherms, and/or other treatment parameters. This information can be used to determine the appropriate ablation algorithm for a patient's specific anatomy. In other embodiments, the three-dimensional visualization of the

regions of influence can be used to illustrate the regions from which the electrodes 136 detect data when measuring bioelectrical properties for anatomical mapping. In this embodiment, the three dimensional visualization can be used to determine which electrode activation pattern should be used to determine the desired properties (e.g., impedance, resistance, etc.) in the desired area. In certain embodiments, it may be better to use dot assessments, whereas in other embodiments it may be more appropriate to detect information from linear or larger contiguous regions.

In some embodiments, the mapped ablation pattern is superimposed on the anatomical mapping to identify what structures (e.g., neural structures, vessels, etc.) will be therapeutically modulated or otherwise affected by the therapy. An image may be provided to the surgeon which includes a digital illustration of a predicted or planned neuromodulation zone in relation to previously identified anatomical structures in a zone of interest. For example, the illustration may show numerous neural structures and, based on the predicted neuromodulation zone, identifies which neural structures are expected to be therapeutically modulated. The expected therapeutically modulated neural structures may be shaded to differentiate them from the non-affected neural structures. In other embodiments, the expected therapeutically modulated neural structures can be differentiated from the non-affected neural structures using different colors and/or other indicators. In further embodiments, the predicted neuromodulation zone and surrounding anatomy (based on anatomical mapping) can be shown in a three dimensional view (and/or include different visualization features (e.g., color-coding to identify certain anatomical structures, bioelectric properties of the target tissue, etc.). The combined predicted ablation pattern and anatomical mapping can be output to the display 112 and/or other user interfaces to allow the clinician to select the appropriate ablation algorithm for a patient's specific anatomy.

The imaging provided by the system 100 allows the clinician to visualize the ablation pattern before therapy and adjust the ablation pattern to target specific anatomical structures while avoiding others to prevent collateral effects. For example, the clinician can select a treatment pattern to avoid blood vessels, thereby reducing exposure of the vessel to the therapeutic neuromodulation energy. This reduces the risk of damaging or rupturing vessels and, therefore, prevents immediate or latent bleeding. Further, the selective energy application provided by the neural mapping reduces collateral effects of the therapeutic neuromodulation,

such as tissue sloughing off during wound healing (e.g., 1-3 weeks post ablation), thereby reducing the aspiration risk associated with the neuromodulation procedure.

The system 100 can be further configured to apply neuromodulation energy (via the electrodes 136) at specific frequencies attuned to the target neural structure and, therefore, specifically target desired neural structures over non-target structures. For example, the specific neuromodulation frequencies can correspond to the frequencies identified as corresponding to the target structure during neural mapping. As described above, the inherent morphology and composition of the anatomical structures react differently to different frequencies. Thus, frequency-tuned neuromodulation energy tailored to a target structure does not have the same modulating effects on non-target structures. More specifically, applying the neuromodulation energy at the target-specific frequency causes ionic agitation in the target neural structure, leading to differentials in osmotic potentials of the targeted neural structures and dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure). This causes degeneration, possibly resulting in vacuolar degeneration and, eventually, necrosis at the target neural structure, but is not expected to functionally affect at least some non-target structures (e.g., blood vessels). Accordingly, the system 100 can use the neural-structure specific frequencies to both (1) identify the locations of target neural structures to plan electrode ablation configurations (e.g., electrode geometry and/or activation pattern) that specifically focus the neuromodulation on the target neural structure; and (2) apply the neuromodulation energy at the characteristic neural frequencies to selectively ablate the neural structures responsive to the characteristic neural frequencies. For example, the end effector 114 of the system 100 may selectively stimulate and/or modulate parasympathetic fibers, sympathetic fibers, sensory fibers, alpha/beta/delta fibers, C-fibers, anoxic terminals of one or more of the foregoing, insulated over non-insulated fibers (regions with fibers), and/or other neural structures. In some embodiments, the system 100 may also selectively target specific cells or cellular regions during anatomical mapping and/or therapeutic modulation, such as smooth muscle cells, sub-mucosal glands, goblet cells, stratified cellular regions within the nasal mucosa. Therefore, the system 100 provides highly selective neuromodulation therapy specific to targeted neural structures, and reduces the collateral effects of neuromodulation therapy to non-target structures (e.g., blood vessels).

The present disclosure provides a method of anatomical mapping and therapeutic neuromodulation. The method includes expanding an end effector (i.e., end effector 114) at a zone of interest ("interest zone"), such as in a portion of the nasal cavity. For example, the end effector 114 can be expanded such that at least some of the electrodes 136 are placed in contact with mucosal tissue at the interest zone. The expanded device can then take bioelectric measurements via the electrodes 136 and/or other sensors to ensure that the desired electrodes are in proper contact with the tissue at the interest zone. In some embodiments, for example, the system 100 detects the impedance and/or resistance across pairs of the electrodes 136 to confirm that the desired electrodes have appropriate surface contact with the tissue and that all of the electrodes are 136 functioning properly.

The method continues by optionally applying an electrical stimulus to the tissue, and detecting bioelectric properties of the tissue to establish baseline norms of the tissue. For example, the method can include measuring resistance, complex impedance, current, voltage, nerve firing rate, neuromagnetic field, muscular activation, and/or other parameters that are indicative of the location and/or function of neural structures and/or other anatomical structures (e.g., glandular structures, blood vessels, etc.). In some embodiments, the electrodes 136 send one or more stimulation signals (e.g., pulsed signals or constant signals) to the interest zone to stimulate neural activity and initiate action potentials. The stimulation signal can have a frequency attuned to a specific target structure (e.g., a specific neural structure, a glandular structure, a vessel) that allows for identification of the location of the specific target structure. The specific frequency of the stimulation signal is a function of the host permeability and, therefore, applying the unique frequency alters the tissue attenuation and the depth into the tissue the RF energy will penetrate. For example, lower frequencies typically penetrate deeper into the tissue than higher frequencies.

Pairs of the non-stimulating electrodes 136 of the end effector 114 can then detect one or more bioelectric properties of the tissue that occur in response to the stimulus, such as impedance or resistance. For example, an array of electrodes (e.g., the electrodes 136) can be selectively paired together in a desired pattern (e.g., multiplexing the electrodes 136) to detect the bioelectric properties at desired depths and/or across desired regions to provide a high level of spatial awareness at the interest zone. In certain embodiments, the electrodes 136 can be paired together in a time-sequenced manner according to an algorithm (e.g., provided by the

mapping/evaluation/feedback algorithms 110). In various embodiments, stimuli can be injected into the tissue at two or more different frequencies, and the resultant bioelectric responses (e.g., action potentials) in response to each of the injected frequencies can be detected via various pairs of the electrodes 136. For example, an anatomical or neural mapping algorithm can cause the end effector 114 to deliver pulsed RF energy at specific frequencies between different pairs of the electrodes 136 and the resultant bioelectric response can be recorded in a time sequenced rotation until the desired interest zone is adequately mapped (i.e., "multiplexing"). For example, the end effector 114 can deliver stimulation energy at a first frequency via adjacent pairs of the electrodes 136 for a predetermined time period (e.g., 1-50 milliseconds), and the resultant bioelectric activity (e.g., resistance) can be detected via one or more other pairs of electrodes 136 (e.g., spaced apart from each other to reach varying depths within the tissue). The end effector 114 can then apply stimulation energy at a second frequency different from the first frequency, and the resultant bioelectric activity can be detected via the other electrodes. This can continue when the interest zone has been adequately mapped at the desired frequencies. As described in further detail below, in some embodiments the baseline tissue bioelectric properties (e.g., nerve firing rate) are detected using static detection methods (without the injection of a stimulation signal).

After detecting the baseline bioelectric properties, the information can be used to map anatomical structures and/or functions at the interest zone. For example, the bioelectric properties detected by the electrodes 136 can be amazed via the mapping/evaluation/feedback algorithms 110, and an anatomical map can be output to a user via the display 112. In some embodiments, complex impedance, dielectric, or resistance measurements can be used to map parasympathetic nerves and, optionally, identify neural structures in a diseased state of hyperactivity. The bioelectric properties can also be used to map other non-target structures and the general anatomy, such as blood vessels, bone, and/or glandular structures. The anatomical locations can be provided to a user (e.g., on the display 112) as a two-dimensional map (e.g., illustrating relative intensities, illustrating specific sites of potential target structures) and/or as a three-dimensional image. This information can be used to differentiate structures on a submicron, cellular level and identify very specific target structures (e.g., hyperactive parasympathetic nerves). The method can also predict the ablation patterns of the end effector 114 based on different electrode neuromodulation protocol and, optionally, superimpose the

predicted neuromodulation patterns onto the mapped anatomy to indicate to the user which anatomical structures will be affected by a specific neuromodulation protocol. For example, when the predicted neuromodulation pattern is displayed in relation to the mapped anatomy, a clinician can determine whether target structures will be appropriately ablated and whether non-target structures (e.g., blood vessels) will be undesirably exposed to the therapeutic neuromodulation energy. Thus, the method can be used for planning neuromodulation therapy to locate very specific target structures, avoid non-target structures, and select electrode neuromodulation protocols.

Once the target structure is located and a desired electrode neuromodulation protocol has been selected, the method continues by applying therapeutic neuromodulation to the target structure. The neuromodulation energy can be applied to the tissue in a highly targeted manner that forms micro-lesions to selectively modulate the target structure, while avoiding non-targeted blood vessels and allowing the surrounding tissue structure to remain healthy for effective wound healing. In some embodiments, the neuromodulation energy can be applied in a pulsed manner, allowing the tissue to cool between modulation pulses to ensure appropriate modulation without undesirably affecting non-target tissue. In some embodiments, the neuromodulation algorithm can deliver pulsed RF energy between different pairs of the electrodes 136 in a time sequenced rotation until neuromodulation is predicted to be complete (i.e., "multiplexing"). For example, the end effector 114 can deliver neuromodulation energy (e.g., having a power of 5-10 W (e.g., 7 W, 8 W, 9 W) and a current of about 50-100 mA) via adjacent pairs of the electrodes 136 until at least one of the following conditions is met: (a) load resistance reaches a predefined maximum resistance (e.g., 350Ω); (b) a thermocouple temperature associated with the electrode pair reaches a predefined maximum temperature (e.g., 80° C.); or (c) a predetermined time period has elapsed (e.g., 10 seconds). After the predetermined conditions are met, the end effector 114 can move to the next pair of electrodes in the sequence, and the neuromodulation algorithm can terminate when all of the load resistances of the individual pairs of electrodes is at or above a predetermined threshold (e.g., 100Ω). In various embodiments, the RF energy can be applied at a predetermined frequency (e.g., 450-500 kHz) and is expected to initiate ionic agitation of the specific target structure, while avoiding functional disruption of non-target structures.

During and/or after neuromodulation therapy, the method continues by detecting and, optionally, mapping the post-therapy bioelectric properties of the target site. This can be performed in a similar manner as described above. The post-therapy evaluation can indicate if the target structures (e.g., hyperactive parasympathetic nerves) were adequately modulated or ablated. If the target structures are not adequately modulated (i.e., if neural activity is still detected in the target structure and/or the neural activity has not decreased), the method can continue by again applying therapeutic neuromodulation to the target. If the target structures were adequately ablated, the neuromodulation procedure can be completed.

Detection of Anatomical Structures and Function

Various embodiments of the present technology can include features that measure bio-electric, dielectric, and/or other properties of tissue at target sites to determine the presence, location, and/or activity of neural structures and other anatomical structures and, optionally, map the locations of the detected neural structures and/or other anatomical structures. For example, the present technology can be used to detect glandular structures and, optionally, their mucoserous functions and/or other functions. The present technology can also be configured to detect vascular structures (e.g., arteries) and, optionally, their arterial functions, volumetric pressures, and/or other functions. The mapping features discussed below can be incorporated into any the system 100 and/or any other devices disclosed herein to provide an accurate depiction of nerves at the target site.

Neural and/or anatomical detection can occur (a) before the application of a therapeutic neuromodulation energy to determine the presence or location of neural structures and other anatomical structures (e.g., blood vessels, glands, etc.) at the target site and/or record baseline levels of neural activity; (b) during therapeutic neuromodulation to determine the real-time effect of the energy application on the neural fibers at the treatment site; and/or (c) after therapeutic neuromodulation to confirm the efficacy of the treatment on the targeted structures (e.g., nerves glands, etc.). This allows for the identification of very specific anatomical structures (even to the micro-scale or cellular level) and, therefore, provides for highly targeted neuromodulation. This enhances the efficacy and efficiency of the neuromodulation therapy. In addition, the anatomical mapping reduces the collateral effects of neuromodulation therapy to non-target sites.

Accordingly, the targeted neuromodulation inhibits damage or rupture of blood vessels (i.e., inhibits undesired bleeding) and collateral damage to tissue that may be of concern during wound healing (e.g., when damage tissue sloughs off of the wall of the nasal wall).

In certain embodiments, the systems disclosed herein can use bioelectric measurements, such as impedance, resistance, voltage, current density, and/or other parameters (e.g., temperature) to determine the anatomy, in particular the neural, glandular, and vascular anatomy, at the target site. The bioelectric properties can be detected after the transmission of a stimulus (e.g., an electrical stimulus, such as RF energy delivered via the electrodes 136; i.e., "dynamic" detection) and/or without the transmission of a stimulus (i.e., "static" detection).

Dynamic measurements include various embodiments to excite and/or detect primary or secondary effects of neural activation and/or propagation. Such dynamic embodiments involve the heightened states of neural activation and propagation and use this dynamic measurement for nerve location and functional identification relative to the neighboring tissue types. For example, a method of dynamic detection can include: (1) delivering stimulation energy to a treatment site via a treatment device (e.g., the end effector 114) to excite parasympathetic nerves at the treatment site; (2) measuring one or more physiological parameters (e.g., resistance, impedance, etc.) at the treatment site via a measuring/sensing array of the treatment device (e.g., the electrodes 136); (4) based on the measurements, identifying the relative presence and position of parasympathetic nerves at the treatment site; and (5) delivering ablation energy to the identified parasympathetic nerves to block the detected para-sympathetic nerves.

Static measurements include various embodiments associated with specific native properties of the stratified or cellular composition at or near the treatment site. The static embodiments are directed to inherent biologic and electrical properties of tissue types at or near the treatment site, the stratified or cellular compositions at or near the treatment site, and contrasting both foregoing measurements with tissue types adjacent the treatment site (and that are not targeted for neuromodulation). This information can be used to localize specific targets (e.g., parasympathetic fibers) and non-targets (e.g., vessels, sensory nerves, etc.). For example, a method of static detection can include: (1) before ablation, utilizing a measuring/sensing array of a treatment device (e.g., the electrodes 136) to determine one or more baseline physiological parameters; (2) geometrically identifying inherent tissue properties within a region of interest based on the measured physiological parameters (e.g., resistance, impedance, etc.); (3) delivering

ablation energy to one or more nerves within the region of via treatment device interest; (4) during the delivery of the ablation energy, determining one or more mid-procedure physiological parameters via the measuring/sensing array; and (5) after the delivery of ablation energy, determining one or more post-procedure physiological parameters via the measurement/sensing array to determine the effectiveness of the delivery of the ablation energy on blocking the nerves that received the ablation energy.

After the initial static and/or dynamic detection of bioelectric properties, the location of anatomical features can be used to determine where the treatment site(s) should be with respect to various anatomical structures for therapeutically effective neuromodulation of the targeted parasympathetic nasal nerves. The bioelectric and other physiological properties described herein can be detected via electrodes (e.g., the electrodes 136 of the end effector 114), and the electrode pairings on a device (e.g., end effector 114) can be selected to obtain the bioelectric data at specific zones or regions and at specific depths of the targeted regions. The specific properties detected at or surrounding target neuromodulation sites and associated methods for obtaining these properties are described below. These specific detection and mapping methods discussed below are described with reference to the system 100 , although the methods can be implemented on other suitable systems and devices that provide for anatomical identification, anatomical mapping and/or neuromodulation therapy.

Neural Identification and Mapping

In many neuromodulation procedures, it is beneficial to identify the portions of the nerves that fall within a zone and/or region of influence (referred to as the "interest zone") of the energy delivered by a neuromodulation device 102, as well as the relative three-dimensional position of the neural structures relative to the neuromodulation device 102. Characterizing the portions of the neural structures within the interest zone and/or determining the relative positions of the neural structures within the interest zone enables the clinician to (1) selectively activate target neural structures over non-target structures (e.g., blood vessels), and (2) sub-select specific targeted neural structures (e.g., parasympathetic nerves) over non-target neural structures (e.g., sensory nerves, subgroups of neural structures, neural structures having certain compositions or morphologies). The target structures (e.g., parasympathetic nerves) and non-target structures

(e.g., blood vessels, sensory nerves, etc.) can be identified based on the inherent signatures of specific structures, which are defined by the unique morphological compositions of the structures and the bioelectrical properties associated with these morphological compositions. For example, unique, discrete frequencies can be associated with morphological compositions and, therefore, be used to identify certain structures. The target and non-target structures can also be identified based on relative bioelectrical activation of the structures to sub-select specific neuronal structures. Further, target and non-target structures can be identified by the differing detected responses of the structures to a tailored injected stimuli. For example, the systems described herein can detect the magnitude of response of structures and the difference in the responses of anatomical structures with respect to differing stimuli (e.g., stimuli injected at different frequencies).

At least for purposes of this disclosure, a nerve can include the following portions that are defined based on their respective orientations relative to the interest zone: terminating neural structures (e.g., terminating axonal structures), branching neural structures (e.g., branching axonal structures), and travelling neural structures (e.g., travelling axonal structures). For example, terminating neural structures enter the zone but do not exit. As such, terminating neural structures are terminal points for neuronal signaling and activation. Branching neural structures are nerves that enter the interest zone and increase number of nerves exiting the interest zone. Branching neural structures are typically associated with a reduction in relative geometry of nerve bundle. Travelling neural structures are nerves that enter the interest zone and exit the zone with no substantially no change in geometry or numerical value.

The system 100 can be used to detect voltage, current, complex impedance, resistance, permittivity, and/or conductivity, which are tied to the compound action potentials of nerves, to determine and/or map the relative positions and proportionalities of nerves in the interest zone. Neuronal cross-sectional area ("CSA") is expected to be due to the increase in axonic structures. Each axon is a standard size. Larger nerves (in cross-sectional dimension) have a larger number of axons than nerves having smaller cross-sectional dimensions. The compound action responses from the larger nerves, in both static and dynamic assessments, are greater than smaller nerves. This is at least in part because the compound action potential is the cumulative action response from each of the axons. When using static analysis, for example, the system 100 can directly measure and map impedance or resistance of nerves and, based on the determined

impedance or resistance, determine the location of nerves and/or relative size of the nerves. In dynamic analysis, the system 100 can be used to apply a stimulus to the interest zone and detect the dynamic response of the neural structures to the stimulus. Using this information, the system 100 can determine and/or map impedance or resistance in the interest zone to provide information related to the neural positions or relative nerve sizes. Neural impedance mapping can be illustrated by showing the varying complex impedance levels at a specific location at differing cross-sectional depths. In other embodiments, neural impedance or resistance can be mapped in a three-dimensional display.

Identifying the portions and/or relative positions of the nerves within the interest zone can inform and/or guide selection of one or more treatment parameters (e.g., electrode ablation patterns, electrode activation plans, etc.) of the system 100 for improving treatment efficiency and efficacy. For example, during neural monitoring and mapping, the system 100 can identify the directionality of the nerves based at least in part on the length of the neural structure extending along the interest zone, relative sizing of the neural structures, and/or the direction of the action potentials. This information can then be used by the system 100 or the clinician to automatically or manually adjust treatment parameters (e.g., selective electrode activation, bipolar and/or multipolar activation, and/or electrode positioning) to target specific nerves or regions of nerves. For example, the system 100 can selectively activate specific electrodes 136, electrode combinations (e.g., asymmetric or symmetric), and/or adjust the bi-polar or multi-polar electrode configuration. In some embodiments, the system 100 can adjust or select the waveform, phase angle, and/or other energy delivery parameters based on the nerve portion/position mapping and/or the nerve proportionality mapping. In some embodiments, structure and/or properties of the electrodes 136 themselves (e.g., material, surface roughening, coatings, cross-sectional area, perimeter, penetrating, penetration depth, surface-mounted, etc.) may be selected based on the nerve portion and proportionality mapping.

In various embodiments, treatment parameters and/or energy delivery parameters can be adjusted to target on-axis or near axis travelling neural structures and/or avoid the activation of traveling neural structures that are at least generally perpendicular to the end effector 114. Greater portions of the on-axis or near axis travelling neural structures are exposed and susceptible to the neuromodulation energy provided by the end effector 114 than a perpendicular travelling neural structure, which may only be exposed to therapeutic energy at a discrete cross-

section. Therefore, the end effector 114 is more likely to have a greater effect on the on-axis or near axis travelling neural structures. The identification of the neural structure positions (e.g., via complex impedance or resistance mapping) can also allow targeted energy delivery to travelling neural structures rather than branching neural structures (typically downstream of the travelling neural structures) because the travelling neural structures are closer to the nerve origin and, therefore, more of the nerve is affected by therapeutic neuromodulation, thereby resulting in a more efficient treatment and/or a higher efficacy of treatment. Similarly, the identification of neural structure positions can be used to target travelling and branching neural structures over terminal neural structures. In some embodiments, the treatment parameters can be adjusted based on the detected neural positions to provide a selective regional effect. For example, a clinician can target downstream portions of the neural structures if only wanting to influence partial effects on very specific anatomical structures or positions.

In various embodiments, neural locations and/or relative positions of nerves can be determined by detecting the nerve-firing voltage and/or current over time. An array of the electrodes 136 can be positioned in contact with tissue at the interest zone, and the electrodes 136 can measure the voltage and/or current associated with nerve-firing. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves in a hyper state (i.e., excessive parasympathetic tone). Rhinitis is at least in part the result of over-firing nerves because this hyper state drives the hyper-mucosal production and hyper-mucosal secretion. Therefore, detection of nerve firing rate via voltage and current measurements can be used to locate the portions of the interest region that include hyper-parasympathetic neural function (i.e., nerves in the diseased state). This allows the clinician to locate specific nerves (i.e., nerves with excessive parasympathetic tone) before neuromodulation therapy, rather than simply targeting all parasympathetic nerves (including non-diseased state parasympathetic nerves) to ensure that the correct tissue is treated during neuromodulation therapy. Further, nerve firing rate can be detected during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy. For example, recording decreases or elimination of nerve firing rate after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In various embodiments, the system 100 can detect neural activity using dynamic activation by injecting a stimulus signal (i.e., a signal that temporarily activates nerves) via one

or more of the electrodes 136 to induce an action potential, and other pairs of electrodes 136 can detect bioelectric properties of the neural response. Detecting neural structures using dynamic activation involves detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The ability to numerically measure, profile, map, and/or image fast neuronal depolarization for generating an accurate index of activity is a factor in measuring the rate of discharge in neurons and their processes. The action potential causes a rapid increase in the voltage across nerve fiber and the electrical impulse then spreads along the fiber. As an action potential occurs, the conductance of a neural cell membrane changes, becoming about 40 times larger than it is when the cell is at rest. During the action potential or neuronal depolarization, the membrane resistance diminishes by about 80 times, thereby allowing an applied current to enter the intracellular space as well. Over a population of neurons, this leads to a net decrease in the resistance during coherent neuronal activity, such as chronic para-sympathetic responses, as the intracellular space will provide additional conductive ions. The magnitude of such fast changes has been estimated to have local resistivity changes with recording near DC is 2.8-3.7% for peripheral nerve bundles (e.g., including the nerves in the nasal cavity).

Detecting neural structures using dynamic activation includes detecting the locations of action potentials within the interest zone by measuring the discharge rate in neurons and the associated processes. The basis of each this discharge is the action potential, during which there is a depolarization of the neuronal membrane of up to 110 mV or more, lasting approximately 2 milliseconds, and due to the transfer of micromolar quantities of ions (e.g., sodium and potassium) across the cellular membrane. The complex impedance or resistance change due to the neuronal membrane falls from 1000 to 25 Ωcm. The introduction of a stimulus and subsequent measurement of the neural response can attenuate noise and improve signal to noise ratios to precisely focus on the response region to improve neural detection, measurement, and mapping.

In some embodiments, the difference in measurements of physiological parameters (e.g., complex impedance, resistance, voltage) over time, which can reduce errors, can be used to create a neural profiles, spectrums, or maps. For example, the sensitivity of the system 100 can be improved because this process provides repeated averaging to a stimulus. As a result, the mapping function outputs can be a unit-less ratio between the reference and test collated data at a

single frequency and/or multiple frequencies and/or multiple amplitudes. Additional considerations may include multiple frequency evaluation methods that consequently expand the parameter assessments, such as resistivity, admittivity, center frequency, or ratio of extra- to intracellular resistivity.

In some embodiments, the system 100 may also be configured to indirectly measure the electrical activity of neural structures to quantify the metabolic recovery processes that accompany action potential activity and act to restore ionic gradients to normal. These are related to an accumulation of ions in the extracellular space. The indirect measurement of electrical activity can be approximately a thousand times larger (in the order of millimolar), and thus are easier to measure and can enhance the accuracy of the measured electrical properties used to generate the neural maps.

The system 100 can perform dynamic neural detection by detecting nerve-firing voltage and/or current and, optionally, nerve firing rate over time, in response to an external stimulation of the nerves. For example, an array of the electrodes 136 can be positioned in contact with tissue at the interest zone, one or more of the electrodes 136 can be activated to inject a signal into the tissue that stimulates the nerves, and other electrodes 136 of the electrode array can measure the neural voltage and/or current due to nerve firing in response to the stimulus. This information can optionally be mapped (e.g., on a display 112) to identify the location of nerves and, in certain embodiments, identify parasympathetic nerves in a hyper state (e.g., indicative of Rhinitis or other diseased state). The dynamic detection of neural activity (voltage, current, firing rate, etc.) can be performed before neuromodulation therapy to detect target nerve locations to select the target site and treatment parameters to ensure that the correct tissue is treated during neuromodulation therapy. Further, dynamic detection of neural activity can be performed during or after neuromodulation therapy to allow the clinician to monitor changes in neural activity to validate treatment efficacy. For example, recording decreases or elimination of neural activity after neuromodulation therapy can indicate that the therapy was effective in therapeutically treating the hyper/diseased nerves.

In some embodiments, a stimulating signal can be delivered to the vicinity of the targeted nerve via one or more penetrating electrodes (e.g., microneedles that penetrate tissue) associated with the end effector 114 and/or a separate device. The stimulating signal generates an action potential, which causes smooth muscle cells or other cells to contract. The location and strength

of this contraction can be detected via the penetrating electrode(s) and, thereby, indicate to the clinician the distance to the nerve and/or the location of the nerve relative to the stimulating needle electrode. In some embodiments, the stimulating electrical signal may have a voltage of typically 1-2 mA or greater and a pulse width of typically 100-200 microseconds or greater. Shorter pulses of stimulation result in better discrimination of the detected contraction, but may require more current. The greater the distance between the electrode and the targeted nerve, the more energy is required to stimulate. The stimulation and detection of contraction strength and/or location enables identification of how close or far the electrodes are from the nerve, and therefore can be used to localize the nerve spatially. In some embodiments, varying pulse widths may be used to measure the distance to the nerve. As the needle becomes closer to the nerve, the pulse duration required to elicit a response becomes less and less.

To localize nerves via muscle contraction detection, the system 100 can vary pulse-width or amplitude to vary the energy (Energy=pulse-width*amplitude) of the stimulus delivered to the tissue via the penetrating electrode(s). By varying the stimulus energy and monitoring muscle contraction via the penetrating electrodes and/or other type of sensor, the system 100 can estimate the distance to the nerve. If a large amount of energy is required to stimulate the nerve/contract the muscle, the stimulating/penetrating electrode is far from the nerve. As the stimulating/penetrating electrode, moves closer to the nerve, the amount of energy required to induce muscle contraction will drop. For example, an array of penetrating electrodes can be positioned in the tissue at the interest zone and one or more of the electrodes can be activated to apply stimulus at different energy levels until they induce muscle contraction. Using an iterative process, localize the nerve (e.g., via the mapping/evaluation/feedback algorithm 110).

In some embodiments, the system 100 can measure the muscular activation from the nerve stimulus (e.g., via the electrodes 136) to determine neural positioning for neural mapping, without the use of penetrating electrodes. In this embodiment, the treatment device targets the smooth muscle cells' varicosities surrounding the submucosal glands and the vascular supply, and then the compound muscle action potential. This can be used to summate voltage response from the individual muscle fiber action potentials. The shortest latency is the time from stimulus artifact to onset of the response. The corresponding amplitude is measured from baseline to negative peak and measured in millivolts (mV). Nerve latencies (mean±SD) in adults typically range about 2-6 milliseconds, and more typically from about 3.4±0.8 to about 4.0±0.5

milliseconds. A comparative assessment may then be made which compares the outputs at each time interval (especially pre- and post-energy delivery) in addition to a group evaluation using the alternative nasal cavity. This is expected to provide an accurate assessment of the absolute value of the performance of the neural functioning because muscular action/activation may be used to infer neural action/activation and muscle action/activation is a secondary effect or by-product whilst the neural function is the absolute performance measure.

In some embodiments, the system 100 can record a neuromagnetic field outside of the nerves to determine the internal current of the nerves without physical disruption of the nerve membrane. Without being bound by theory, the contribution to the magnetic field from the current inside the membrane is two orders of magnitude larger than that from the external current, and that the contribution from current within the membrane is substantially negligible. Electrical stimulation of the nerve in tandem with measurements of the magnetic compound action fields ("CAFs") can yield sequential positions of the current dipoles such that the location of the conduction change can be estimated (e.g., via the least-squares method). Visual representation (e.g., via the display 112) using magnetic contour maps can show normal or non-normal neural characteristics (e.g., normal can be equated with a characteristic quadrupolar pattern propagating along the nerve), and therefore indicate which nerves are in a diseases, hyperactive state and suitable targets for neuromodulation.

During magnetic field detection, an array of the electrodes 136 can be positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes 136 can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire), and therefore changing magnetic fields are indicative of the nerve nerve-firing rate. The changing magnetic field caused by neural firing can induce a current detected by nearby sensor wire (e.g., the sensor 314) and/or wires associated with the nearby electrodes 136. By measuring this current, the magnetic field strength can be determined. The magnetic fields can optionally be mapped (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. Further, the magnetic field information can be used during or after neuromodulation

therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In other embodiments, the neuromagnetic field is measured with a Hall Probe or other suitable device, which can be integrated into the end effector 114 and/or part of a separate device delivered to the interest zone. Alternatively, rather than measuring the voltage in the second wire, the changing magnetic field can be measured in the original wire (i.e. the nerve) using a Hall probe. A current going through the Hall probe will be deflected in the semi-conductor. This will cause a voltage difference between the top and bottom portions, which can be measured. In some aspects of this embodiments, three orthogonal planes are utilized.

In some embodiments, the system 100 can be used to induce electromotive force ("EMF") in a wire (i.e., a frequency-selective circuit, such as a tunable/LC circuit) that is tunable to resonant frequency of a nerve. In this embodiment, the nerve can be considered to be a current carrying wire, and the firing action potential is a changing voltage. This causes a changing current which, in turn, causes a changing magnetic flux (i.e., the magnetic field that is perpendicular to the wire). Under Faraday's Law of Induction/Faraday's Principle, the changing magnetic flux induces EMF (including a changing voltage) in a nearby sensor wire (e.g., integrated into the end effector 114, the sensor 314, and/or other structure), and the changing voltage can be measured via the system 100.

In further embodiments, the sensor wire (e.g., the sensor 314) is an inductor and, therefore, provides an increase of the magnetic linkage between the nerve (i.e., first wire) and the sensor wire (i.e., second wire), with more turns for increasing effect. (e.g., $V2,rms=V1,rms(N2/N1)$). Due to the changing magnetic field, a voltage is induced in the sensor wire, and this voltage can be measured and used to estimate current changes in the nerve. Certain materials can be selected to enhance the efficiency of the EMF detection. For example, the sensor wire can include a soft iron core or other high permeability material for the inductor.

During induced EMF detection, the end effector 114 and/or other device including a sensor wire is positioned in contact with tissue at the interest zone and, optionally, one or more of the electrodes 136 can be activated to inject an electrical stimulus into the tissue. As the nerves in the interest zone fire (either in response to a stimulus or in the absence of it), the nerve generates a magnetic field (e.g., similar to a current carrying wire) that induces a current in the sensor wire (e.g., the sensor 314). This information can be used to determine neural location

and/or map the nerves (e.g., on a display 112) to identify the location of nerves and select target nerves (nerves with excessive parasympathetic tone) before neuromodulation therapy to ensure that the desired nerves are treated during neuromodulation therapy. EMF information can also be used during or after neuromodulation therapy so that the clinician can monitor changes in nerve firing rate to validate treatment efficacy.

In some embodiments, the system 100 can detect magnetic fields and/or EMF generated at a selected frequency that corresponds to a particular type of nerve. The frequency and, by extension, the associated nerve type of the detected signal can be selected based on an external resonant circuit. Resonance occurs on the external circuit when it is matched to the frequency of the magnetic field of the particular nerve type and that nerve is firing. In manner, the system 100 can be used to locate a particular sub-group/type of nerves.

In some embodiments, the system 100 can include a variable capacitor frequency-selective circuit to identify the location and/or map specific nerves (e.g., parasympathetic nerve, sensory nerve, nerve fiber type, nerve subgroup, etc.). The variable capacitor frequency-selective circuit can be defined by the sensor 314 and/or other feature of the end effector 114. Nerves have different resonant frequencies based on their function and structure. Accordingly, the system 100 can include a tunable LC circuit with a variable capacitor (C) and/or variable inductor (L) that can be selectively tuned to the resonant frequency of desired nerve types. This allows for the detection of neural activity only associated with the selected nerve type and its associated resonant frequency. Tuning can be achieved by moving the core in and out of the inductor. For example, tunable LC circuits can tune the inductor by: (i) changing the number of coils around the core; (ii) changing the cross-sectional area of the coils around the core; (iii) changing the length of the coil; and/or (iv) changing the permeability of the core material (e.g., changing from air to a core material). Systems including such a tunable LC circuit provide a high degree of dissemination and differentiation not only as to the activation of a nerve signal, but also with respect to the nerve type that is activated and the frequency at which the nerve is firing.

Anatomical Mapping

In various embodiments, the system 100 is further configured to provide minimally-invasive anatomical mapping that uses focused energy current/voltage stimuli from a spatially localized source (e.g., the electrodes 136) to cause a change in the conductivity of the of the tissue at the interest zone and detect resultant biopotential and/or bioelectrical measurements (e.g., via the electrodes 136). The current density in the tissue changes in response to changes of voltage applied by the electrodes 136, which creates a change in the electric current that can be measured with the end effector 114 and/or other portions of the system 100. The results of the bioelectrical and/or biopotential measurements can be used to predict or estimate relative absorption profilometry to predict or estimate the tissue structures in the interest zone. More specifically, each cellular construct has unique conductivity and absorption profiles that can be indicative of a type of tissue or structure, such as bone, soft tissue, vessels, nerves, types of nerves, and/or certain neural structures. For example, different frequencies decay differently through different types of tissue. Accordingly, by detecting the absorption current in a region, the system 100 can determine the underlying structure and, in some instances, to a sub-microscale, cellular level that allows for highly specialized target localization and mapping. This highly specific target identification and mapping enhances the efficacy and efficiency of neuromodulation therapy, while also enhancing the safety profile of the system 100 to reduce collateral effects on non-target structures.

To detect electrical and dielectric tissue properties (e.g., resistance, complex impedance, conductivity, and/or, permittivity as a function of frequency), the electrodes 136 and/or another electrode array is placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli (current/voltage) to the tissue. The electrical properties of the tissue between the source and the receiver electrodes 136 are measured, as well as the current and/or voltage at the individual receiver electrodes 136. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest and, in certain embodiments, the location of firing nerves. For example, the anatomical mapping can be provided as a color-coded or gray-scale three-dimensional or two-dimensional map showing differing intensities of certain bioelectric properties (e.g., resistance, impedance, etc.), or the information can be processed to map the actual anatomical structures for the clinician. This information can also be used during neuromodulation therapy to monitor treatment progression with respect to the anatomy, and after

neuromodulation therapy to validate successful treatment. In addition, the anatomical mapping provided by the bioelectrical and/or biopotential measurements can be used to track the changes to non-target tissue (e.g., vessels) due to neuromodulation therapy to avoid negative collateral effects. For example, a clinician can identify when the therapy begins to ligate a vessel and/or damage tissue, and modify the therapy to avoid bleeding, detrimental tissue ablation, and/or other negative collateral effects.

Furthermore, the threshold frequency of electric current used to identify specific targets can subsequently be used when applying therapeutic neuromodulation energy. For example, the neuromodulation energy can be applied at the specific threshold frequencies of electric current that are target neuronal-specific and differentiated from other non-targets (e.g., blood vessels, non-target nerves, etc.). Applying ablation energy at the target-specific frequency results in an electric field that creates ionic agitation in the target neural structure, which leads to differentials in osmotic potentials of the targeted neural structures. These osmotic potential differentials cause dynamic changes in neuronal membronic potentials (resulting from the difference in intra-cellular and extra-cellular fluidic pressure) that lead to vacuolar degeneration of the targeted neural structures and, eventually, necrosis. Using the highly targeted threshold neuromodulation energy to initiate the degeneration allows the system 100 to delivery therapeutic neuromodulation to the specific target, while surrounding blood vessels and other non-target structures are functionally maintained.

In some embodiments, the system 100 can further be configured to detect bioelectrical properties of tissue by non-invasively recording resistance changes during neuronal depolarization to map neural activity with electrical impedance, resistance, bio-impedance, conductivity, permittivity, and/or other bioelectrical measurements. Without being bound by theory, when a nerve depolarizes, the cell membrane resistance decreases (e.g., by approximately 80×) so that current will pass through open ion channels and into the intracellular space. Otherwise the current remains in the extracellular space. For non-invasive resistance measurements, tissue can be stimulated by applying a current of less than 100 Hz, such as applying a constant current square wave at 1 Hz with an amplitude less than 25% (e.g., 10%) of the threshold for stimulating neuronal activity, and thereby preventing or reducing the likelihood that the current does not cross into the intracellular space or stimulating at 2 Hz. In either case,

the resistance and/or complex impedance is recorded by recording the voltage changes. A complex impedance or resistance map or profile of the area can then be generated.

For impedance/conductivity/permittivity detection, the electrodes 136 and/or another electrode array are placed on tissue at an interest region, and an internal or external source (e.g., the generator 106) applies stimuli to the tissue, and the current and/or voltage at the individual receiver electrodes 136 is measured. The stimuli can be applied at different frequencies to isolate different types of nerves. These individual measurements can then be converted into an electrical map/image/profile of the tissue and visualized for the user on the display 112 to identify anatomical features of interest. The neural mapping can also be used during neuromodulation therapy to select specific nerves for therapy, monitor treatment progression with respect to the nerves and other anatomy, and validate successful treatment.

In some embodiments of the neural and/or anatomical detection methods described above, the procedure can include comparing the mid-procedure physiological parameter(s) to the baseline physiological parameter(s) and/or other, previously-acquired mid-procedure physiological parameter(s) (within the same energy delivery phase). Such a comparison can be used to analyze state changes in the treated tissue. The mid-procedure physiological parameter(s) may also be compared to one or more predetermined thresholds, for example, to indicate when to stop delivering treatment energy. In some embodiments of the present technology, the measured baseline, mid-, and post-procedure parameters include a complex impedance. In some embodiments of the present technology, the post-procedure physiological parameters are measured after a pre-determined time period to allow the dissipation of the electric field effects (ionic agitation and/or thermal thresholds), thus facilitating accurate assessment of the treatment.

In some embodiments, the anatomical mapping methods described above can be used to differentiate the depth of soft tissues within the nasal mucosa. The depth of mucosa on the turbinates is great whilst the depth off the turbinate is shallow and, therefore, identifying the tissue depth in the present technology also identifies positions within the nasal mucosa and where precisely to target. Further, by providing the micro-scale spatial impedance mapping of epithelial tissues as described above, the inherent unique signatures of stratified layers or cellular bodies can be used as identifying the region of interest. For example, different regions have

larger or small populations of specific structures, such as submucosal glands, so target regions can be identified via the identification of these structures.

In some embodiments, the system 100 includes additional features that can be used to detect anatomical structures and map anatomical features. For example, the system 100 can include an ultrasound probe for identification of neural structures and/or other anatomical structures. Higher frequency ultrasound provides higher resolution, but less depth of penetration. Accordingly, the frequency can be varied to achieve the appropriate depth and resolution for neural/anatomical localization. Functional identification may rely on the spatial pulse length ("SPL") (wavelength multiplied by number of cycles in a pulse). Axial resolution (SPL/2) may also be determined to locate nerves.

In some embodiments, the system 100 can further be configured to emit stimuli with selective parameters that suppress rather than fully stimulate neural activity. for example, in embodiments where the strength-duration relationship for extracellular neural stimulation is selected and controlled, a state exists where the extracellular current can hyperpolarize cells, resulting in suppression rather than stimulation spiking behavior (i.e., a full action potential is not achieved). Both models of ion channels, HH and RGC, suggest that it is possible to hyperpolarize cells with appropriately designed burst extracellular stimuli, rather than extending the stimuli. This phenomenon could be used to suppress rather than stimulate neural activity during any of the embodiments of neural detection and/or modulation described herein.

In various embodiments, the system 100 could apply the anatomical mapping techniques disclosed herein to locate or detect the targeted vasculature and surrounding anatomy before, during, and/or after treatment.

Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment. Thus, appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments.

The terms and expressions which have been employed herein are used as terms of description and not of limitation, and there is no intention, in the use of such terms and expressions, of excluding any equivalents of the features shown and described (or portions

thereof), and it is recognized that various modifications are possible within the scope of the claims. Accordingly, the claims are intended to cover all such equivalents.

Incorporation by Reference

References and citations to other documents, such as patents, patent applications, patent publications, journals, books, papers, web contents, have been made throughout this disclosure. All such documents are hereby incorporated herein by reference in their entirety for all purposes.

Equivalents

Various modifications of the invention and many further embodiments thereof, in addition to those shown and described herein, will become apparent to those skilled in the art from the full contents of this document, including references to the scientific and patent literature cited herein. The subject matter herein contains important information, exemplification and guidance that can be adapted to the practice of this invention in its various embodiments and equivalents thereof.

Claims

What is claimed is:

1. A device for treating a condition within a sino-nasal cavity of a patient, the device comprising:

an elongate body comprising one or more of a first set of electrodes provided along a length thereof; and

a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon.

2. The device of claim 1, wherein the elongate body comprises a shaft to which the end effector is coupled.

3. The device of claim 2, wherein the shaft comprises an outer sheath surrounding a hypotube or metallic member, wherein at least one of the outer sheath and hypotube and metallic member includes the one or more of the first set of electrodes provided thereon.

4. The device of claim 1, wherein the elongate body comprises one or more of a plurality of support elements forming at least a portion of the end effector.

5. The device of claim 1, wherein each of the first set of electrodes is positioned on separate respective portion of the elongate body.

6. The device of claim 5, wherein one or more of the separate respective portions of the elongate body are transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

7. The device of claim 1, wherein each of the first set of electrodes is configured to deliver energy to a first target site associated with an inferior or middle turbinate within a nasal cavity of

a patient at a level sufficient to reduce engorgement of tissue associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient.

8. The device of claim 1, wherein the end effector comprises a proximal segment that is spaced apart from a separate distal segment.

9. The device of claim 8, wherein:

the proximal segment comprises a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate; and

the distal segment comprises a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate.

10. The device of claim 9, wherein each of the second set of electrodes is configured to deliver energy to a second target site associated with a sphenopalatine foramen within the nasal cavity of the patient at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the patient.

11. A method for treating a condition within a nasal cavity of a patient, the method comprising:

providing a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon,

advancing the elongate body and end effector through a nasal passage and into a sino-nasal cavity of a patient until a length of the elongate body is positioned at a first target site and the end effector is positioned at a separate second target site; and

delivering energy, via the first and second sets of electrodes, to tissue at the respective first and second target sites.

12. The method of claim 11, wherein the elongate body comprises a shaft to which the end effector is coupled.

13. The method of claim 12, wherein the shaft comprises an outer sheath surrounding a hypotube or metallic member, wherein at least one of the outer sheath and hypotube and metallic member includes the one or more of the first set of electrodes provided thereon.

14. The method of claim 11, wherein the elongate body comprises one or more of a plurality of support elements forming at least a portion of the end effector.

15. The method of claim 11, wherein each of the first set of electrodes is positioned on separate respective portion of the elongate body.

16. The method of claim 15, wherein one or more of the separate respective portions of the elongate body are transformable between a retracted configuration and an expanded configuration such that, when in the expanded configuration, each separate respective portion of the elongate body is configured to position a separate associated one of the first set of electrodes into contact with a first target site.

16. The method of claim 11, wherein the first target site associated with an inferior or middle turbinate of the patient and the second target site associated with a sphenopalatine foramen within the nasal cavity of the patient.

17. The method of claim 16, wherein delivering energy via the first set of electrodes comprises delivering energy at level sufficient to disrupt multiple neural signals to and/or result in local hypoxia or coagulation necrosis of mucus producing and/or mucosal engorgement elements associated with the inferior turbinate to thereby increase volumetric flow through a nasal passage of the patient.

18. The method of claim 16, wherein the end effector comprises a proximal segment that is spaced apart from a separate distal segment.

19. The method of claim 18, wherein:

the proximal segment comprises a first set of flexible support elements arranged in a deployed configuration to fit around at least a portion of a middle turbinate at an anterior position relative to a lateral attachment and a posterior-inferior edge of the middle turbinate; and

the distal segment comprises a second set of flexible support elements configured in a deployed configuration to contact a plurality of tissue locations in a cavity at a posterior position relative to the lateral attachment and posterior-inferior edge of the middle turbinate.

20. The method of claim 19, wherein delivering energy via the second set of electrodes comprises delivering energy at a level sufficient to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at foramina and or microforamina of a palatine bone of the patient.

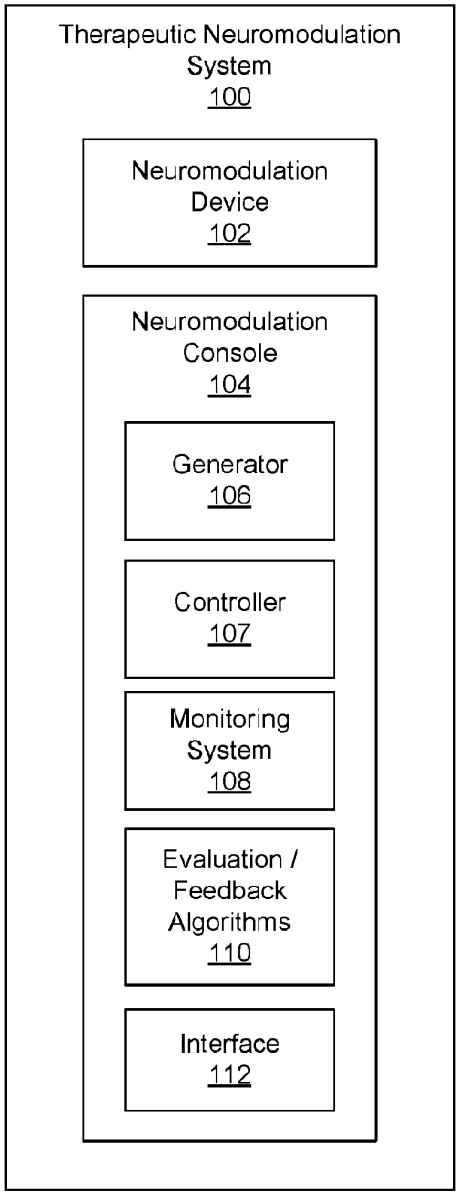

Therapeutic Neuromodulation System
100
Neuromodulation Device
102
Neuromodulation Console
104
Generator
106
Controller
107
Monitoring System
108
Evaluation / Feedback Algorithms
110
Interface
112

FIG. 1A

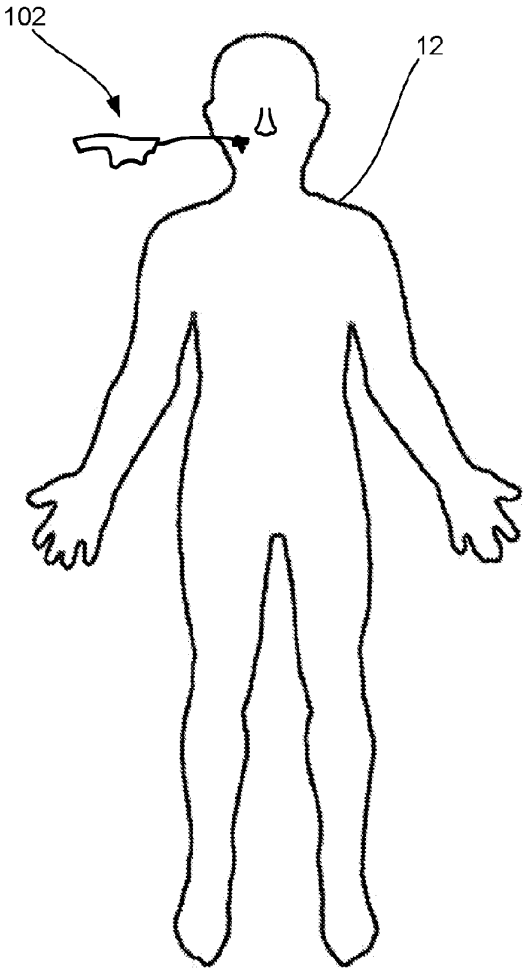

102
12

FIG. 1B

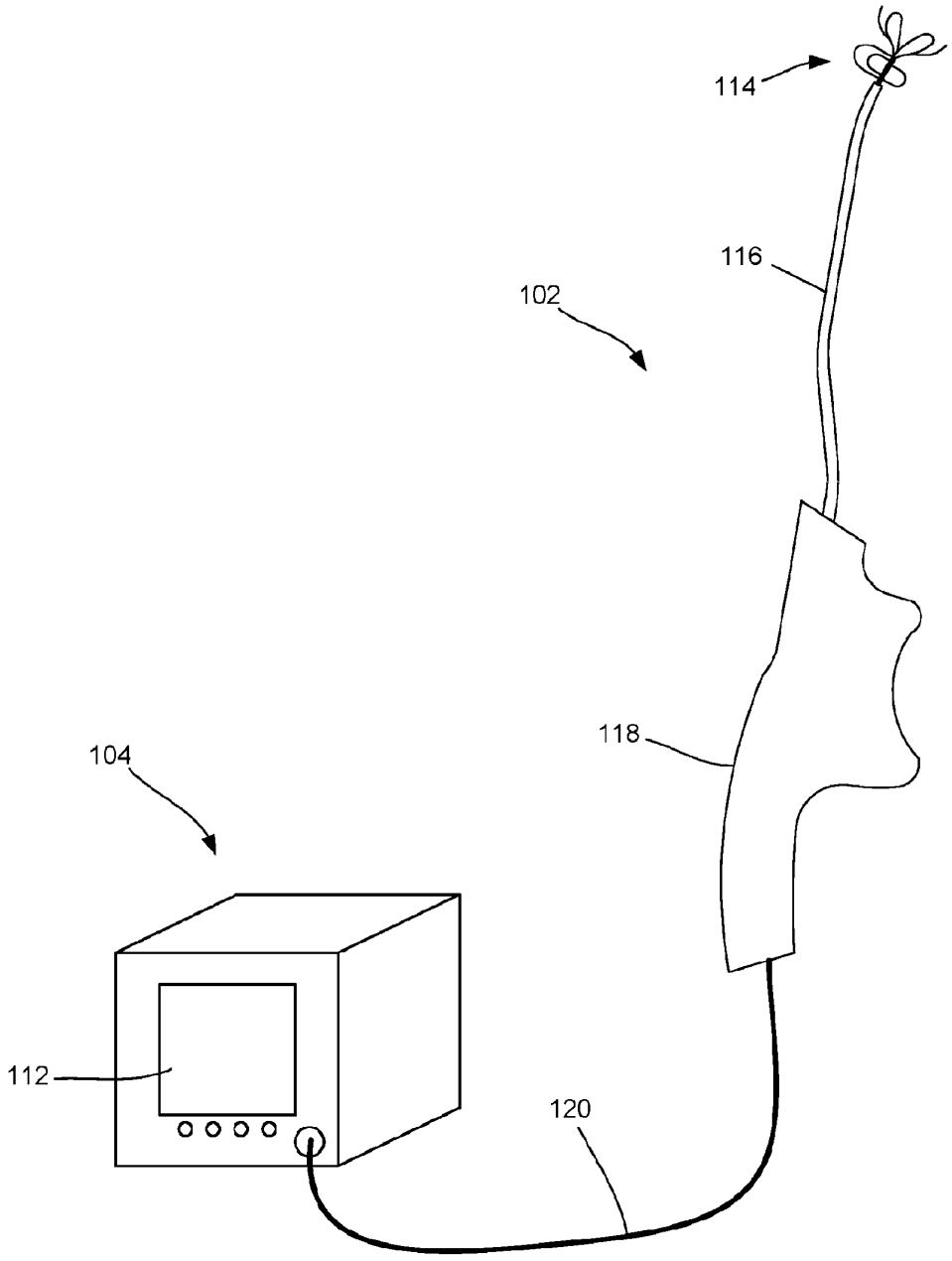


FIG. 2

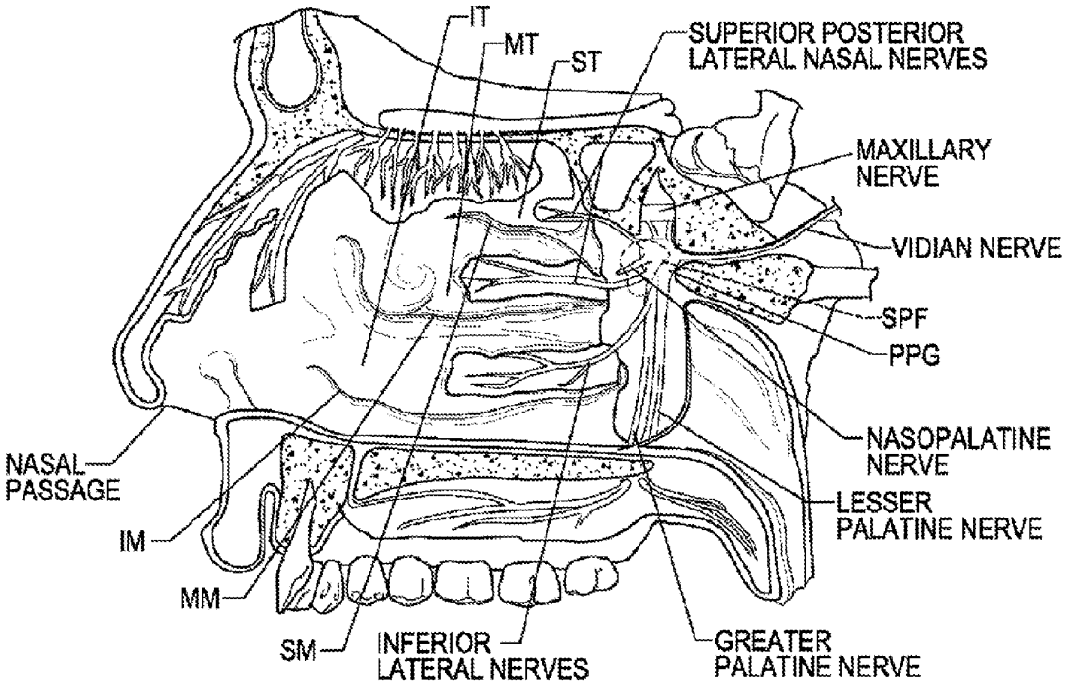

IT
MT
ST
SUPERIOR POSTERIOR LATERAL NASAL NERVES
MAXILLARY NERVE
VIDIAN NERVE
SPF
PPG
NASOPALATINE NERVE
LESSER PALATINE NERVE
NASAL PASSAGE
IM
MM
SM
INFERIOR LATERAL NERVES
GREATER PALATINE NERVE

FIG. 3A

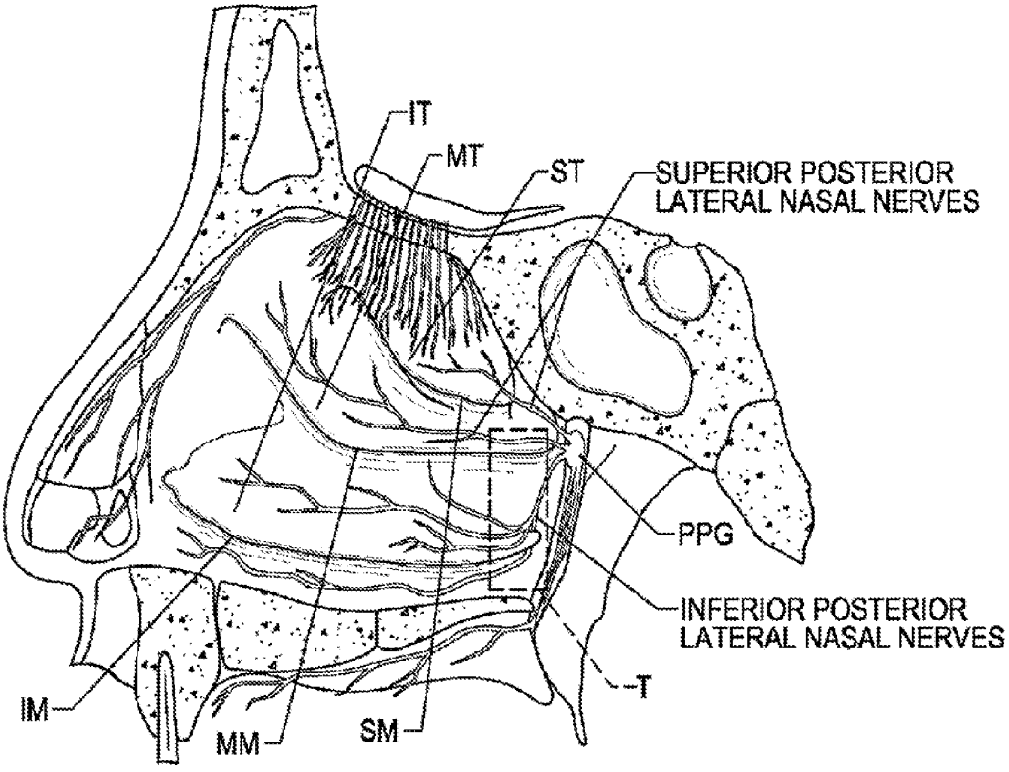

IT
MT
ST
SUPERIOR POSTERIOR
LATERAL NASAL NERVES
PPG
INFERIOR POSTERIOR
LATERAL NASAL NERVES
T
IM
MM
SM

FIG. 3B

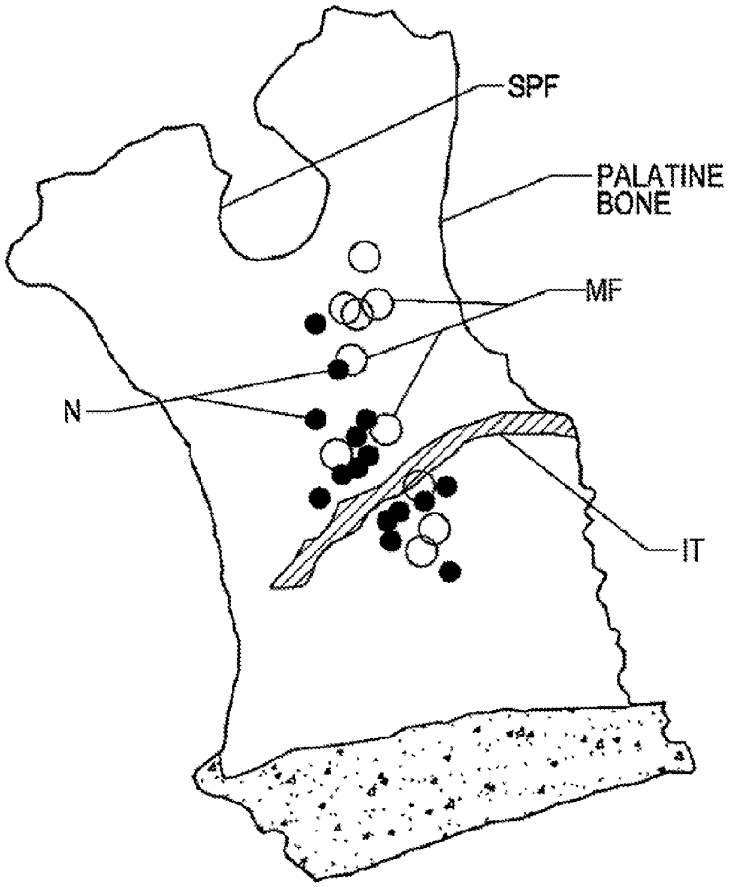


FIG. 3C

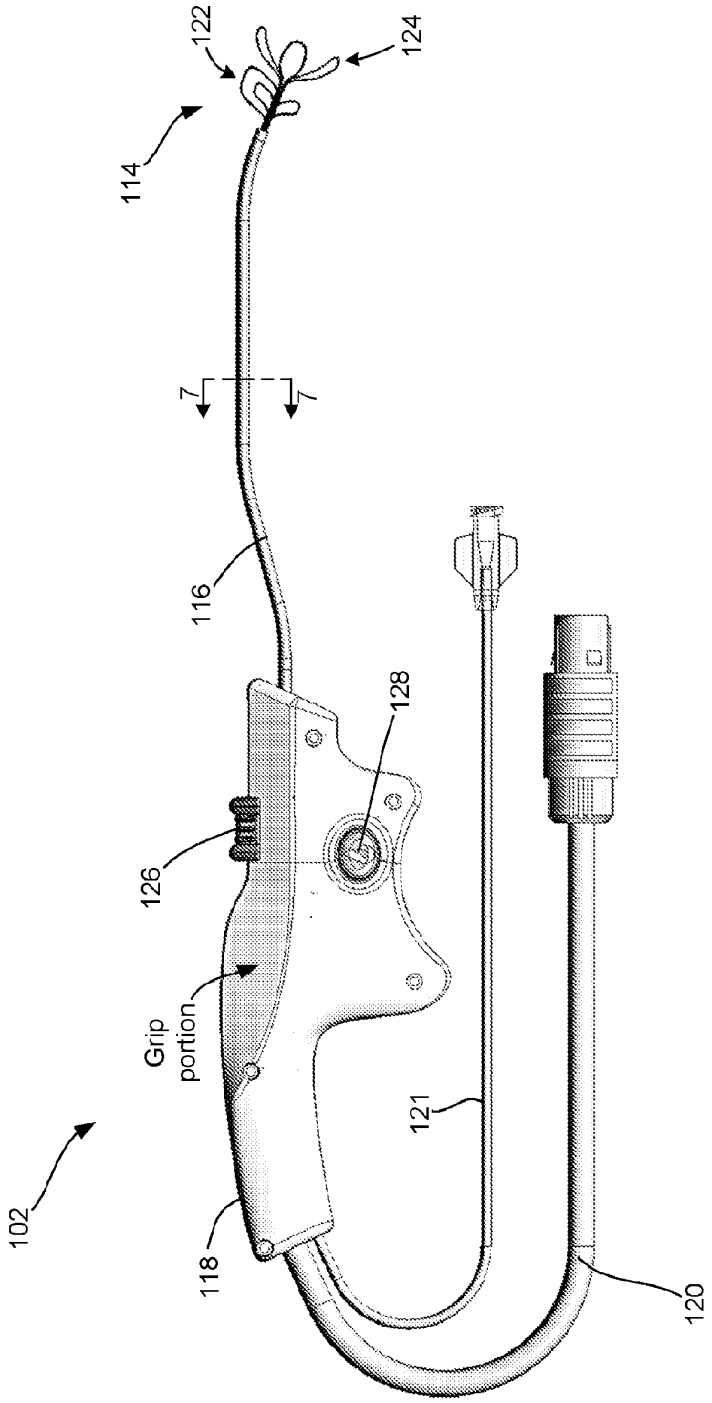


FIG. 4

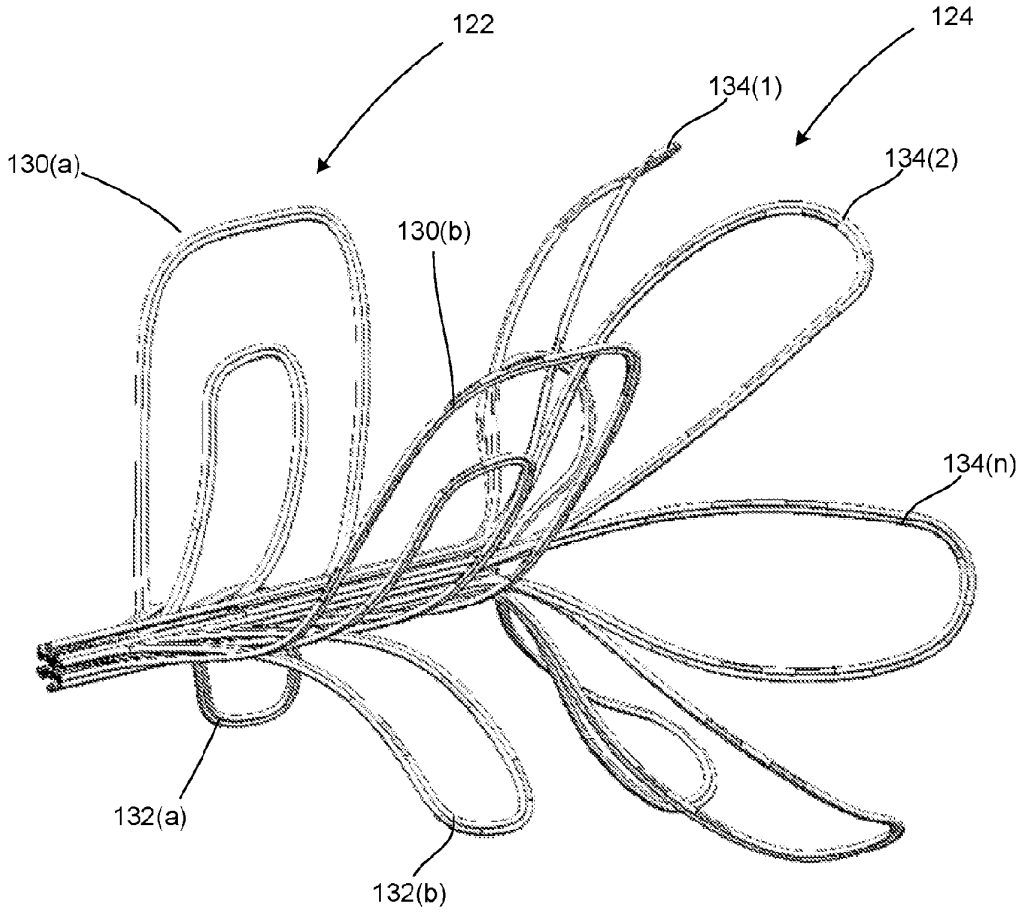


FIG. 5A

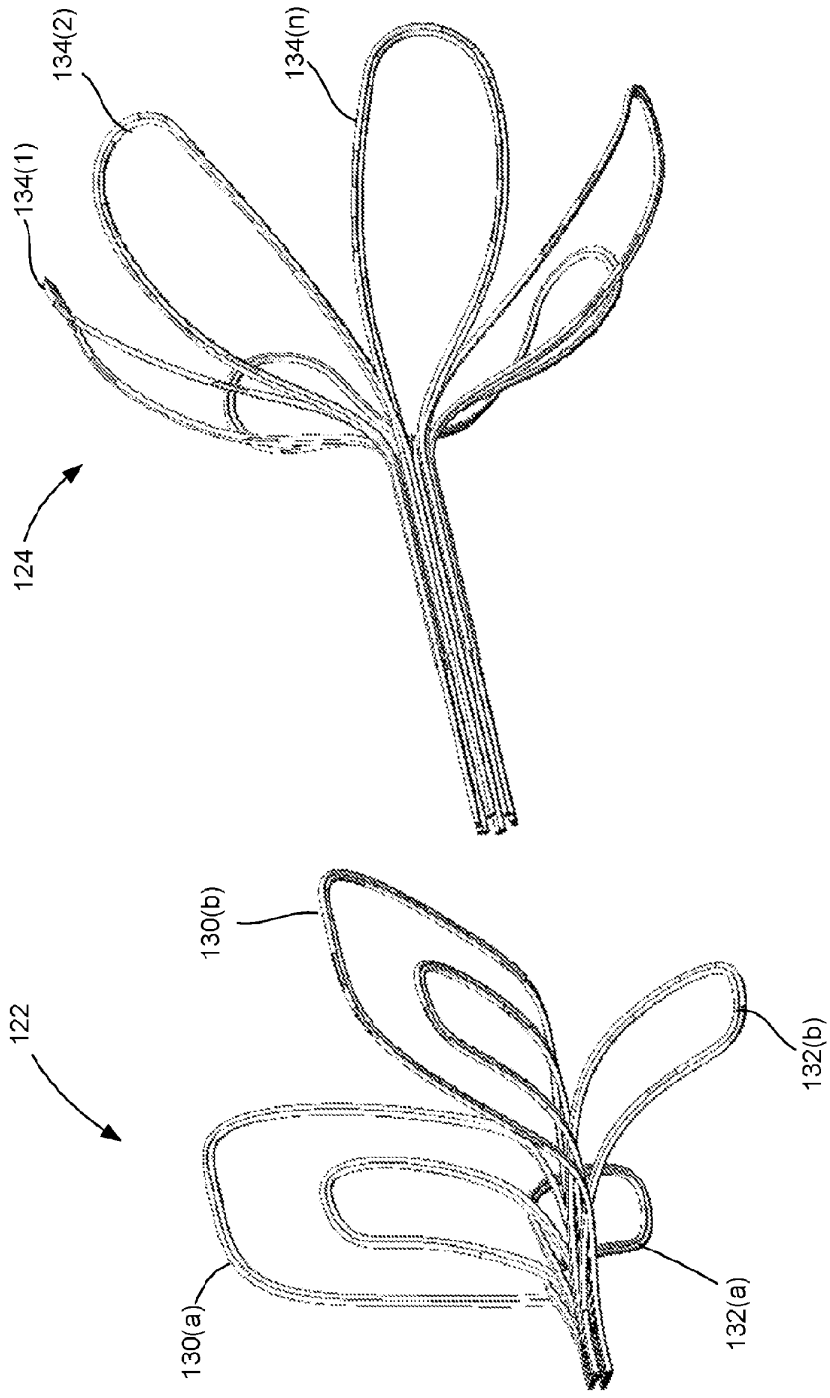


FIG. 5B

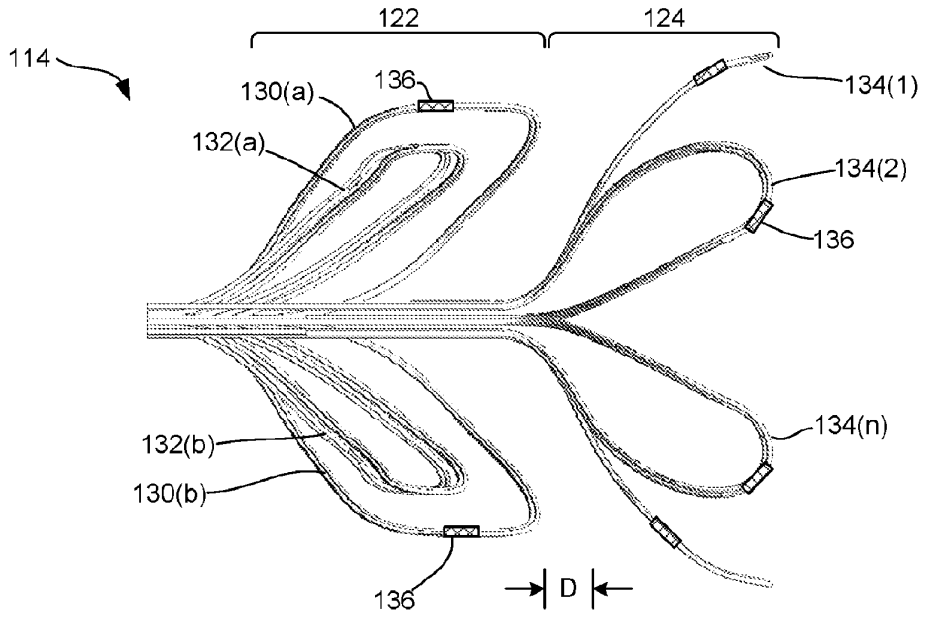

122
124
114
130(a)
136
134(1)
132(a)
134(2)
136
132(b)
134(n)
130(b)
136
D

FIG. 5C

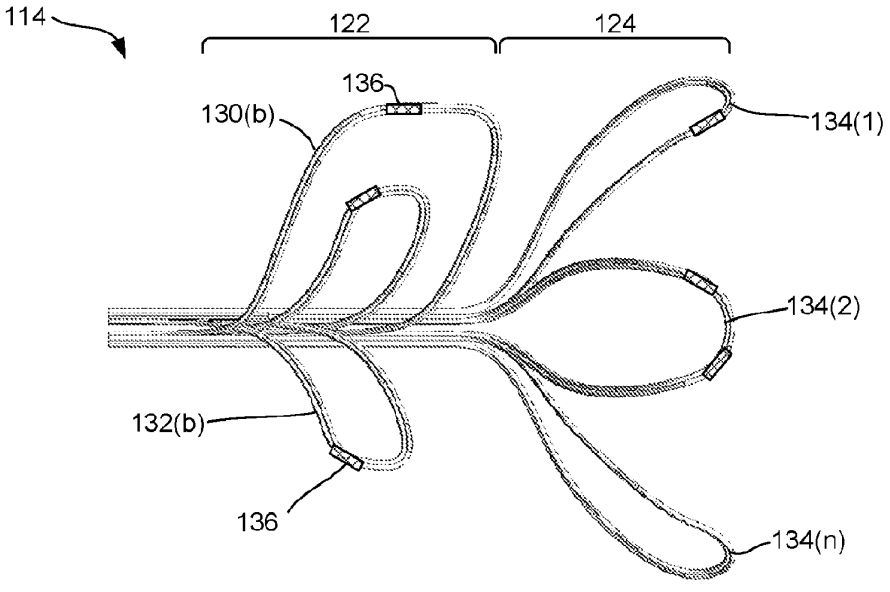

114
122
124
136
130(b)
134(1)
134(2)
132(b)
136
134(n)

FIG. 5D

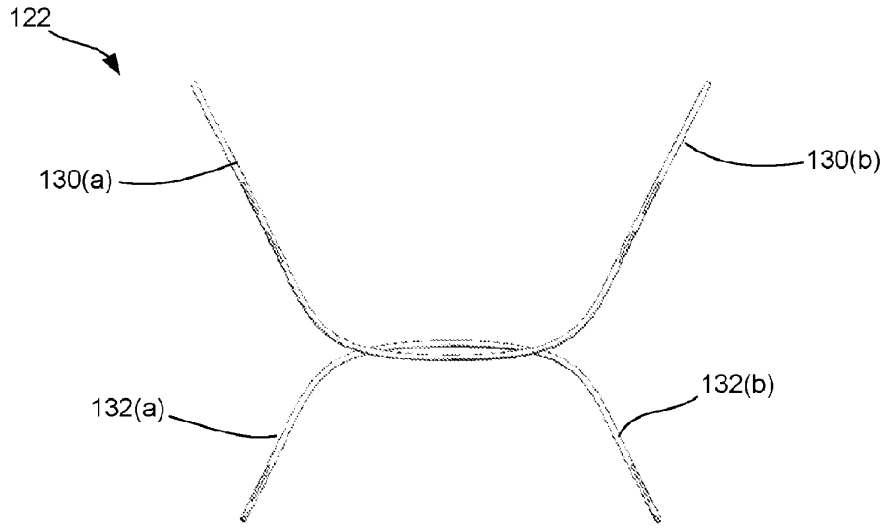


FIG. 5E

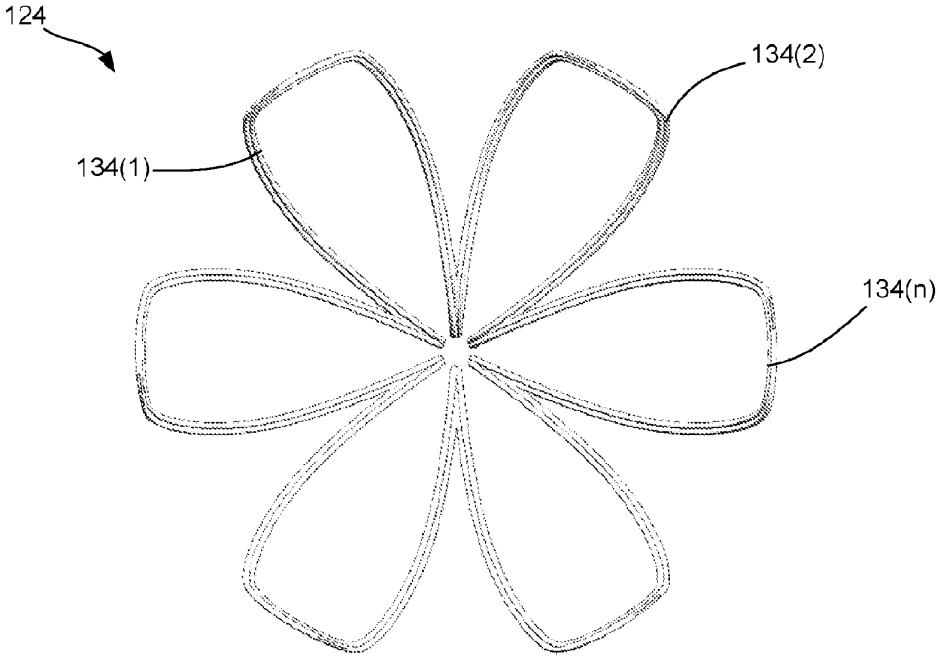


FIG. 5F

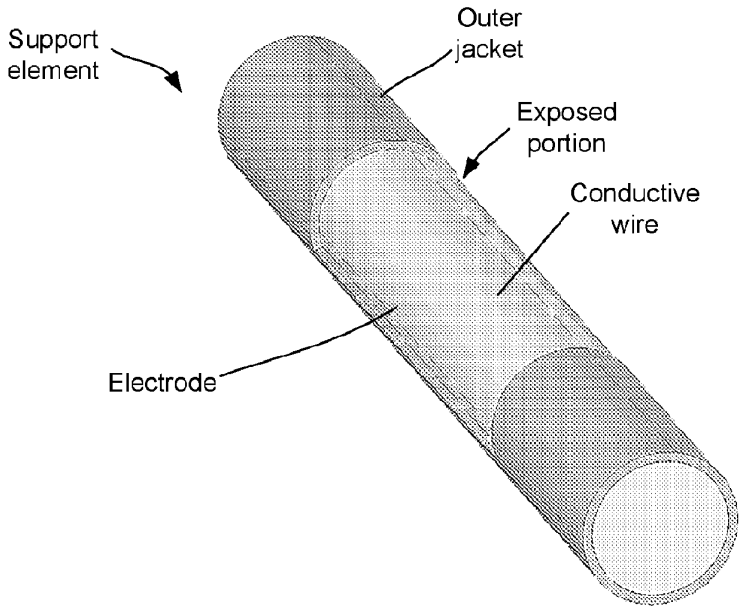

Support element
Outer jacket
Exposed portion
Conductive wire
Electrode

FIG. 6

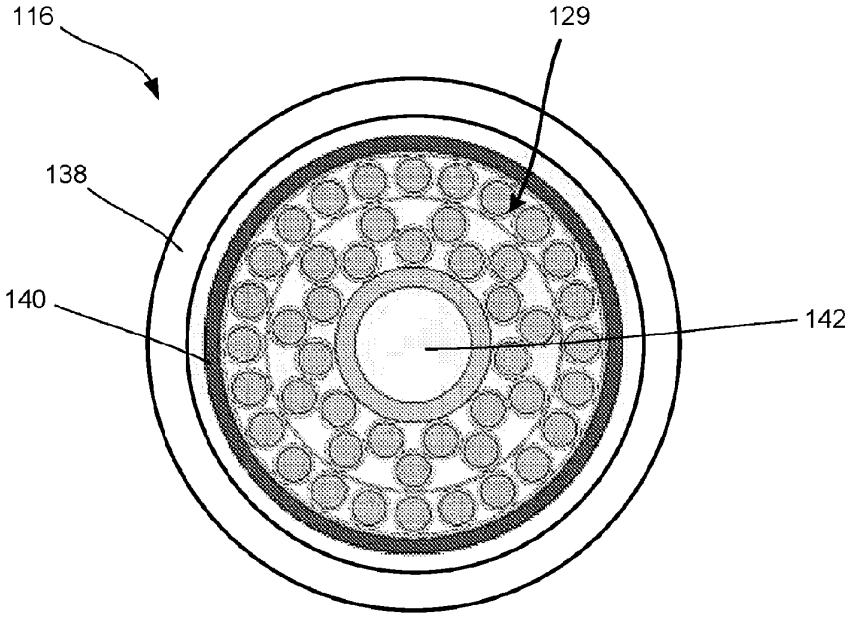

116
129
138
140
142

FIG. 7

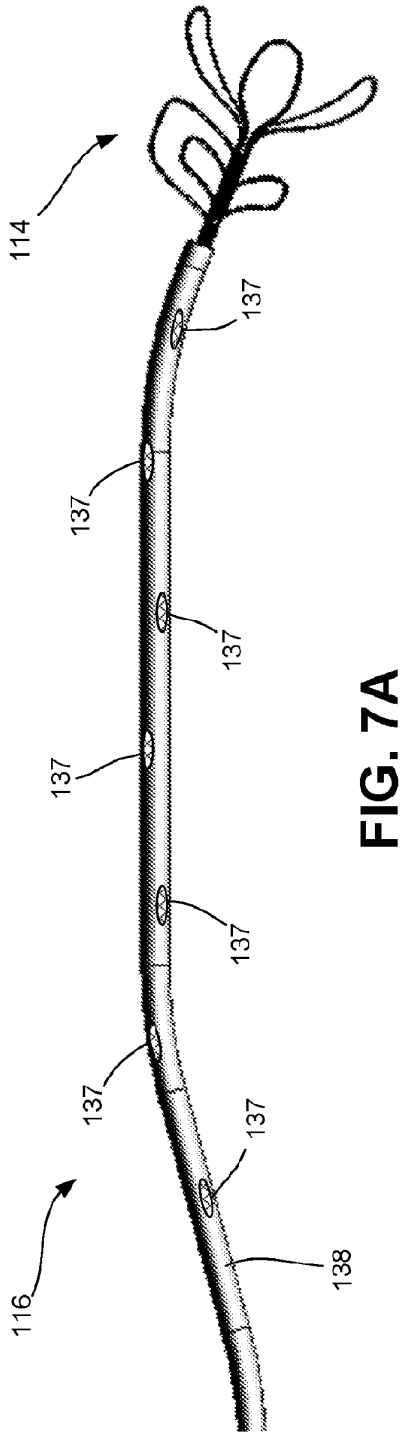


FIG. 7A

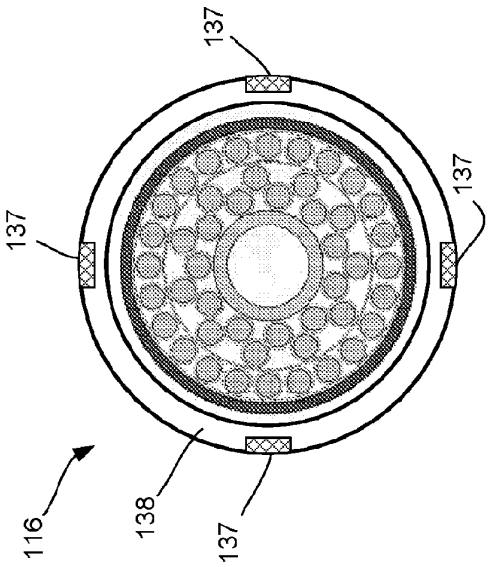


FIG. 7B

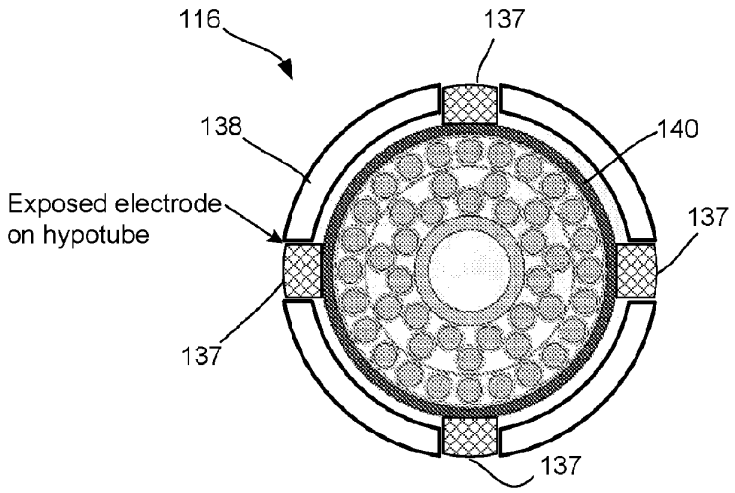

116
137
138
140
Exposed electrode on hypotube
137
137
137

FIG. 7C

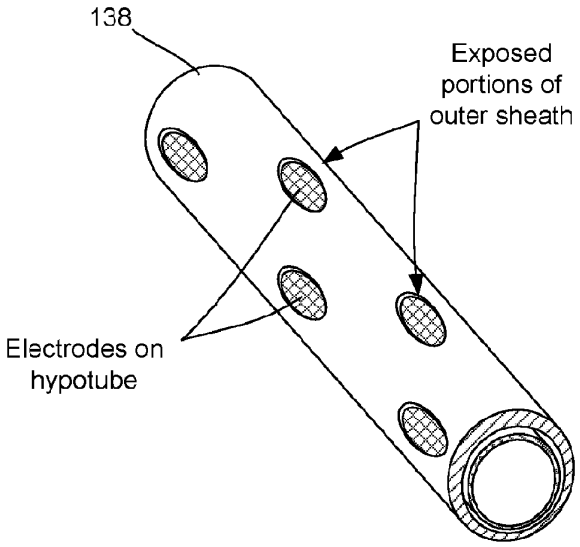

138
Exposed portions of outer sheath
Electrodes on hypotube

FIG. 7D

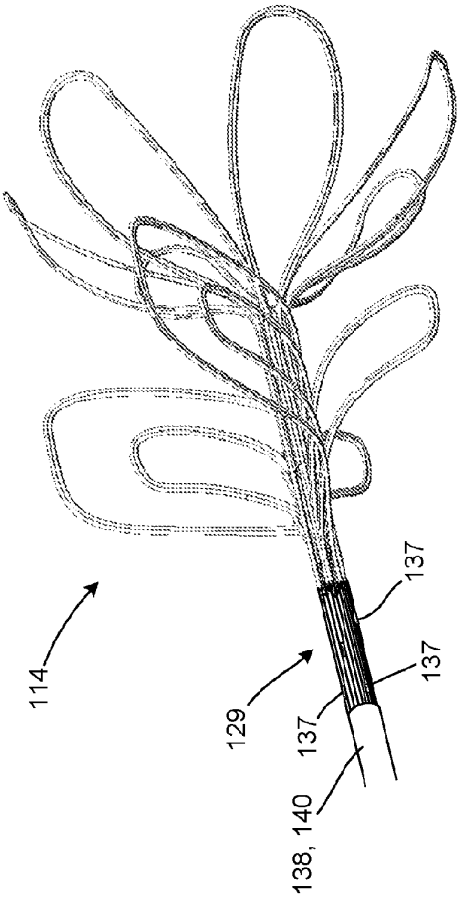


FIG. 7F

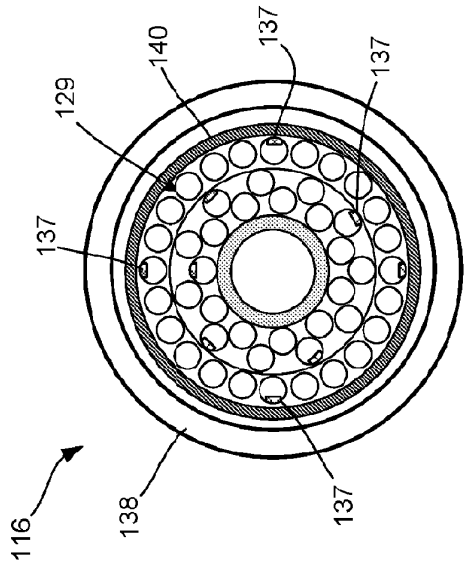


FIG. 7E

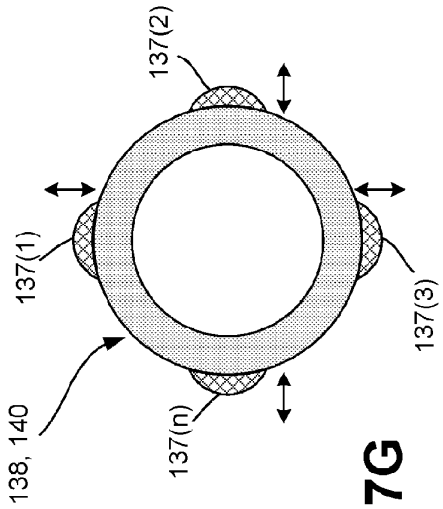


FIG. 7G

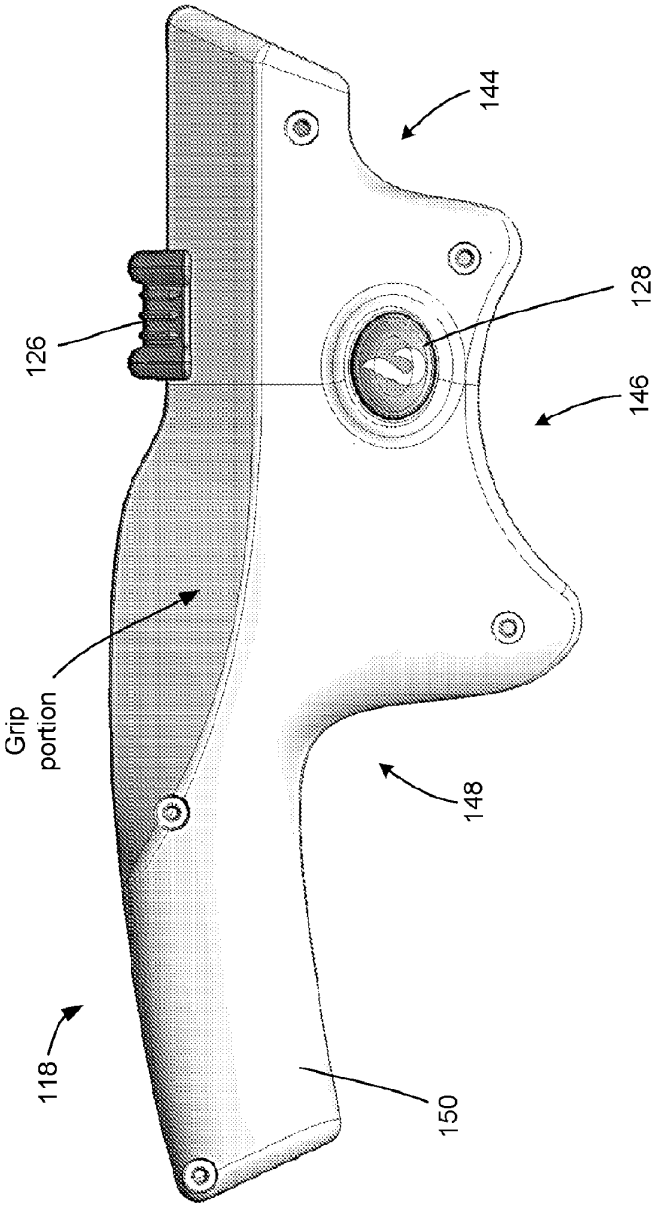


FIG. 8

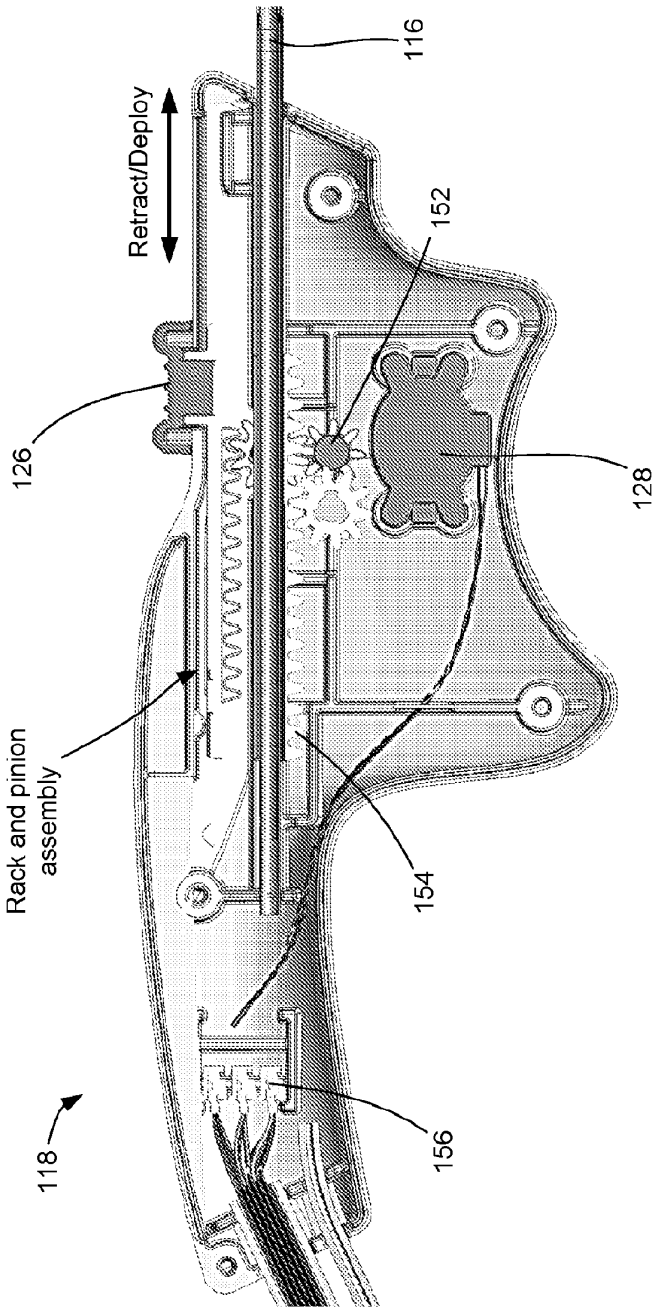

116
Retract/Deploy
152
126
128
Rack and pinion assembly
154
156
118

FIG. 9

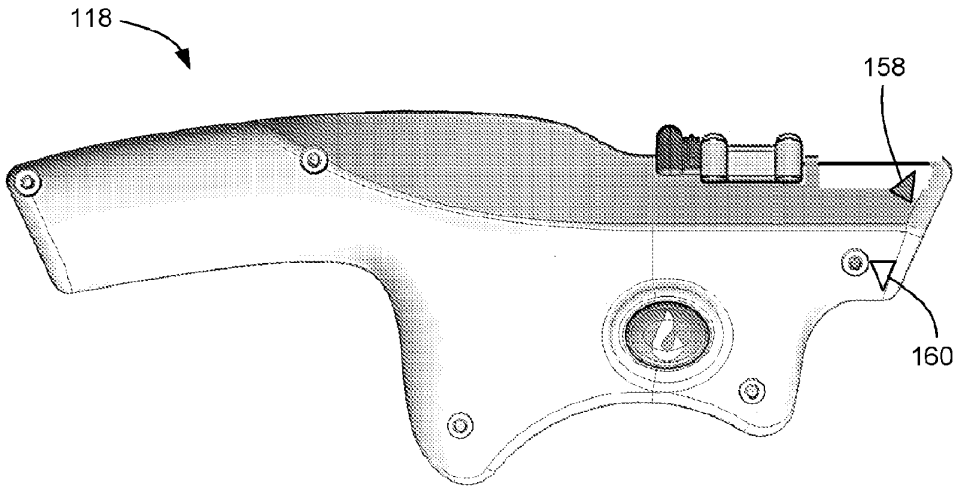


FIG. 10

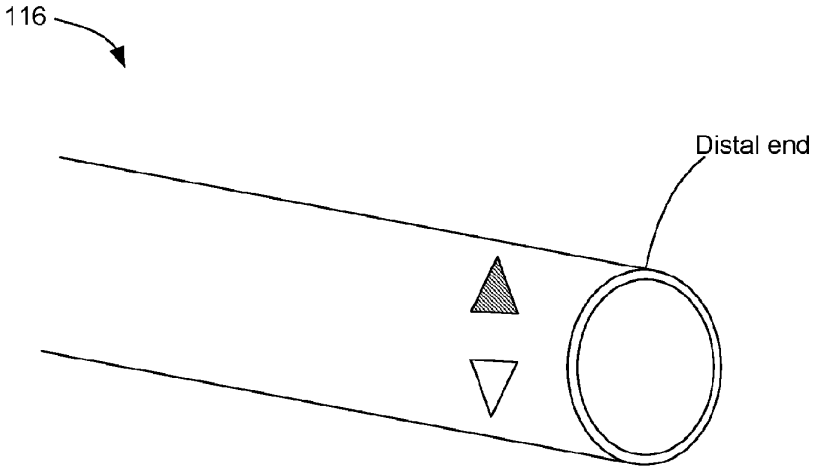


FIG. 11

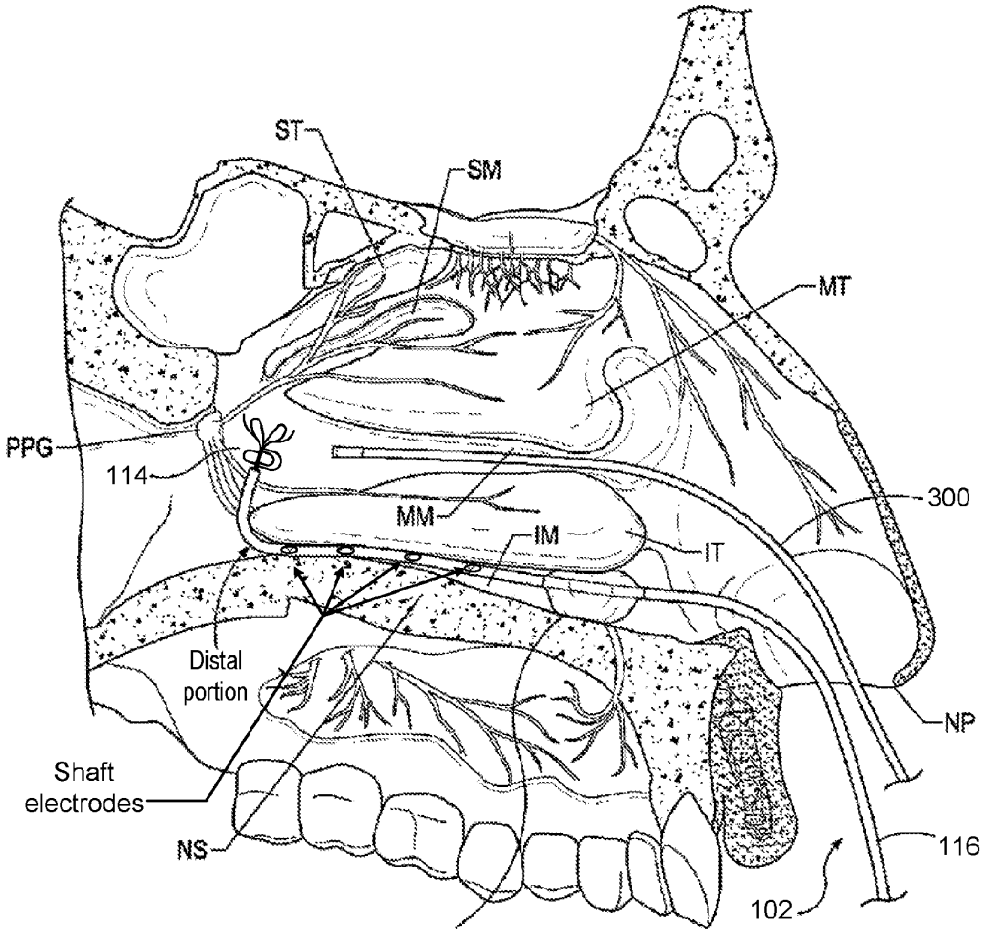

ST
SM
MT
PPG
114
300
MM
IM
IT
Distal
portion
NP
Shaft
electrodes
NS
116
102

FIG. 12

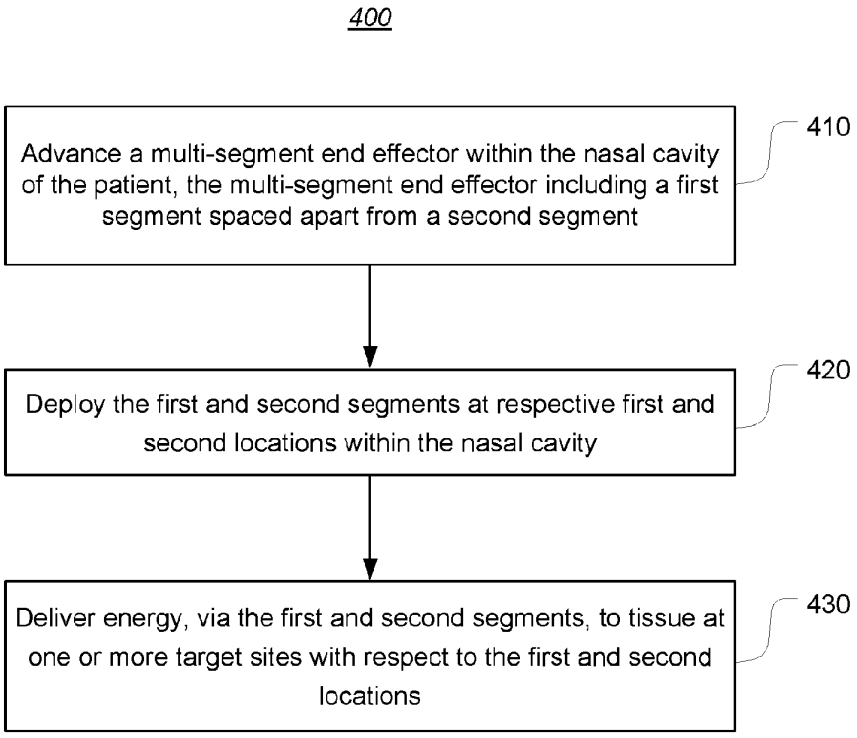

400
Advance a multi-segment end effector within the nasal cavity of the patient, the multi-segment end effector including a first segment spaced apart from a second segment
410
Deploy the first and second segments at respective first and second locations within the nasal cavity
420
Deliver energy, via the first and second segments, to tissue at one or more target sites with respect to the first and second locations
430

FIG. 13

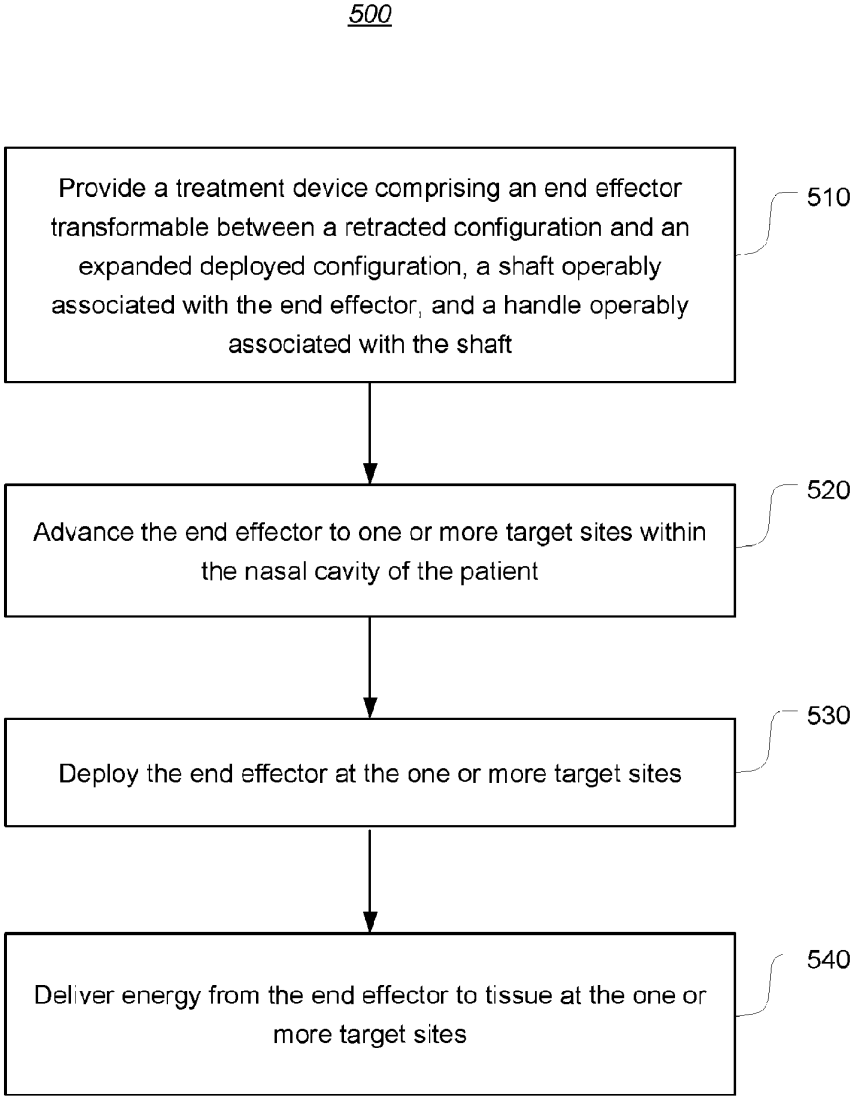

500
Provide a treatment device comprising an end effector transformable between a retracted configuration and an expanded deployed configuration, a shaft operably associated with the end effector, and a handle operably associated with the shaft
510
Advance the end effector to one or more target sites within the nasal cavity of the patient
520
Deploy the end effector at the one or more target sites
530
Deliver energy from the end effector to tissue at the one or more target sites
540

FIG. 14

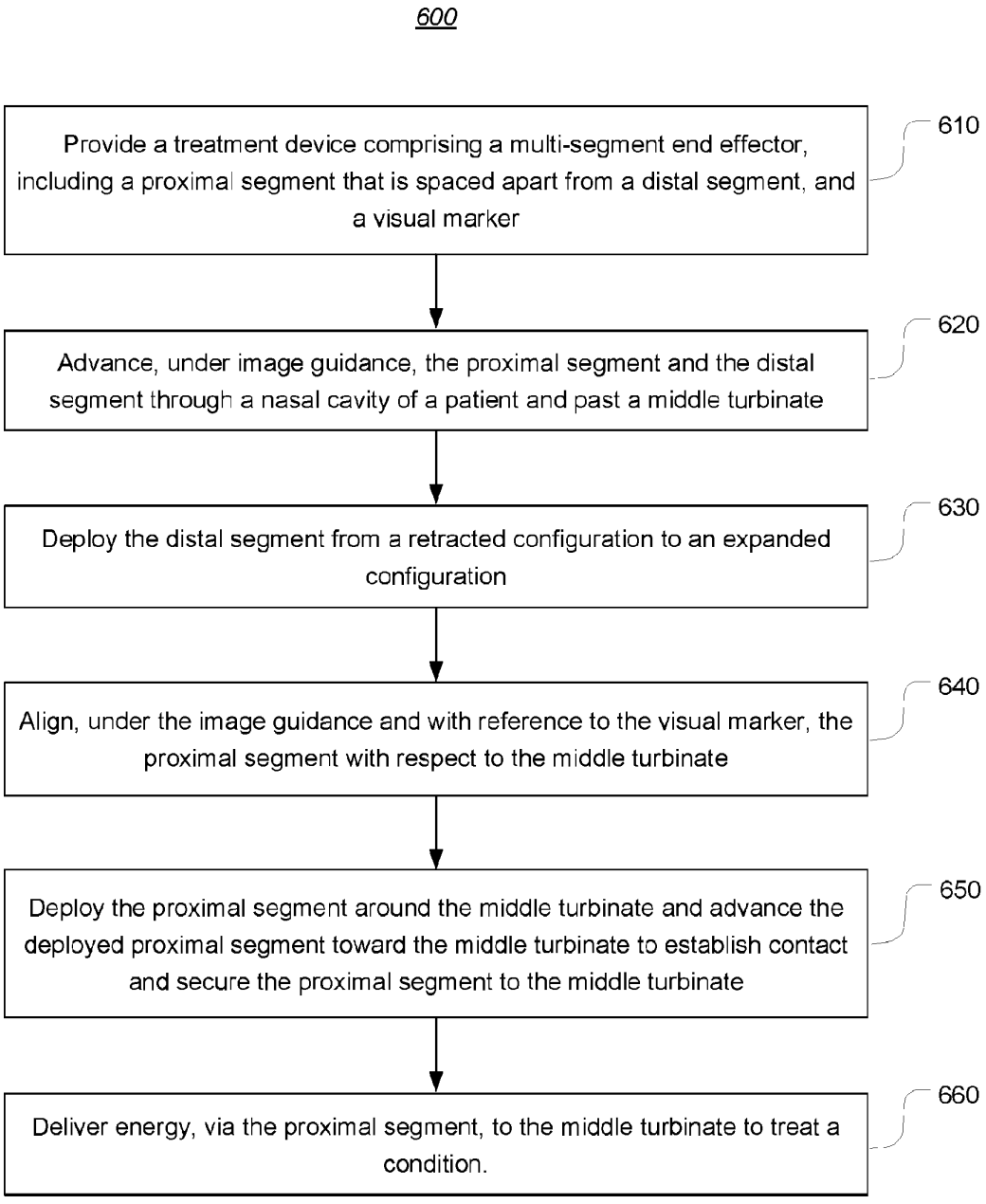

600
Provide a treatment device comprising a multi-segment end effector, including a proximal segment that is spaced apart from a distal segment, and a visual marker
610
Advance, under image guidance, the proximal segment and the distal segment through a nasal cavity of a patient and past a middle turbinate
620
Deploy the distal segment from a retracted configuration to an expanded configuration
630
Align, under the image guidance and with reference to the visual marker, the proximal segment with respect to the middle turbinate
640
Deploy the proximal segment around the middle turbinate and advance the deployed proximal segment toward the middle turbinate to establish contact and secure the proximal segment to the middle turbinate
650
Deliver energy, via the proximal segment, to the middle turbinate to treat a condition.
660

FIG. 15

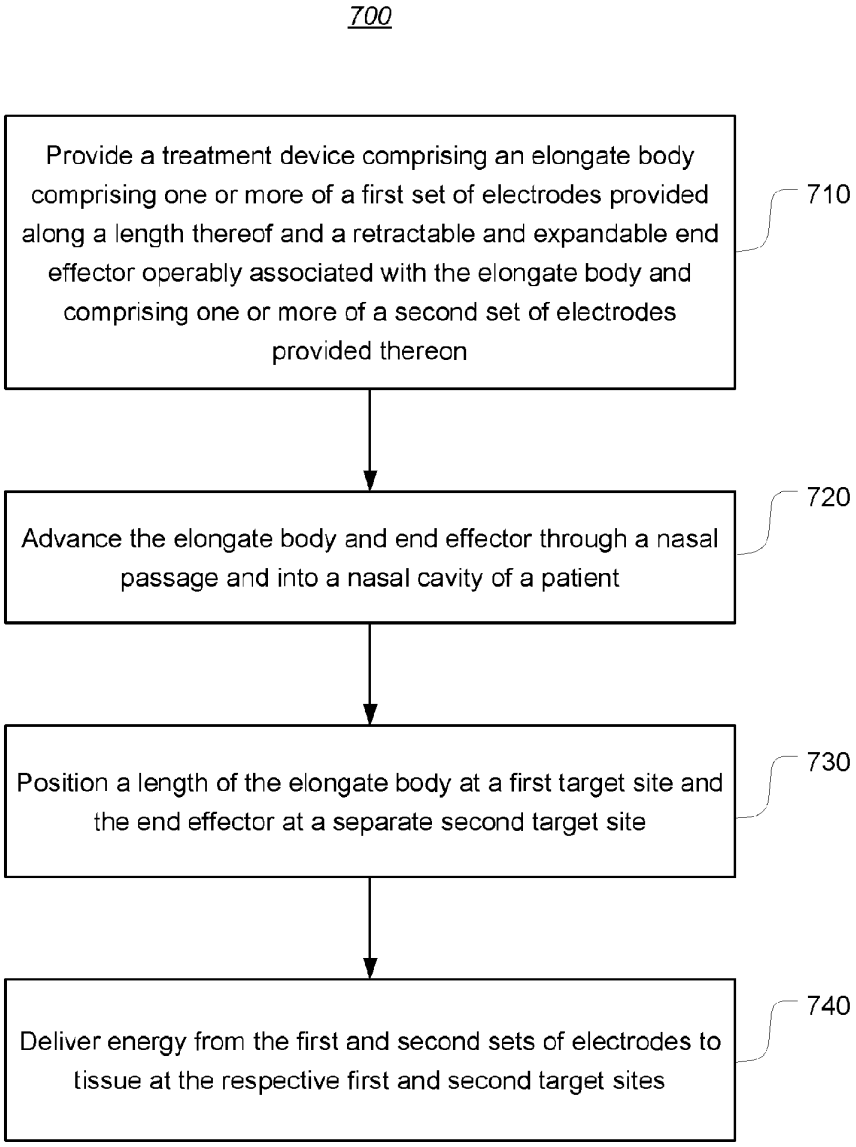

700
Provide a treatment device comprising an elongate body comprising one or more of a first set of electrodes provided along a length thereof and a retractable and expandable end effector operably associated with the elongate body and comprising one or more of a second set of electrodes provided thereon
710
Advance the elongate body and end effector through a nasal passage and into a nasal cavity of a patient
720
Position a length of the elongate body at a first target site and the end effector at a separate second target site
730
Deliver energy from the first and second sets of electrodes to tissue at the respective first and second target sites
740

FIG. 16

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000234

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/02 A61B18/08 A61B18/14
ADD. A61B18/00

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)
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, BIOSIS, COMPENDEX, INSPEC, 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 2016/331459 A1 (TOWNLEY DAVID [IE] ET AL) 17 November 2016 (2016-11-17) cited in the application	1-8
Y	paragraphs [0002], [0058], [0066], [0102]; figures 1-5,10	9,10
Y	US 2017/151014 A1 (PERFLER ENRICO [IT]) 1 June 2017 (2017-06-01) paragraphs [0101] - [0104]; figures 11,12	9,10
A	US 2018/125560 A1 (SAADAT VAHID [US] ET AL) 10 May 2018 (2018-05-10) cited in the application the whole document	1-10

☐ 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 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 July 2021	06/08/2021

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	Aronsson, Fredrik

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000234

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.: 11-20
because they relate to subject matter not required to be searched by this Authority, namely:

The subject-matter of claims 11-20 refers to a surgical and therapeutic treatment.According to the PCT neither search (Rule 39.1(iv) PCT) nor examination (Rule 67.1(iv) PCT) is required for such subject-matter.

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.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000234

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最終頁に続く

(54)【発明の名称】患者の鼻腔内治療を促進するためのシステムおよび装置

(57)【要約】
患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するためのシステムが開示される。同様に、即時システムが、急性痛状態に対処するために効果的であり、医師助手、看護師、および他の十分な訓練を受けた施術者によって行われるほど十分に洗練されている。関与する装置は、実施形態において、シースハブと、カテーテルハブと、抑止要素と、係合要素とを含む。抑止要素と係合要素との間の係合は、カテーテルハブに対するシースハブの回転を防止する。

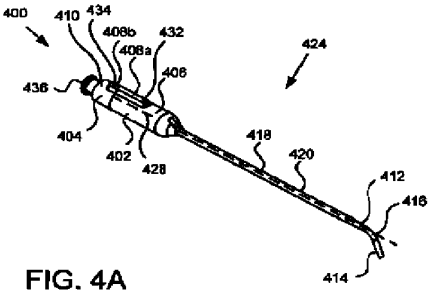


FIG. 4A

【特許請求の範囲】
【請求項１】
患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進する装置であって、
内面に対向する外面を有する、シースハブであって、前記内面は、カテーテルハブ受容空間を画定する、シースハブと、
前記カテーテルハブ受容空間内で摺動可能に受容されるカテーテルハブであって、前記カテーテルハブは、前記シースハブの長手方向軸に沿って位置付け可能である、カテーテルハブと、
前記カテーテルハブおよび前記シースハブのうちの一方の上の抑止要素と、
前記カテーテルハブおよび前記シースハブのうちの他方の上の係合要素であって、前記抑止要素は、前記カテーテルハブが前記シースハブの前記長手方向軸に沿って再配置されたときに前記係合要素に連続的に係合し、前記抑止要素と前記係合要素との間の係合は、前記カテーテルハブに対する前記シースハブの回転を防止する、係合要素と、
を組み合わせで備える、装置。
【請求項２】
カテーテルと、回転配向インジケータとをさらに備える請求項１に記載の装置であって、前記カテーテルは、前記カテーテルハブに連結され、前記カテーテルの少なくとも一部分は、内部屈曲部を含み、前記回転配向インジケータは、前記カテーテルの前記内部屈曲部の回転配向を識別する、装置。
【請求項３】
前記回転配向インジケータは、前記シースハブおよび前記カテーテルハブのうちの少なくとも１つに沿って長手方向に延在する、隆起部を備える、請求項２に記載の装置。
【請求項４】
前記カテーテルハブに連結されるカテーテルをさらに備える請求項２に記載の装置であって、前記カテーテルは挿入端および連結端を備え、前記挿入端は、前記カテーテルの長手方向軸に対して内部屈曲部を有し、前記回転配向インジケータは、前記カテーテルの前記内部屈曲部の配向を識別する、装置。
【請求項５】
前記シースハブに連結されるシースと、前記カテーテルハブに連結されるカテーテルとをさらに備える請求項１に記載の装置であって、前記カテーテルは、前記シース内で受容され、前記カテーテルは、挿入端と、連結端とを備え、前記挿入端は、前記カテーテルの長手方向軸に対して内部屈曲部を有し、前記カテーテルハブは、挿入位置と拡張位置との間で位置付け可能であり、前記シースは、前記カテーテルハブが前記拡張位置に位置付けられたときに、前記カテーテルの前記内部屈曲部をまっすぐにし、前記カテーテルハブは、前記シースの導入端に対する前記カテーテルの前記挿入端の位置を示す、少なくとも１つの深度インジケータを含む、装置。
【請求項６】
前記カテーテルハブに連結されるカテーテルと、前記シースハブに連結されるシースとをさらに備える請求項１に記載の装置であって、前記カテーテルは、前記シース内で受容され、前記カテーテルハブは、挿入位置と拡張位置との間で位置付け可能であり、前記カテーテルは、先端が丸みを帯びるように湾曲した先端を有する、挿入端を備え、前記シースは、頂点まで傾斜している最外縁を有する、導入端を備え、前記頂点は、前記カテーテルハブが前記拡張位置に位置付けられたときに、前記カテーテルの前記丸みを帯びた先端の湾曲の開始と整合する、装置。
【請求項７】
前記頂点と前記カテーテルの前記丸みを帯びた先端の前記湾曲の前記開始との間の移行部は、前記カテーテルハブが前記拡張位置に位置付けられたときに連続的である、請求項６に記載の装置。
【請求項８】
前記カテーテルハブに連結されるカテーテルをさらに備える請求項１に記載の装置であ

って、前記カテーテルは、挿入端および連結端を備え、前記挿入端は、前記カテーテルの長手方向軸に対して内部屈曲部を有し、前記カテーテルの前記挿入端の先端は、球状である、装置。

【請求項９】

前記抑止要素は、前記カテーテルハブの外面および前記シースハブの内面のうちの一方に連結され、そこから垂直に延在するフランジを備え、前記係合要素は、前記シースハブの前記内面および前記カテーテルハブの前記外面のうちの他方に沿って縦方向に延在する陥凹を備え、前記フランジは、前記カテーテルハブが前記シースハブの前記長手方向軸に沿って再配置されたときに、前記陥凹内に位置付けられ、それに沿って移動する、請求項１に記載の装置。

【請求項１０】

前記カテーテルハブおよび前記シースハブのうちの１つに連結される停止要素をさらに備える請求項１に記載の装置であって、前記カテーテルハブは、挿入位置と拡張位置との間で前記シースハブの前記長手方向軸に沿って位置付け可能であり、前記停止要素は、前記抑止要素に係合して、前記カテーテルハブが前記カテーテルハブ受容空間から除去されることを止めるように構成される、装置。

【請求項１１】

急性痛状態に対処するためのシステムであって、

内面に対向する外面を有する、シースハブであって、前記内面は、カテーテルハブ受容空間を画定する、シースハブと、

前記カテーテルハブ受容空間内で摺動可能に受容されるカテーテルハブであって、前記カテーテルハブは、前記シースハブの長手方向軸に沿って位置付け可能である、カテーテルハブと、

前記カテーテルハブおよび前記シースハブのうちの一方の上の抑止要素と、

前記カテーテルハブおよび前記シースハブのうちの他方の上の係合要素であって、前記抑止要素は、前記カテーテルハブが前記シースハブの前記長手方向軸に沿って再配置されたときに、前記係合要素に連続的に係合し、前記抑止要素と前記係合要素との間の係合は、前記カテーテルハブに対する前記シースハブの回転を防止する、係合要素と、

前記シースハブおよび前記カテーテルハブのうちの少なくとも１つの回転配向を識別する、回転配向インジケータと、

を備える、システム。

【請求項１２】

前記回転配向インジケータは、前記シースハブおよび前記カテーテルハブのうちの少なくとも１つに沿って縦方向に延在する、隆起部を備え、前記隆起部は、前記シースハブおよび前記カテーテルハブのうちの少なくとも１つの前記回転配向を視覚的および触覚的に識別する、請求項１１に記載のシステム。

【請求項１３】

前記カテーテルハブに連結されるカテーテルをさらに備える請求項１１に記載のシステムであって、前記カテーテルは挿入端および連結端を備え、前記挿入端は、前記カテーテルの長手方向軸に対して内部屈曲部を有し、前記回転配向インジケータは、前記カテーテルの前記内部屈曲部の配向を識別する、システム。

【請求項１４】

前記抑止要素は、前記カテーテルハブの外面および前記シースハブの内面のうちの一方に連結され、そこから垂直に延在するフランジを備え、前記係合要素は、前記シースハブの前記内面および前記カテーテルハブの前記外面のうちの他方に沿って縦方向に延在する陥凹を備え、前記フランジは、前記カテーテルハブが前記シースハブの前記長手方向軸に沿って再配置されたときに、前記陥凹内に位置付けられ、それに沿って移動する、請求項１１に記載のシステム。

【請求項１５】

前記シースハブに連結されるシースをさらに備える請求項１１に記載のシステムであっ

て、前記カテーテルハブは、挿入位置と拡張位置との間に位置付け可能であり、前記シースは、前記カテーテルハブが前記拡張位置に位置付けられたときに、前記カテーテルの前記内部屈曲部をまっすぐにする、システム。

【請求項１６】

前記カテーテルの前記挿入端の先端は、前記先端が丸みを帯びるように湾曲しており、前記シースは、導入端と、接続端とを備え、前記導入端の最外縁は、頂点まで傾斜し、前記頂点は、前記カテーテルハブが前記シースハブ内で前記拡張位置に再配置されたときに、前記カテーテルの前記丸みを帯びた先端の湾曲の開始と整合し、前記カテーテルハブは、前記シースの前記導入端に対する前記カテーテルの前記挿入端の位置を示す、少なくとも１つの深度インジケータを含む、請求項１５に記載のシステム。

【請求項１７】

前記カテーテルは、
頭頸部癌、
複合性局所疼痛症候群、
反射性交感神経性ジストロフィ、
血管運動神経性鼻炎、
口腔および顎顔面手術における術前および術後感覚脱失、
群発性頭痛、
頭痛、
頸部けいれん、
任意のレベルの椎間板疾患またはヘルニア、
腰痛、
腰仙部けいれん、
梨状筋けいれん症候群、
痙性（けいれん性）斜頸、
ＳＰＧ神経痛（スルダー症候群）、
三叉神経痛（疼痛性チック）、
帯状疱疹後神経痛、
自律神経痛、
非定型顔面痛、
椎間板膨隆、
腰仙椎間板、
カウザルギー、
反射性交感神経性ジストロフィ（ＲＳＤ）、
頚椎症、
片頭痛、
副鼻洞性頭痛、
脳脊髄液（ＣＳＦ）漏出頭痛、
慢性副鼻腔炎、
緊張性頭痛、
筋筋膜疼痛症候群、
圧迫神経、
坐骨神経痛、
椎間板脱出、
副鼻腔痛、
顎関節症候群（ＴＭＪ）、
むち打ち、
アレルギー性鼻炎、
血管運動神経性鼻炎、
喘息、

ベル麻痺（顔面神経麻痺）、
骨痛、
癌疼痛、
気管支けいれん、
慢性気管支炎、
月経困難症、
子宮内膜症、
線維筋痛症、
けいれんを伴う多発性硬化症、
末梢神経障害（神経障害性疼痛）、
レイノー現象、
関節リウマチ（発赤）、
帯状疱疹（帯状ヘルペス）、
脊髄狭窄、
慢性疲労症候群、
慢性吃逆、
糖尿病性神経障害、
多汗症、
脳圧低下頭痛、
幻肢／歯痛、
感覚異常、
反復性ストレス損傷、および
耳鳴（低頻度）
のうちの少なくとも１つのための適用に対処するように設計されている、
請求項１６に記載のシステム。
【請求項１８】
前記システムは、ナース・プラクティショナー、医師助手、外科医、神経科医、および介入医師の群から選択される医療専門家によって施されるように設計されている、請求項１７に記載のシステム。
【請求項１９】
患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するためのシステムであって、
シースハブ、カテーテルハブ、抑止要素、および係合要素によって画定される除去可能なツールを組み合わせで備え、
使用中に、前記システムは、患者の鼻腔で解剖学的に制約された空間の中へ前進させられ、
それにより、使用中に、前記システムは、少なくとも前記蝶口蓋／翼口蓋陥凹内の標的組織部位に隣接して配置され、
薬学、生物学、電気／電子刺激、音波、機械およびパルス状またはストリーム状エネルギーから本質的になるその他のものから群より選択される、少なくとも１つの医療処置が、少なくとも前記標的組織部位に送達される、
システム。
【請求項２０】
請求項１７に記載の患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するためのシステムであって、前記システムは、使用中に、神経科医、神経外科医、介入医師、外科医、ナース・プラクティショナー、および医師助手から本質的に成る群より選択される、少なくとも１人の医療専門家によって行われる、システム。
【発明の詳細な説明】
【技術分野】
【０００１】
本主題は、自律および侵害受容神経遮断に関し、より具体的には、蝶口蓋／翼口蓋神経

節の遮断に関する。具体的には、本主題は、使用中に、多数の適応症に起因する疼痛を軽減、緩和、および改善する、システムおよび装置を提示する。

【背景技術】

【０００２】

自律神経痛は、自律神経系の機能の異常により生じる、一種の神経痛である。自律神経痛があると、神経節と呼ばれる神経群の異常が、臓器または体内の領域に疼痛を引き起こす。自律神経介在疼痛を治療するために、医師は、身体の特定の領域への注射または薬剤の適用により、神経節を遮断することができる。急性痛を治療的に処置するために、医師は、罹患神経節に局所麻酔薬を注射または適用する。この種類の治療は、神経ブロックと呼ばれ得る。

【０００３】

１９０８年に、Ｇｒｅｅｎｆｉｅｌｄ Ｓｌｕｄｅｒ医学博士が、「Ｔｈｅ ｒｏｌｅ ｏｆ ｔｈｅ ｓｐｈｅｎｏｐａｌｉｔｉｎｅ ｇａｎｇｌｉｏｎ ｉｎ ｎａｓａｌ ｈｅａｄａｃｈｅｓ」という論文をＮｅｗ Ｙｏｒｋ Ｍｅｄｉｃａｌ Ｊｏｕｒｎａｌに発表した。彼は、蝶口蓋神経節（ＳＰＧ）にコカインを注射して、ある重度の再発性頭痛を治療するために、顔の側面を通して長い針を使用することを主張した。医学の１世紀以上にわたって、蝶口蓋神経節遮断（ＳＰＧＢ）が頭痛管理において有益なツールであるＳｌｕｄｅｒの基本前提が立証されてきた。しかしながら、本教示の前に、ツールの不足が同治療に存在する。

【０００４】

ＳＰＧは、鼻腔の後部の内側を覆う薄い組織の直下に静置する、神経細胞の集合である。それを通過する神経接続により、ＳＰＧは、種々の種類の頭痛で本質的な役割を果たす。ＳＰＧを通したインパルス伝導の一時的な中断が、しばしば頭痛を中断し、時には、頭痛患者に長期緩和を提供することができる。

【０００５】

発表された文献の中でＳＰＧＢに応答することが示されている他の症状は、本明細書で論議され、以下で請求されるように、いくつかある適応症の中でも、三叉神経痛、歯痛、分娩後頸痛および背痛、複合性局所疼痛症候群、帯状ヘルペス（帯状疱疹）、顎関節（ＴＭＪ）痛、および原発性多汗症を含む。

【０００６】

再発する重度の頭痛を経験する者が苦しむ個人的な疼痛は別として、社会にとっての膨大な財務費用は、推定または把握することが困難である。米国での３千万人の片頭痛患者だけで、年間の直接医療費は、＄１２０億を超えると推定され、雇用主に負担をかける生産性の損失はさらに＄１２０億である。これらの数字は、世界の他の地域、または世界保健機関の頭痛分類方式で見出される他の２４種類の頭痛を含まない。

【０００７】

人口の推定４～５％が、定義上、少なくとも３ヶ月にわたって、少なくとも１ヶ月に少なくとも１５日間、個人の機能する能力に影響を及ぼす、慢性的な日常の頭痛に苦しんでいる。これらの患者のうち、３０％は、比較的安価な薬剤で管理され、１７％は、＄５００／月を超える薬理学的投薬計画を必要とし、半分以上が、現代医学の事実上の失敗に苦しみ続けている。

【０００８】

頭痛の発症または持続時間を低減させる任意の介入は、個人の苦痛を劇的に低減させ、かつ患者、会社、および政府の大金を節約する可能性を有する。カテーテルシステムのＳｐｈｅｎｏＣａｔｈ™ブランドは、全体を通して説明され、以下で請求されるように、単純、安全、かつ安価な介入を提供する。

【０００９】

ＳＰＧ／翼口蓋神経節は、主に、中鼻甲介の後方にある翼口蓋窩内で頭部の中心に位置する、神経構造である。ＳＰＧ／翼口蓋神経節は、脳の外側の頭部内に交感神経ニューロンの最大集合を備える。ＳＰＧ／翼口蓋神経節は、神経インパルスを相互作用させ、頭部

の自律神経または副交感神経経路の大部分に方向付ける。したがって、この構造への任意の異常または損傷が、重度の疼痛を引き起こし得る。ＳＰＧ／翼口蓋神経節の神経ブロックは、頭痛から腰痛に及ぶ種々の疼痛症状を緩和し得る。加えて、ＳＰＧ／翼口蓋神経節および周辺構造の局所麻酔遮断、および／または他の薬理学的増強あるいは機械的改変によって、頭痛障害および他の神経学的症状等の他の疾患プロセスを抑止または改善することができる。

【００１０】

残念ながら、ＳＰＧ／翼口蓋神経節の解剖学的位置により、該構造は、局所麻酔液で遮断することが非常に困難である。ＳＰＧ／翼口蓋神経節の解剖学的な場所は、多くの極めて重要かつ繊細な中脳構造に危険なほど近い。麻酔薬をＳＰＧ／翼口蓋神経節に投与するために、直接針配置を蛍光透視誘導下で採用することができるが、大抵の施術者は、技術的困難かつ異常な針配置という極度の危険により、該手技を行おうとしないであろう。

【００１１】

従来のデバイスでＳＰＧ／翼口蓋神経節を治療するようにＳＰＧ／翼口蓋陥凹にアクセスすることは、従来のデバイスが、典型的には、蝶口蓋／翼口蓋陥凹にアクセスするための曲率を含まないという点で困難である。さらに、たとえ従来の針が蝶口蓋／翼口蓋陥凹にアクセスするように湾曲していても、いったん湾曲した針が患者の鼻腔に挿入されると、医師または他の医療専門家は、針の湾曲の方向を識別できないであろう。蛍光透視誘導がないと、針の挿入端が、極めて重要かつ繊細な中脳構造に接触および／または損傷し得る。現在まで、この制限が、サービス提供者および患者の両方が大幅に関与することを制限してきた。

【発明の概要】

【課題を解決するための手段】

【００１２】

前述の論議から、段階的変化のために、すなわち、それを成功させることができる、トップレベルの片手で数えられる程度の医療専門家以外の者によっても、やがて、安全に行うことができるようになる、患者の鼻腔内治療を促進するための装置およびシステムの必要性が存在することが明白となるはずである。有益なこととして、そのような装置およびシステムは、薬剤を蝶口蓋／翼口蓋神経節に直接投与するであろう。

【００１３】

本主題は、現在の最新技術に応じて、具体的には、現在利用可能な鼻腔内治療装置、システム、および方法によって、まだ完全には解決されていない問題および必要性に応じて、開発されている。したがって、本主題は、当技術分野における上記の欠点の多くまたは全てを克服する、患者の鼻腔内治療のための装置およびシステムを提供するように開発されている。

【００１４】

患者のＳＰＧ／翼口蓋陥凹の鼻腔内治療を促進する装置は、ある実施形態では、シースハブと、カテーテルハブと、抑止要素と、係合要素とを含む。シースハブは、内面に対向する外面を有する。内面は、カテーテルハブ受容空間を画定する。カテーテルハブは、カテーテルハブ受容空間内で摺動可能に受容され、シースハブの長手方向軸に沿って位置付け可能である。抑止要素は、カテーテルハブおよびシースハブのうちの一方の上に位置付けられ、係合要素は、カテーテルハブおよびシースハブのうちの他方の上に位置付けられる。抑止要素は、カテーテルハブがシースハブの長手方向軸に沿って位置付けられたときに係合要素に連続的に係合する。抑止要素と係合要素との間の係合は、カテーテルハブに対するシースハブの回転を防止する。

【００１５】

本装置は、一実施形態では、カテーテルと、回転配向インジケータとを含む。カテーテルは、カテーテルハブに連結され、カテーテルの少なくとも一部分は、内部屈曲部を含む。回転配向インジケータは、カテーテルの内部屈曲部の回転配向を識別する。ある実施形態では、回転配向インジケータは、シースハブおよびカテーテルハブのうちの少なくとも

１つに沿って長手方向に延在する、隆起部を備える。他の実施形態では、回転配向インジケータは、カテーテルの内部屈曲部の回転配向の視覚的指示のみを提供する。

【００１６】

実施形態によれば、カテーテルは、挿入端と、連結端とを含む。そのような実施形態では、挿入端は、カテーテルの長手方向軸に対する内部屈曲部を含んでもよく、回転配向インジケータは、カテーテルの内部屈曲部の回転配向を識別する。

【００１７】

ある実施形態では、本装置は、シースハブに連結されるシースと、カテーテルハブに連結され、シース内で受容されるカテーテルとを含む。カテーテルは、挿入端と、連結端とを含み、挿入端は、カテーテルの長手方向軸に対する内部屈曲部を有する。そのような実施形態では、カテーテルハブは、挿入位置と拡張位置との間で位置付け可能である。カテーテルハブが拡張位置に位置付けられると、シースは、カテーテルの内部屈曲部をまっすぐにする。

【００１８】

カテーテルは、いくつかの実施形態では、先端が丸みを帯びるように湾曲した先端を有する、挿入端を含む。シースは、頂点まで傾斜している最外縁を有する、導入端を含む。そのような実施形態では、カテーテルハブが拡張位置に位置付けられたときに、頂点は、カテーテルの丸みを帯びた先端の湾曲の開始と整合する。ある実施形態では、頂点とカテーテルの丸みを帯びた先端の湾曲の開始との間の移行部は、カテーテルハブが拡張位置に位置付けられたときに連続的である。一実施形態では、カテーテルの挿入端の先端は、球状である。

【００１９】

抑止要素は、ある実施形態では、カテーテルハブの外面またはシースハブの内面のいずれか一方に連結され、そこから垂直に延在するフランジである。そのような実施形態では、係合要素は、シースハブの内面またはカテーテルハブの外面の他方に沿って縦方向に延在する陥凹である。フランジは、カテーテルハブがシースハブの長手方向軸に沿って再配置されたときに、陥凹内に位置付けられ、それに沿って移動する。

【００２０】

ある実施形態では、本装置は、カテーテルハブまたはシースハブのいずれか一方に連結される停止要素を含む。停止要素は、抑止要素に係合して、カテーテルハブがカテーテルハブ受容空間から除去されることを止めるように構成される。一実施形態では、停止要素は、カテーテルハブが拡張位置に位置付けられたときに、シースの頂点を、カテーテルの丸みを帯びた先端の湾曲の開始と整合させるように構成される。

【００２１】

ある実施形態では、本装置は、シースハブと、カテーテルハブと、抑止要素と、係合要素と、回転配向インジケータとを含む。シースハブは、内面に対向する外面を有する。内面は、カテーテルハブ受容空間を画定する。カテーテルハブは、カテーテルハブ受容空間内で摺動可能に受容され、シースハブの長手方向軸に沿って位置付け可能である。抑止要素は、カテーテルハブまたはシースハブのいずれか一方に連結されるか、またはその上に位置付けられる。係合要素は、カテーテルハブおよびシースハブのうちの他方に連結されるか、またはその上に位置付けられる。抑止要素は、カテーテルハブがシースハブの長手方向軸に沿って再配置されたときに、係合要素に連続的に係合する。抑止要素と係合要素との間の係合は、カテーテルハブに対するシースハブの回転を防止する。回転配向インジケータは、シースハブおよびカテーテルハブのうちの少なくとも１つの回転配向を識別する。

【００２２】

ある実施形態では、転配向インジケータは、シースハブおよびカテーテルハブのうちの少なくとも１つに沿って縦方向に延在する、隆起部である。隆起部は、シースハブおよびカテーテルハブのうちの少なくとも１つの回転配向を視覚的および触覚的の両方で識別する。

【００２３】
実施形態によれば、本装置は、カテーテルハブに連結されるカテーテルを含む。カテーテルは、挿入端および連結端を有し、挿入端は、カテーテルの長手方向軸に対する内部屈曲部を有する。そのような実施形態では、回転配向インジケータは、カテーテルの内部屈曲部の配向を識別する。
【００２４】
抑止要素は、ある実施形態では、カテーテルハブの外面またはシースハブの内面のいずれか一方に連結され、そこから垂直に延在するフランジを含む。そのような実施形態では、係合要素は、シースハブの内面およびカテーテルハブの外面のうちの他方に沿って縦方向に延在する陥凹を含む。抑止要素のフランジは、カテーテルハブがシースハブの長手方向軸に沿って再配置されたときに、係合要素の陥凹内に位置付けられ、それに沿って移動する。
【００２５】
ある実施形態では、本装置はさらに、シースハブに連結されるシースを含み、カテーテルハブは、挿入位置と拡張位置との間に位置付け可能である。拡張位置では、シースは、カテーテルの内部屈曲部をまっすぐにする。一実施形態では、カテーテルの挿入端の先端は、先端が丸みを帯びるように湾曲した。そのような実施形態では、シースは、導入端と、接続端とを含む。導入端の最外縁は、頂点まで傾斜し、頂点は、カテーテルハブがシースハブ内で拡張位置に再配置されたときに、カテーテルの丸みを帯びた先端の湾曲の開始と整合する。
【００２６】
シースハブと、カテーテルハブと、抑止要素と、係合要素と、シースと、カテーテルとを含む、患者のＳＰＧ／翼口蓋陥凹の鼻腔内治療を促進するための装置も開示される。シースハブは、内面に対向する外面を有する。内面は、カテーテルハブ受容空間を画定し、カテーテルハブは、カテーテルハブ受容空間内で摺動可能に受容される。カテーテルハブは、シースハブの長手方向軸に沿って位置付け可能である。抑止要素は、カテーテルハブまたはシースハブのいずれか一方の上に配置される。係合要素は、カテーテルハブまたはシースハブの他方の上または中に位置付けられる。抑止要素は、カテーテルハブが挿入位置と拡張位置との間でシースハブの長手方向軸に沿って再配置されたときに、係合要素に連続的に係合する。シースは、シースハブに連結され、最外縁を有する、導入端を含む。カテーテルは、シース内で受容され、カテーテルハブに連結される。カテーテルは、先端が丸みを帯びるように湾曲した先端を有する、挿入端を含む。シースの最外縁は、カテーテルハブが拡張位置に位置付けられたときに、カテーテルの丸みを帯びた先端の湾曲の開始と整合する。
【００２７】
ある実施形態では、シースの導入端の最外縁は、頂点まで傾斜する。そのような実施形態では、頂点は、カテーテルが拡張位置に位置付けられたときに、カテーテルの丸みを帯びた先端の湾曲の開始と整合する。一実施形態では、頂点とカテーテルの丸みを帯びた先端の湾曲の開始との間の移行部は、カテーテルハブが拡張位置に位置付けられたときに連続的である。別の実施形態では、カテーテルの挿入端の先端は、球状である。そのような実施形態では、カテーテルの挿入端の球状先端は、シースが患者の鼻腔内の繊細な組織に引っ掛かることを防止するようにシースを保護してもよい。
【００２８】
実施形態によれば、急性痛に対処するためのシステムおよび装置が開示されており、適応症は、頭頸部癌、複合性局所疼痛症候群、反射性交感神経性ジストロフィ、血管運動神経性鼻炎、口腔および顎顔面手術における術前および術後感覚脱失、群発性頭痛、頭痛、頸部けいれん、任意のレベルの椎間板疾患またはヘルニア、腰痛、腰仙部けいれん、梨状筋けいれん症候群、痙性（けいれん性）斜頸、ＳＰＧ神経痛（スルダー症候群）、三叉神経痛（疼痛性チック）、帯状疱疹後神経痛、自律神経痛、非定型顔面痛、椎間板膨隆（ｂｕｌｇｉｎｇ　ｄｉｓｃ）、腰仙椎間板、カウザルギー、反射性交感神経性ジストロフィ

（ＲＳＤ）、頚椎症、片頭痛、副鼻洞性頭痛（ｓｉｎｕｓ　ｈｅａｄａｃｈｅ）、脳脊髄液（ＣＳＦ）漏出頭痛（ｃｅｒｅｂｒｏｓｐｉｎａｌ　ｆｌｕｉｄ　ｌｅａｋ　ｈｅａｄａｃｈｅ）、慢性副鼻腔炎、緊張性頭痛、筋筋膜疼痛症候群、圧迫神経（ｐｉｎｃｈｅｄ　ｎｅｒｖｅ）、坐骨神経痛、椎間板脱出（ｓｌｉｐｐｅｄ　ｄｉｓｃ）、副鼻腔痛（ｓｉｎｕｓ　ｐａｉｎ）、顎関節症候群（ＴＭＪ）、むち打ち、アレルギー性鼻炎、血管運動神経性鼻炎、喘息、ベル麻痺（顔面神経麻痺）、骨痛、癌疼痛、気管支けいれん、慢性気管支炎、月経困難症、子宮内膜症、線維筋痛症、けいれんを伴う多発性硬化症、末梢神経障害（神経障害性疼痛）、レイノー現象、関節リウマチ（発赤）、帯状疱疹（帯状ヘルペス）、脊髄狭窄、慢性疲労症候群、慢性吃逆、糖尿病性神経障害、多汗症、脳圧低下頭痛、幻肢／歯痛、感覚異常、反復性ストレス損傷、および耳鳴（低頻度）のうちの少なくとも１つについて存在する。

【００２９】

実施形態によれば、本明細書で開示され、以下で請求される、使用説明書および改良型システムを含む、キットが開示されている。

【００３０】

特徴、利点、またな類似用語の本明細書の全体を通した言及は、本主題で実現され得る特徴および利点の全てが、本主題の任意の単一の実施形態の中にあるべき、またはあることを示唆しない。むしろ、特徴および利点を指す用語は、実施形態と関連して説明される特定の特徴、利点、または特性が、本主題の少なくとも１つの実施形態に含まれることを意味すると理解される。したがって、特徴および利点の論議、ならびに類似用語は、本明細書の全体を通して、同一の実施形態を指し得るが、必ずしもそうとは限らない。

【００３１】

さらに、本主題の説明された特徴、利点、および特性は、１つ以上の実施形態において任意の好適な様式で組み合わせられてもよい。当業者であれば、特定の実施形態の特定の特徴または利点のうちの１つ以上を伴わずに、本主題が実践されてもよいことを認識するであろう。他の場合において、本主題の全ての実施形態で存在するわけではない場合がある、付加的な特徴および利点が、ある実施形態で認識されてもよい。

【００３２】

本主題のこれらの特徴および利点は、以下の説明および添付の請求項から、より完全に明白となり、または以降で記載される本主題の実践によって習得され得る。

【００３３】

本主題の利点が容易に理解されるために、添付図面で図示される具体的実施形態を参照することにより、上記で簡潔に説明される本主題のより具体的な説明が提供されるであろう。これらの図面が、本主題の典型的な実施形態のみを描写し、したがって、その範囲を限定すると見なされないものであると理解して、本主題は、添付図面の使用を通して、付加的な特異性および詳細を伴って描写および説明されるであろう。

【図面の簡単な説明】

【００３４】

【図１】図１は、本発明の装置、システム、および方法が採用され得る、患者の顔面生体構造の一実施形態を図示する、断面図である。

【図２】図２は、頭痛を治療する従来技術の方法を図示する、断面図である。

【図３】図３は、頭痛を治療する従来技術の方法を図示する、断面図である。

【図４】図４Ａは、本主題による、カテーテルハブがシースハブ内で挿入位置に位置付けられている（薬剤送達の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するための装置の一実施形態を図示する、斜視図である。図４Ｂは、本主題による、カテーテルハブがシースハブ内で拡張位置に位置付けられている（デバイス挿入の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するための装置の一実施形態を図示する、斜視図である。

【図５】図５Ａは、本主題による、カテーテルハブがシースハブ内で拡張位置に位置付けられている（デバイス挿入の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治

療を促進するための装置の一実施形態を図示する、上面図である。図５Ｂは、本主題による、カテーテルハブがシースハブ内で拡張位置に位置付けられている（デバイス挿入の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するための装置の一実施形態を図示する、側面断面図である。

【図６】図６Ａは、本主題による、カテーテルハブがシースハブ内で挿入位置に位置付けられている（薬剤送達の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するための装置の一実施形態を図示する、上面図である。図６Ｂは、本主題による、カテーテルハブがシースハブ内で挿入位置に位置付けられている（薬剤送達の準備ができている）、患者の蝶口蓋／翼口蓋陥凹の鼻腔内治療を促進するための装置の一実施形態を図示する、側面断面図である。

【図７】図７は、本主題による、カテーテルハブの一実施形態を図示する、斜視図である。

【図８】図８Ａは、本主題による、カテーテルハブの一実施形態を図示する、上面図である。図８Ｂは、本主題による、カテーテルハブおよびカテーテルの一実施形態を図示する、側面断面図である。

【図９】図９Ａは、本主題による、カテーテルハブの治療受容端の方向に得られたカテーテルハブの一実施形態を描写する、端面図である。図９Ｂは、本主題による、カテーテルハブの治療送達端の方向に得られたカテーテルハブの一実施形態を描写する、端面図である。

【図１０】図１０Ａは、本主題による、シースハブおよびシースの一実施形態を図示する、上面図である。図１０Ｂは、本主題による、シースハブおよびシースの一実施形態を図示する、側面断面図である。

【図１１】図１１は、本主題による、停止要素を含むシースハブの領域の拡大図である。

【図１２】図１２は、本主題による、シースハブのシース受容端の方向に得られたシースハブの一実施形態を描写する、端面図である。

【図１３】図１３Ａは、シースの頂点がカテーテルの挿入端の湾曲の開始と整合する、シースの導入端およびカテーテルの挿入端の一実施形態を図示する、断面図である。図１３Ｂは、シースの頂点がカテーテルの挿入端の湾曲の開始と整合していない、シースの導入端およびカテーテルの挿入端の一実施形態を図示する、断面図である。図１３Ｃは、シースの頂点がカテーテルの挿入端の湾曲の開始と整合していない、シースの導入端およびカテーテルの挿入端の一実施形態を図示する、断面図である。

【発明を実施するための形態】

【００３５】

本発明者らは、強化システムにより、免許を持つ医師ではない者（免許を持つ医療専門家による訓練を受けている、外科的に訓練されていない施術者）が、予想を上回る成功率でＳＰＧ問題に対処することを可能にできることを発見した。

【００３６】

ＳｐｈｅｎｏＣａｔｈ™ブランドの医療デバイスは、設計通りに使用されたとき、針、鎮痛剤、または麻酔剤がない診療室環境で、適切な用量の薬剤を安全に無痛でＳＰＧに送達するために必要な方向制御を任意の施術者にもたらす。

【００３７】

本明細書の全体を通した「一実施形態」、「実施形態」、または類似用語という言及は、実施形態と関連して説明される特定の特徴、構造、または特性が、本主題の少なくとも１つの実施形態に含まれることを意味する。したがって、本明細書の全体を通した「一実施形態では」、「実施形態では」という語句、または類似用語の出現は、全て同一の実施形態を指し得るが、必ずしもそうとは限らない。

【００３８】

さらに、本主題の説明された特徴、構造、または特性は、１つ以上の実施形態において任意の好適な様式で組み合わせられてもよい。以下の説明では、多数の具体的詳細が、本主題の実施形態の徹底的な理解のために提供される。しかしながら、当業者であれば、具

体的詳細のうちの１つ以上を伴わずに、または他の方法、構成要素、材料等を伴って、本主題が実践されてもよいことを認識するであろう。他の場合において、周知の構造、材料、または動作は、本主題の側面を曖昧にすることを回避するために、詳細に示されない、または説明されない。

【００３９】

図１は、本デバイスおよびシステムが動作する、１つの環境の説明図である。具体的には、図１は、典型的なヒトの鼻腔の解剖学的特徴の断面図を描写する。当業者であれば、ヒトの鼻腔のある解剖学的特徴および構造が、本主題の実践に関連する構造を曖昧にすることを回避するために、省略されていることを認識するであろう。読者を正しい方向に導くのに役立つために、口１０６が、歯１０８および舌１１０とともに図示されている。本主題の１つの実践に関連する解剖学的構造は、鼻腔１０４から口腔１０２を分離する口蓋１００、下鼻甲介１１２、中鼻甲介１１４、および上鼻甲介１１６、ならびに鼻骨１２２を含む。中鼻甲介１１４および上鼻甲介１１６は、蝶口蓋／翼口蓋陥凹１１８を画定する。蝶口蓋／翼口蓋陥凹１１８の奥深く、蝶口蓋／翼口蓋陥凹１１８の後部１２４に、蝶口蓋／翼口蓋神経節１２０が位置する。

【００４０】

当業者であれば、医学会が蝶口蓋または翼口蓋神経節に関する用語で統一していないことを認識するであろう。ある施術者が蝶口蓋を使用する一方で、他の施術者は翼口蓋を使用する。したがって、本説明は、１２０で標識された神経節をＳＰＧ／翼口蓋神経節１２０と呼ぶ。同様に、１１８で標識された陥凹は、ＳＰＧ／翼口蓋陥凹１１８と呼ばれるであろう。しかしながら、この用語は、本主題が意図される構造でいかようにも限定的ではない。施術者または科学者が蝶口蓋神経節または翼口蓋神経節を区別する場合、本開示は、いずれか一方の構造を適用すると理解されるであろう。

【００４１】

蝶口蓋／翼口蓋神経節１２０は、主に、中鼻甲介１１４の後方にある翼口蓋窩内で頭部の中心に位置する、神経構造である。蝶口蓋／翼口蓋神経節１２０は、脳の外側の頭部内に交感神経ニューロンの最大集合を備える。蝶口蓋／翼口蓋神経節１２０は、神経インパルスを相互作用させ、頭部の自律神経または副交感神経経路の大部分に方向付ける。したがって、この構造へのいかなる異常または損傷も、重度の疼痛を引き起こし得る。蝶口蓋／翼口蓋神経節１２０の神経ブロックは、頭痛から腰痛に及ぶ種々の疼痛症状を緩和するのに効果的であり得る。加えて、蝶口蓋／翼口蓋神経節１２０および周辺構造の局所麻酔遮断、および／または他の薬理学的増強あるいは機械的改変によって、頭痛障害および他の神経学的症状等の他の疾患プロセスを抑止または改善することができる。

【００４２】

残念ながら、蝶口蓋／翼口蓋神経節１２０の解剖学的位置により、該構造は、いくつかの一般的に実践されている技法を使用して局所麻酔液で遮断することが非常に困難であり得る。蝶口蓋／翼口蓋神経節１２０の解剖学的な場所は、多くの極めて重要かつ繊細な中脳構造に危険なほど近い。麻酔薬を蝶口蓋／翼口蓋神経節１２０に投与するために、直接針配置を蛍光透視誘導下で採用することができるが、大抵の施術者は、技術的困難かつ異常な針配置という極度の危険により、該手技を行おうとしないであろう。

【００４３】

図２で描写される従来技術の説明図に示されるように、蝶口蓋／翼口蓋神経節１２０は、蝶口蓋／翼口蓋陥凹１１８の奥深くに位置する。疼痛の専門医、神経科医、および神経外科医によって着手される従来の方法は、局所麻酔薬で飽和した８インチの綿棒２００の使用を含む。綿棒２００が使用されるため、本手技は、「綿棒（Ｑ－先端）」手技と呼ばれる。綿棒２００は、濃縮局所麻酔液のバイアルに浸される。ある実施形態では、麻酔液は、リドカイン、コカイン、エチドカイン、またはプリロカイン、あるいは他の非特定局所麻酔薬である。次いで、綿棒２００は、鼻孔２０２の中へ、および鼻腔１０４を通して前進させられる。蝶口蓋／翼口蓋陥凹１１８の中の蝶口蓋／翼口蓋神経節１２０に到達するために、綿棒２００は、鼻腔１０４の中へ、中鼻甲介１１４を過ぎて、および蝶口蓋／

翼口蓋陥凹１１８の中へ前進させられなければならない。

【００４４】

図３は、従来技術の綿棒２００が蝶口蓋／翼口蓋陥凹１１８に到達するために横断しなければならない蛇行経路を図示する。手技を行うために、患者は、仰臥位で置かれる。綿棒２００は、濃縮局所麻酔液または他の薬理作用物質のバイアルに浸される。次いで、医師が、患者の鼻孔２０２の中へ、および鼻腔１０４を通して綿棒２００を挿入する。中鼻甲介１１４の前隆起３０２を通過するように、綿棒２００が患者の顔とほとんど平行に挿入されなければならないため、蝶口蓋／翼口蓋陥凹１１８の中へ直線の剛性綿棒２００を前進させることには、困難で患者にとって苦痛であり得る。次いで、綿棒２００は、鼻骨１２２の下面３０４を回避して蝶口蓋／翼口蓋陥凹１１８にアクセスするように、ほぼ９０度に屈曲しなければならない。綿棒２００は、副鼻腔粘膜を通した局所麻酔薬または他の薬理作用物質の拡散を可能にして蝶口蓋／翼口蓋神経節１２０を変調し、神経伝達を一時的に遮断するか、または永久的に除去するように、患者の蝶口蓋／翼口蓋陥凹１１８の中で約２０分間放置される。

【００４５】

いくつかの非常に敏感で血管が豊富であり、砕けやすく、高度に神経支配された構造の周囲で、いくつかのかなり蛇行性の方向変更を行わなければならない、直線の剛性綿棒２００の使用は、多くの施術者がそれを試行しないであろうほど、手技を複雑にする。既知の合併症は、極度の患者不快感、鼻血、および静脈を刺激する妨害、動脈出血、吸引、血便、またはさらに死亡を含む、鼻血と関連付けられる合併症を含む。他の合併症は、局所麻酔薬毒性、発作、折れた綿棒２００等の医原性異物、副鼻腔粘膜裂傷、および感染症を含む。

【００４６】

任意の神経構造の麻酔遮断は、麻酔液と標的組織との間の直接物理的相互作用を必要とする。したがって、機能するために、綿棒２００は、麻酔液を蝶口蓋／翼口蓋神経節１２０に直接送達しなければならない。綿棒２００の正しい配置は、技術的に困難であり、多くの施術者は、単純に、手技を行おうとするときに、所望の構造である蝶口蓋／翼口蓋神経節１２０を外す。蝶口蓋／翼口蓋陥凹１１８に到達するために必要とされる複雑な屈曲を行うのに役立つために、多くの施術者は、綿棒２００の最上部の２インチを浸し、患者があまり刺激されず、出血のリスクが減少させられるように、柄を操作して可撓性にするであろう。可撓性綿棒２００でさえも、手技は困難である。一般的な配置の失敗は、鼻骨１２２の下面３０４、および中鼻甲介１１４の前隆起３０２を含む。綿棒２００が誤留置されたとき、麻酔薬が蝶口蓋／翼口蓋神経節１２０に送達される前に綿棒から絞り出され、効果のない手技をもたらす、「絞り出し」効果が起こり得る。さらに、上記で論議されるように、鼻腔１０４の豊富な血管および神経構造が、綿棒２００のいかなる誤留置も危険かつ苦痛なものにする。

【００４７】

図４Ａは、患者の蝶口蓋／翼口蓋陥凹１１８の鼻腔内治療を促進するための装置４００の一実施形態の斜視図を描写する。装置４００は、ある実施形態では、シースハブ４０２と、カテーテルハブ４０４と、カテーテル４１２と、シース４２０とを含む。図４Ａの装置４００は、シースハブ４０２内で挿入位置４２４に位置付けられたカテーテルハブ４０４を伴って描写されている。図４Ｂは、カテーテルハブ４０４がシースハブ４０２内で拡張位置４２６に位置付けられた、図４Ａの装置４００の一実施形態の斜視図を描写する。

【００４８】

シースハブ４０２は、内面５０２（図５Ｂ）に対向する外面４０６を含む。カテーテルハブ４０４の内面５０２は、カテーテルハブ受容空間５０４（図５Ｂ）を画定する。カテーテルハブ４０４の少なくとも一部分４２２は、カテーテルハブ受容空間５０４内で受容され、カテーテルハブ４０４は、シースハブ４０２の長手方向軸４２８に沿って再配置可能である。ある実施形態では、カテーテルハブ４０４は、図４Ａで図示されるような挿入位置４２４と、図４Ｂで図示されるような拡張位置４２６との間で再配置可能である。

【００４９】
一実施形態では、カテーテルハブ４０４は、停止表面４２５を含む。カテーテルハブ４０４がカテーテルハブ受容空間５０４に完全に挿入されたとき、カテーテルハブ４０４の停止表面４２５は、カテーテルハブ受容空間５０４内のカテーテルハブ４０４のさらなる挿入を抑止するように、シースハブ４０２に接触する。停止表面４２５がシースハブ４０２に接触する点まで、カテーテルハブ４０４がカテーテルハブ受容空間５０４内に完全に位置付けられると、カテーテルハブ４０４は、シースの遠位先端を越えて完全に拡張された内部カテーテルを伴って完全挿人位置４２４に位置付けられたと見なされてもよい。カテーテルハブ４０４が矢印４０７によって示される方向にカテーテルハブ受容空間５０４内から引き出されるにつれて、カテーテルハブ４０４は、完全拡張位置４２６に位置付けられたと見なされてもよい。

【００５０】
描写した実施形態では、シースハブ４０２の外形およびカテーテルハブ４０４の外形は、実質的に円形である。他の実施形態では、シースハブ４０２およびカテーテルハブ４０６は、三角形の外形、正方形の外形、長方形の外形、多角形の外形、楕円形の外形、または任意の他の幾何学的形状を有する外形を有してもよい。

【００５１】
カテーテル４１２は、カテーテル４１２の連結端５０６（図５Ｂ参照）においてカテーテルハブ４０４に連結される。カテーテル４１２の挿入端（遠位先端）４１４は、カテーテル４１２の長手方向軸４１８に対する内部屈曲部４１６を含む。カテーテル４１２の挿入端４１４は、カテーテル４１２の連結端５０６の反対側に配置される。カテーテル４１２の挿入端４１４の部曲率４１６は、シース４２０の遠位先端を越えて前進させられたときに、カテーテル４１２の挿入端４１４を屈曲させる。装置４００が患者の鼻腔１０４に挿入されたとき、患者の鼻腔１０４の繊細な周辺構造に接触することなく、医師または他の医療専門家が、シース４２０の遠位先端を越えたカテーテルを患者の蝶口蓋／翼口蓋陥凹１１８より直接上側の空間の中へ前進させるまで、挿入端４１４の内部屈曲部４１６は、シース４２０の中へ後退させられる。

【００５２】
カテーテル４１２が最初に患者の鼻腔１０４に挿入されたとき、カテーテル４１２は、患者の蝶口蓋／翼口蓋陥凹１１８にアクセスするように、中鼻甲介１１４の前隆起３０２を過ぎて、比較的直線の経路で移動しなければならない。したがって、患者の鼻腔に挿入されると、カテーテル４１２は、比較的直線となるべきである。カテーテル４１２の挿入端４１４の内部屈曲部４１６をまっすぐにするために、カテーテル４１２は、カテーテル４１２の挿入端４１４の内部屈曲部４１６をまっすぐにするように十分な構造的剛性を有する、シース４２０内で受容される。シース４２０は、シースハブ４０２に連結され、カテーテル４１２は、シース４２０内で受容される。

【００５３】
カテーテル４１２がカテーテルハブ４０４に連結され、シース４２０がシースハブ４０２に連結されるため、カテーテルハブ４０４が拡張位置４２６に位置付けられたとき、カテーテル４１２は、図４Ｂで図示されるようにシース４２０に引き込まれる。カテーテル４１２がシース４２０に引き込まれると、シース４２０の構造的剛性が、カテーテル４１２の挿入端４１４の内部屈曲部４１６をまっすぐにし、医師または他の医療専門家が、中鼻甲介１１４の前隆起３０２を過ぎてカテーテル４１２の挿入端４１４を操作することを可能にする。

【００５４】
いったんカテーテル４１２の挿入端４１４が中鼻甲介１１４の前隆起３０２を通過すると、医師または他の医療専門家は、カテーテルハブ４０４を挿入位置４２４まで前進させることができる。カテーテルハブ４０４が挿入位置４２４に再配置されると、カテーテル４１２の挿入端４１４の内部屈曲部４１６は、シース４２０内に位置付けられず、したがって、シース４２０によってまっすぐにされない。カテーテル４１２の挿入端４１４の内

部屈曲部４１６は、カテーテル４１２の挿入端４１４を屈曲させる。カテーテル４１２の屈曲は、医師または他の医療専門家が、カテーテル４１２の挿入端４１４を患者の蝶口蓋／翼口蓋陥凹１１８の中へ方向付けることを可能にし、そこで、医師または他の医療専門家は、治療を患者の蝶口蓋／翼口蓋神経節１２０に送達することができる。

【００５５】

本論議は、蝶口蓋／翼口蓋神経節１２０を治療するための蝶口蓋／翼口蓋陥凹１１８のアクセスを対象とするが、当業者であれば、他の実施形態では、患者の他の領域にアクセスするために装置４００が使用されてもよいことを認識するであろう。例えば、装置４００は、進入点を参照して配置されるカテーテル４１２の挿入端４１４を、線形ではない患者上の任意の領域の中で位置付けるために、医師または他の医療専門家によって使用されてもよい。そのような領域の実施例は、患者の耳腔、静脈、動脈等を含んでもよい。

【００５６】

ある実施形態では、送達される治療は、カテーテル４１２を通した蝶口蓋／翼口蓋神経節１２０への神経遮断薬の分注であってもよい。他の実施形態では、カテーテル４１２は、電気刺激を蝶口蓋／翼口蓋神経節１２０に送達するように構成される電極を含んでもよい。当業者であれば、他の医療処置が蝶口蓋／翼口蓋神経節１２０に送達されてもよいことを認識するであろう。

【００５７】

医師または他の医療専門家が、カテーテル４１２の挿入端を患者の鼻腔に挿入するとき、カテーテル４１２の挿入端４１４の医師または他の医療専門家の視界が、患者の鼻の周辺構造によって妨害され得る。加えて、医師または他の医療専門家は、内部屈曲部４１６がカテーテル４１２の挿入端４１４を患者の蝶口蓋／翼口蓋陥凹１１８の中へ前進させる位置に配向されているか否かを判定するために、内部屈曲部４１６またはカテーテル４１２の挿入端４１４の配向を見ることができない。カテーテル４１２の挿入端４１４を患者の蝶口蓋／翼口蓋陥凹１１８の中へ前進させるのに医師または他の医療専門家を支援するために、ある実施形態では、装置４００は、回転配向インジケータ４０８を含む。一実施形態では、回転配向インジケータ４０８は、カテーテルの挿入端４１４の配向を判定するのに医師または他の医療専門家を支援するように、カテーテル４１２の内部屈曲部４１６の回転配向を識別する。ある実施形態では、回転配向インジケータ４０８は、シースハブ４０２の外面４０６、カテーテルハブ４０４の外面４１０、または両方の上に位置付けられる、線、点、または他の指示等の視覚的指示であってもよい。

【００５８】

図４Ａおよび４Ｂで図示される実施形態では、回転配向インジケータ４０８は、シースハブ４０２の外面４０６上に位置付けられる第１の回転配向インジケータ４０８ａと、カテーテルハブ４０４の外面４１０上に位置付けられる第２の回転配向インジケータ４０８ｂとを含む。他の実施形態では、シースハブ４０２またはカテーテルハブ４０４のうちの１つのみが、回転配向インジケータ４０８を含む。

【００５９】

一実施形態では、シースハブ４０２上の回転配向インジケータ４０８ａは、シースハブ４０２の少なくとも一部分に沿って縦方向に延在する、隆起部４３２である。隆起部４３２は、カテーテル４１２の内部屈曲部４１６の配向に関する触覚フィードバックを医師または他の医療専門家に提供するように、シースハブ４０２の外面４０６から実質的に垂直に延在する。したがって、医師または他の医療専門家が、カテーテル４１２の挿入端４１４を患者の鼻腔１０４の中へ前進させるとき、医師または他の医療専門家は、患者の鼻腔１０４内のカテーテル４１２の深度等の手技に影響を及ぼし得る他の要因に視覚的注意を集中することができる。

【００６０】

ある実施形態では、カテーテルハブ４０４上の回転配向インジケータ４０８ｂもまた、隆起部４３４であってもよい。そのような実施形態では、隆起部４３４は、カテーテルハブ４０４の少なくとも一部分に沿って縦方向に延在する。隆起部４３２は、カテーテル４

１２の内部屈曲部４１６の配向に関する触覚フィードバックを医師または他の医療専門家に提供するように、カテーテルハブ４０４の外面４１０から実質的に垂直に延在する。シースハブ４０２およびカテーテルハブ４０４の両方が、回転配向インジケータ４０８の役割を果たす隆起部４３２および４３４を含む、実施形態では、医師または他の医療専門家は、どの構成要素（カテーテルハブ４０４またはシースハブ４０２）を医師または他の医療専門家が操作しているかにかかわらず、カテーテル４１２の内部屈曲部４１６の配向を判定することができる。

【００６１】

ある実施形態では、シースハブ４０２およびカテーテルハブ４０４上の隆起部４３２および４３４は、同一の軸に沿って整合させられる。他の実施形態では、シースハブ４０２上の隆起部４３２は、カテーテルハブ４０４上の隆起部４３４からオフセットされてもよい。さらに別の実施形態では、上記で論議されるように、シースハブ４０２またはカテーテルハブ４０４のうちの１つのみが、回転配向インジケータ４０８を含む。そのような実施形態では、装置４００は、シースハブ４０２の外面４０６上の隆起部４３２、またはカテーテルハブ４０４の外面４１０上の隆起部４３４のいずれか一方を含んでもよい。

【００６２】

一実施形態では、装置４００は、薬物治療を受容する治療受容ポート４３６を含む。例えば、ある実施形態では、治療受容ポート４３６は、注射器または他の薬剤送達デバイスに連結可能である。治療受容ポート４３６は、カテーテル４１２を通して蝶口蓋／翼口蓋神経節１２０へ薬剤を送達することができるように、カテーテル４１２と流体連通している。

【００６３】

他の実施形態では、他の治療送達デバイスが治療受容ポート４３６に連結されてもよい。例えば、一実施形態では、治療送達デバイスは、電流を装置４００に伝送するように構成される電気刺激デバイスを含んでもよい。そのような実施形態では、カテーテル４１２は、治療受容ポート４３６からカテーテル４１２の挿入端４１４へ電流を伝導する、電気導管を含んでもよい。カテーテル４１２の挿入端４１４の上に位置付けられる電極が、電流を患者に送達する。

【００６４】

図５Ａは、患者の蝶口蓋／翼口蓋陥凹１１８の鼻腔内治療を促進するための装置４００の一実施形態の上面図を描写する。図５Ａで描写される実施形態では、カテーテルハブ４０４は、拡張位置４２６に位置付けられる。ある実施形態では、シース４２０は、シース４２０の導入端５０５全体が、患者の鼻腔１０４の組織に引っ掛かる任意の縁を伴わない平滑な傾斜を形成するように、頂点５０８まで傾斜している導入端５０５を含む。

【００６５】

一実施形態では、カテーテル４１２の挿入端４１４は、カテーテル４１２の挿入端４１４の先端５１０が丸みを帯びるように湾曲した。カテーテル４１２の挿入端４１４の上に丸みを帯びた先端５１０を含むことによって、医師または他の医療専門家は、カテーテル４１２の挿入端４１４で患者の鼻腔１０４の繊細な組織を捕捉する、または引っ掛ける可能性が低い。以下でさらに説明されるように、ある実施形態では、カテーテルハブ４０４が拡張位置４２６に位置付けられたとき、シース４２０の導入端５０５における頂点５０８は、カテーテル４１２とシース４２０との間の移行部５１２が、連続的で平滑であり、実質的に縁を含まないように、カテーテル４１２の丸みを帯びた先端５１０の湾曲の開始と整合する。カテーテル４１２とシース４２０との間の平滑な移行部５１２は、患者の鼻腔１０４内の組織を捕捉することを回避するのに役立つ。

【００６６】

ある実施形態では、治療受容ポート４３６は、装置４００を治療送達デバイスに連結するための連結部材５１４を含む。例えば、一実施形態では、連結部材５１４は、治療受容ポート４３６の円周の周囲に配置される複数のネジ山であってもよい。連結部材５１４のネジ山は、治療送達デバイスを治療受容ポート４３６に連結するように、注射器または他

の治療送達デバイス上のネジ山に係合する。

【００６７】

図５Ｂは、患者の蝶口蓋／翼口蓋陥凹１１８の鼻腔内治療を促進するための装置４００の一実施形態の側面断面図を描写する。図５Ｂで描写される実施形態では、カテーテルハブ４０４は、拡張位置４２６に位置付けられる。図５Ｂで描写される実施形態は、図５Ａの線Ａ－Ａに沿って得られ、シースハブ４０２の内面５０２およびカテーテルハブ受容空間５０４の一実施形態をより明確に図示する。

【００６８】

ある実施形態では、シースハブ４０２は、内面５０２に対面する外面４０６を有する。シースハブ４０２の内面５０２は、カテーテルハブ受容空間５０４を画定する。カテーテルハブ４０４の一部分４２２は、縮小した直径を有し、カテーテルハブ４０４がシースハブ４０２の長手方向軸４２８（図４Ａおよび４Ｂ参照）に沿った縦方向に配置可能であるように、カテーテルハブ受容空間５０４内で摺動可能に受容される。

【００６９】

ある実施形態では、装置４００は、カテーテルハブ４０４またはシースハブ４０２のいずれか一方の上に抑止要素５１６を含む。図５Ｂで図示される実施形態では、抑止要素５１６は、カテーテルハブ４０４の縮小直径部分４２２の外面５１８に連結され、そこから垂直に延在する、フランジである。

【００７０】

一実施形態では、装置４００はまた、カテーテルハブ４０４またはシースハブ４０２のいずれか一方の上に係合要素５２０も含む。図５Ｂで図示される実施形態では、係合要素５２０は、シースハブ４０２の内面５０２に沿って縦方向に延在する陥凹である。抑止要素５１６のフランジは、カテーテルハブ４０４がシースハブ４０２の長手方向軸４２８に沿って再配置されたときに、係合要素５２０の陥凹内に位置付けられ、それに沿って移動する。抑止要素５１６と係合要素５２０との間の協調は、シースハブ４０２に対するカテーテルハブ４０４の回転を制限しながら、カテーテルハブ４０４がカテーテルハブ受容空間５０４内で摺動可能に受容されることを可能にする。したがって、ある実施形態では、抑止要素５１６のフランジは、カテーテルハブ４０４がシースハブ４０２の長手方向軸４２８に沿って再配置されたときに、係合要素５２０の陥凹内で連続的に係合させられる。抑止要素５１６と係合要素５２０との間の係合は、カテーテルハブ４０４に対するシースハブ４０２の回転を防止する。

【００７１】

シースハブ４０２に対するカテーテルハブ４０４の回転を制限することによって、医師または他の医療専門家は、カテーテルハブ４０４上の回転配向インジケータ４０８ａの位置によって、カテーテル４１２の内部屈曲部４１４の配向を判定することができ、シースハブ４０２上の回転配向インジケータ４０８ｂは、不必要であり得る。

【００７２】

ある実施形態では、装置４００はまた、カテーテルハブ４０４またはシースハブ４０２のいずれか一方に連結される停止要素５２２も含む。停止要素５２２は、抑止要素５１６に係合して、カテーテルハブ４０４がカテーテルハブ受容空間５０４から除去されることを止めるように構成される。図５Ｂで図示される実施形態では、停止要素５２２は、カテーテルハブ４０４がカテーテルハブ受容空間５０４から除去されることを止めるように抑止要素５１６に係合する、実質的に剛性の壁である。ある実施形態では、停止要素５２２はまた、カテーテルハブ４０４が拡張位置４２６に位置付けられたときに、カテーテル４１２とシース４２０との間の移行部５１２が、連続的で平滑であり、実質的に縁を含まないように、カテーテル４１２の丸みを帯びた先端５１０の湾曲の開始とのシース４２０の導入端５０５における頂点５０８の整合も促進する。

【００７３】

当然ながら、当業者であれば、ある実施形態では、抑止要素５１６、係合要素５２０、および停止要素５２２の位置が反転されてもよいことを認識するであろう。例えば、一実

施形態では、抑止要素５１６は、シースハブ４０２の内面５０２に連結されてもよく、係合要素５２０の陥凹は、カテーテルハブ４０４の縮小直径部分５０６の外面５１８内に位置付けられてもよい。同様に、一実施形態では、停止要素５２２は、カテーテルハブ４０４がシースハブ４０２の中のカテーテルハブ受容空間５０４内から除去されることを制限するように、カテーテルハブ４０４の縮小直径部分５０６に連結されてもよい。

【００７４】

図６Ａは、患者の蝶口蓋／翼口蓋陥凹１１８の鼻腔内治療を促進するための装置４００の一実施形態の上面図を描写する。図６Ａで図示される実施形態では、カテーテルハブ４０４は、挿入位置４２４に位置付けられる。

【００７５】

図６Ｂは、患者の蝶口蓋／翼口蓋陥凹１１８の鼻腔内治療を促進するための装置の一実施形態の側面断面図である。図６Ｂで描写される実施形態では、カテーテルハブ４０４は、挿入位置４２４に位置付けられる。図６Ｂで描写される実施形態は、図６Ａの線Ｂ－Ｂに沿って得られる。

【００７６】

一実施形態では、カテーテルハブ４０４がカテーテルハブ受容空間５０４に完全に挿入されたとき、カテーテルハブ４０４の停止表面４２５は、カテーテルハブ受容空間５０４内のカテーテルハブ４０４のさらなる挿入を抑止するように、シースハブ４０２の端部６０２に接触する。他の実施形態では、カテーテルハブ４０４の縮小直径部分４２２の端部６０４は、カテーテルハブ受容空間５０４内のカテーテルハブ４０４のさらなる挿入を抑止するように、カテーテルハブ受容空間５０４内の内壁６０６に接触する。停止表面４２５がシースハブ４０２に接触する点まで、カテーテルハブ４０４がカテーテルハブ受容空間５０４内に完全に位置付けられると、カテーテルハブ４０４は、完全挿入位置４２４に位置付けられたと見なされてもよい。

【００７７】

図７Ａは、本開示による、カテーテルハブ４０４の一実施形態の斜視図を描写する。図７Ａで図示される実施形態では、シースハブ４０２およびカテーテル４１２は、カテーテルハブ４０４をより良く図示するように省略されている。

【００７８】

ある実施形態では、カテーテルハブ４０４は、治療送達端７０４の反対側に配置される治療受容端７０２を含む。一実施形態では、カテーテルハブ４０４は、操作部分７０６と、挿入部分７０８と、連結部分７１０とを含む。描写した実施形態では、操作部分７０６、挿入部分７０８、および連結部分７１０は、実質的に円筒形である。他の実施形態では、操作部分７０６、挿入部分７０８、および／または連結部分７１０は、三角形の外形、正方形の外形、長方形の外形、多角形の外形、楕円形の外形、または任意の他の幾何学的形状を有する外形を有してもよい。

【００７９】

一実施形態では、カテーテルハブ４０４の挿入部分７０８は、カテーテルハブ４０４の縮小直径部分４２２を含む。挿入部分７０８は、ある実施形態では、カテーテルハブ４０４の停止表面４２５から始まり、カテーテルハブ４０４の治療送達端７０４まで延在する。

【００８０】

カテーテルハブ４０４の連結部分７１０は、挿入部分７０８の反対側に位置付けられ、治療受容ポート４３６を含む。麻酔薬、薬剤、電流、または任意の他の治療が、治療受容ポート４３６で受容され、治療受容端７０２から治療送達端７０４までカテーテルハブ４０４を通して配置される管腔７１２を通して、治療送達端７０４へ送達される。カテーテル４１２が管腔７１２の中に位置付けられるとき、カテーテルは、治療を受容し、それを患者の蝶口蓋／翼口蓋陥凹１１８等の所望の領域へ送達する。

【００８１】

カテーテルハブ４０４の操作部分７０６は、ある実施形態では、挿入部分７０８に対し

て増加した直径を有し、連結部分７１０と挿入部分７０８との間に位置付けられる。カテーテルハブ４０４の操作部分７０６の増加した直径は、医師または他の医療専門家によるカテーテルハブ４０４の操作を促進する。

【００８２】

抑止要素５１６は、カテーテルハブ４０４の挿入部分７０８の外面５１８に連結され、そこから実質的に垂直に延在する。抑止要素５１６は、一実施形態では、傾斜面７１５を含む。例えば、一実施形態では、カテーテルハブ４０４の治療送達端７０４に隣接する抑止要素５１６の端部７１１は、カテーテルハブ４０４の治療受容端７０２により近い抑止要素５１６の端部７１４よりも実質的に小さい距離で、カテーテルハブ４０４の挿入部分７０８の外面５１８から延在する。抑止要素５１６の傾斜面７１５は、抑止要素５１６のフランジが、停止要素５２２を過ぎて係合要素５２０の陥凹に挿入されることを可能にする。抑止要素５１６の後面７１６は、カテーテルハブ４０４の縮小直径部分４２２の外面５１８から実質的に垂直に延在する。カテーテルハブ４０４がカテーテルハブ受容空間５０４内から引き出されたとき、抑止要素５１６の後面７１６は、カテーテルハブ４０４がカテーテルハブ受容空間５０４内から除去されることを止めるように停止要素５２２に係合する。ある実施形態では、抑止要素５１６の後面と停止要素５２２との間の相互作用は、シース４２０の導入端５０５における頂点５０８が、カテーテル４１２の丸みを帯びた先端５１０の湾曲の開始と整合するように、シース４２０内にカテーテル４１２を位置付ける。この位置で、カテーテル４１２とシース４２０との間の移行部５１２は、連続的で平滑であり、実質的に縁を含まない。

【００８３】

図８Ａは、本発明による、カテーテルハブ４０４およびカテーテル４１２の実施形態の側面図を描写する。図８Ａで図示される実施形態では、連結部材５１４のネジ山が、より明確に図示されている。他の実施形態では、連結部材５１４は、スナップ嵌合取付部、治療送達デバイスを化学的に接着するための周縁、または治療送達デバイスをカテーテルハブ４０４に取り付けるか、あるいは添着するための任意の他の手段であってもよい。

【００８４】

ある実施形態では、カテーテルハブ４０４は、規則的間隔でカテーテルハブ４０４の挿入部分７０８に沿って配置される、複数の深度インジケータ８０６を含む。図８Ａで図示される実施形態では、深度インジケータ８０６は、カテーテルハブ４０４の挿入部分７０８の円周の周囲に位置付けられる線である。他の実施形態では、深度インジケータ８０６は、点、正方形、円、三角形、または任意の他の視覚的インジケータ等の他の形状を含んでもよい。一実施形態では、深度インジケータ８０６はまた、カテーテルハブ受容空間５０４内にカテーテルハブ４０４の深度の数値的指示を含んでもよい。

【００８５】

初期神経ブロックを行うために、カテーテルハブ４０４が拡張位置４２６に位置付けられると、医師または他の医療専門家が、シース４２０およびカテーテル４１２を患者の鼻腔１０４の中へ前進させる。いったんカテーテルの挿入端４１４が中鼻甲介１１４の前隆起３０２を通過すると、医師または他の医療専門家は、カテーテルハブ受容空間５０４のより奥深くにカテーテルハブ４０４を前進させ、シース４２０の導入端５０５を過ぎてカテーテル４１２の挿入端４１４を前進させる。いったんシース４２０がカテーテル４１２の内部屈曲部４１６をもはや含まなくなる位置までカテーテル４１２の挿入端４１４が前進させられると、カテーテル４１２が屈曲する。医師または他の医療専門家が、カテーテル４１２が回転配向インジケータ４０８の配向によって屈曲される方向を把握しているため、医師または他の医療専門家は、神経ブロックまたは他の治療を蝶口蓋／翼口蓋神経節１２０に送達するように、カテーテル４１２の挿入端４１４を蝶口蓋／翼口蓋陥凹１１８の中へ方向付けることができる。

【００８６】

当業者に明白となるように、患者の鼻腔１０４の生体構造は、個人によって異なる。したがって、ある患者は、他の患者よりも深い蝶口蓋／翼口蓋陥凹１１８を有するであろう

。カテーテルハブ４０４の挿入部分７０８上の深度インジケータ８０６は、カテーテル４１２の挿入端４１４が患者の蝶口蓋／翼口蓋陥凹１１８内に位置付けられたときに、医師または他の医療専門家がカテーテル４１２の挿入端４１４の深度を判定することを可能にする。一実施形態では、特定の患者の蝶口蓋／翼口蓋神経節１２０の初期治療中に、医師または他の医療専門家は、患者の蝶口蓋／翼口蓋陥凹１１８の深度を記録してもよい。患者の蝶口蓋／翼口蓋神経節１２０の後続の治療において、医師または他の医療専門家は、指針として記録された深度を使用することができる。

【００８７】

図８Ｂは、本開示による、カテーテルハブ４０４の一実施形態の断面図を描写する。図８Ｂで描写される実施形態は、図８Ａの線Ｃ－Ｃに沿って得られている。

【００８８】

ある実施形態では、カテーテル４１２は、カテーテルハブ４０４の中の管腔７１２内に位置付けられ、少なくとも部分的に管腔７１２の中へ延在する。他の実施形態では、カテーテル４１２は、カテーテル４１２の治療送達端７０４において端面８０２に添着されてもよい。いずれか一方の実施形態では、カテーテル４１２は、薬剤、麻酔薬、または他の化学物質を患者に分注することができるカテーテル４１２の挿入端４１４に送達するように、管腔７１２と流体連通して連通可能である。

【００８９】

他の実施形態では、ワイヤ等の電気導管が、カテーテル４１２の中の管腔７１２を通して、およびカテーテルの中の管腔８０４を通して位置付けられる。そのような実施形態では、電気導管は、電流をカテーテル４１２の挿入端４１４に位置付けられる電極に送達するように、電源に連結されてもよい。電極は、電流を患者に送達するように構成される。

【００９０】

図９Ａは、本開示による、カテーテルハブ４０４の一実施形態を描写する端面図である。図９Ａで図示される実施形態は、カテーテルハブ４０４の治療受容端７０２の方向に得られている。

【００９１】

ある実施形態では、カテーテルハブ４０４は、治療受容ポート４３６の内周９０４の上に位置付けられる、１つ以上の連結フランジ９０２ａおよび９０２ｂを含む。そのような実施形態では、連結フランジ９０２は、注射器または他の治療送達デバイスをカテーテルハブに連結するように構成される。

【００９２】

図９Ｂは、本開示による、カテーテルハブ４０４の一実施形態を描写する端面図である。図９Ａで図示される実施形態は、カテーテルハブ４０４の治療送達端７０４の方向に得られている。

【００９３】

図１０Ａは、本開示による、シース４２０に連結されたシースハブ４０２の一実施形態の上面図である。シースハブ４０２は、ある実施形態では、カテーテルハブ受容端１００２と、シース受容端１００４とを含む。図１０Ａで図示される実施形態では、シース４２０は、シースハブ４０２のシース受容端１００４に連結される。

【００９４】

ある実施形態では、シースハブ４０６は、実質的に円筒形の部分１００６と、先細部分１００８とを含む。円筒形部分１００６内には、カテーテルハブ受容空間５０４が配置される。ある実施形態では、カテーテルハブ受容空間５０４はまた、シースハブ４０６の中の実質的に円筒形の空隙である。そのような実施形態では、カテーテルハブ４０４の挿入部分７０８がカテーテルハブ受容空間内で受容され得るように、カテーテルハブ４０４の挿入部分７０８もまた、円筒形である。他の実施形態では、カテーテルハブ４０４の挿入部分７０８の形状およびカテーテルハブ受容空間５０４の空隙の形状が、任意の他の幾何学的形状であってもよい一方で、シースハブ４０２の外面４０６は、円筒形のままである。当然ながら、一実施形態では、逆のことが当てはまり得る。つまり、ある実施形態では

、シースハブ４０２の外面４０６が、円筒形以外の形状であってもよい一方で、カテーテルハブ４０４の挿入部分７０８の形状およびカテーテルハブ受容空間５０４の空隙の形状は、円筒形である。

【００９５】

シースハブ４０２の先細部分１００８は、円筒形部分１００６からシースハブ４０２のシース受容端１００４まで延在する。シース受容端１００４におけるシースハブ４０２の直径は、シースハブ４０２の先細部分１００８がシースハブ４０２の先細部分１００８に向かって傾斜するように、円筒形部分１００６と先細部分１００８との間の界面１０１０におけるシースハブ４０２の直径よりも実質的に小さい。

【００９６】

ある実施形態では、シース４２０は、規則的間隔でシース４２０の外面１０１８の少なくとも一部分に沿って配置される、複数の深度インジケータ１０１６を含んでもよい。図１０Ａで図示される実施形態では、深度インジケータ１０１６は、シース４２０の外面１０１８上に配置される線である。他の実施形態では、深度インジケータ１０１６は、点、正方形、円、三角形、または任意の他の視覚的インジケータ等の他の形状を含んでもよい。一実施形態では、深度インジケータ１０１６は、シース４２０が患者の鼻腔１０４内に位置付けられたときのシース４２０の深度の数値的指示を含んでもよい。

【００９７】

上記で論議されるように、患者の鼻腔１０４の生体構造は、個人によって異なる。したがって、中鼻甲介１１４の前隆起３０２の深度は、患者によって異なる。初期治療中に、医師または他の医療専門家は、特定の患者の中鼻甲介１１４の前隆起３０２の深度を記録するために、シース４２０上の深度インジケータ１０１６を使用してもよい。ある実施形態では、医師または他の医療専門家はまた、患者の鼻骨１２２の下面３０４の深度を記録してもよい。後続の治療のために、医師または他の医療専門家は、患者の鼻腔１０４内の繊細な組織に接触または損傷することを回避するように、記録された深度を参照することができる。

【００９８】

一実施形態では、初期治療のために、医師または他の医療専門家は、患者のある特性に従って、患者の中鼻甲介１１４の前隆起３０２の平均深度および鼻骨１２２の下面３０４の平均深度を記載する、表（図示せず）を参照してもよい。例えば、一実施形態では、表は、所与の年齢層の中鼻甲介１１４の前隆起３０２の平均深度および鼻骨１２２の下面３０４の平均深度を記載してもよい。表はまた、所与の年齢層の蝶口蓋／翼口蓋陥凹１１８の平均深度を記載してもよい。ある実施形態では、表はさらに、性別分類に分けられてもよい。別の実施形態では、表は、患者の外鼻生体構造で得られる測定値に従って、平均深度を記載してもよい。

【００９９】

図１０Ｂは、本開示による、シース４２０に連結されたシースハブ４０２の一実施形態の断面図を描写する。図１０Ｂで描写される実施形態は、図１０Ａの線Ｄ－Ｄに沿って得られている。

【０１００】

ある実施形態では、先細部分は、シースハブ４０２の中のカテーテルハブ受容空間５０４からシースハブ４０２のシース受容端１００４まで先細部分を通って延在する、空洞１０１２を含む。シース４２０は、シースをシースハブ４０２に連結するように空洞１０１２内で受容される。

【０１０１】

図１０Ｂで図示される実施形態では、係合要素５２０は、シースハブ４０２の内面５０２に沿って縦方向に延在する陥凹として、より明確に示されている。ある実施形態では、係合要素５２０の陥凹は、シースハブ４０２の円筒形部分１００６内のみに位置付けられる。そのような実施形態では、係合要素５２０の陥凹は、停止要素５２２から円筒形部分１００６と先細部分１００８との間の界面１０１０まで延在してもよい。図１０Ｂで図示

される実施形態等の他の実施形態では、係合要素５２０の陥凹は、シースハブ４０２の先細部分１００８を通って延在してもよい。

【０１０２】

図１１は、本開示の一実施形態による、停止要素５２２を含むシースハブ４０２の領域１０１４の拡大図を描写する。ある実施形態では、停止要素５２２は、シースハブ４０２のカテーテルハブ受容端１００２に隣接して配置される傾斜面１１０２を含む。停止要素５２２の傾斜面１１０２は、カテーテルハブ受容空間５０４の中へのカテーテルハブ４０４の挿入部分７０８の容易な挿入を促進するように、抑止要素５１６のフランジの傾斜面７１５によって係合されてもよい。ある実施形態では、停止要素５２２、抑止要素５１６のフランジ、または両方は、カテーテルハブ受容空間５０４の中へのカテーテルハブ４０４の挿入部分７０８の容易な挿入を促進するように、柔軟または半柔軟な材料で作製されてもよい。他の実施形態では、カテーテルハブ４０２全体、シースハブ４０２全体、または両方とも、柔軟または半柔軟な材料で作製されてもよい。

【０１０３】

停止要素５２２の停止表面１１０４は、シースハブ４０２の内面５０２から実質的に垂直に延在する。カテーテルハブ４０４がカテーテルハブ受容空間５０４内から拡張位置４２６へ引き出されたとき、停止要素５２２の停止表面１１０４は、カテーテルハブ受容空間５０４内からのカテーテルハブ４０４のさらなる引き出しを止めるように、抑止要素５１６の後面７１６に係合する。

【０１０４】

図１２は、本開示による、シースハブ４０２の一実施形態の端面図を描写する。図１２で図示される実施形態は、シースハブ４０２のシース受容端１００４の方向に得られており、シース４２０は明確にするために除去されている。

【０１０５】

図１２で図示される実施形態では、係合要素５２０の陥凹は、シースハブ４０２の先細部分１００８を通ってシース受容端１００４まで延在する。ある実施形態では、係合要素５２０の陥凹は、シースハブ４０２の長手方向軸に対して回転配向インジケータ４０８ｂと同一の回転配向で整合させられる。他の実施形態では、係合要素５２０の陥凹は、回転配向インジケータ４０８ｂからオフセットされてもよい。

【０１０６】

図１３Ａは、シース４２０の導入端５０５およびカテーテル４１２の挿入端４１４の一実施形態の断面図を図示する。図１３Ａで図示される実施形態では、シース４２０の導入端５０５およびカテーテル４１２の挿入端４１４は、カテーテルハブ４０４（図示せず）が拡張位置４２６に位置付けられたときにシース４２０の導入端５０５およびカテーテル４１２の挿入端４１４が配置される位置に、位置付けられる。

【０１０７】

ある実施形態では、カテーテル４１２の挿入端４１４の先端５１０は、先端５１０が丸みを帯びるように湾曲した１３０６。シース４２０の導入端５０５における最外縁１３０２は、頂点５０８まで傾斜している。一実施形態では、カテーテルハブ４０４が拡張位置４２６に位置付けられたとき、シース４２０の導入端５０５における頂点５０８は、カテーテル４１２の丸みを帯びた先端５１０の湾曲１３０６の開始１３０４と整合させられる。そのような実施形態では、カテーテル４１２とシース４２０との間の移行部５１２は、連続的で平滑であり、実質的に縁を含まない。一実施形態では、カテーテル４１２とシース４２０との間の嵌合は、緊密である。つまり、一実施形態では、カテーテル４１２とシース４２０との間には実質的に間隙がない。一実施形態では、カテーテル４１２とシース４２０との間の間隙の欠如は、シース４２０の導入端５０５における頂点５０８が、患者の鼻腔１０４内の繊細な組織に引っ掛かるか、または別様に損傷するであろう可能性を低減させる。

【０１０８】

図１３Ｂは、シース４２０の導入端５０５およびカテーテル４１２の挿入端４１４の一

実施形態の断面図を図示する。図１３Ｂで図示される実施形態では、カテーテル４１２の外径１３０８は、シース１４２０の内径１３１０よりも実質的に小さい。そのような実施形態では、カテーテル４１２とシース４２０との間の移行部５１２は、平滑ではなく、シース４２０の導入端５０５上の頂点５０８は、患者の鼻腔１０４内の繊細な組織に引っ掛かり、または別様に損傷し得る、鋭い縁を形成してもよい。したがって、ある実施形態では、カテーテル４１２およびシース４２０は、カテーテル４１２とシース４２０との間の嵌合が鋭い縁を回避するよう緊密であるように、設計されてもよい。

【０１０９】

図１３Ｃは、シース４２０の導入端５０５およびカテーテル４１２の挿入端４１４の別の実施形態の断面図を図示する。図１３Ｃで図示される実施形態では、カテーテル４１２は、カテーテル４１２の挿入端４１４における湾曲１３０６の開始１３０４を越えてシース４２０の頂点５０８を延在させる位置で、シース４２０内に位置付けられる。そのような実施形態では、カテーテル４１２とシース４２０との間の移行部５１２は、平滑ではなく、シース４２０の導入端５０５上の頂点５０８は、患者の鼻腔１０４内の繊細な組織に引っ掛かり、または別様に損傷し得る、鋭い縁を形成してもよい。したがって、一実施形態では、停止要素５２２は、シース４２０の導入端５０５上の頂点５０８を、カテーテル４１２の挿入端４１４における湾曲１３０６の開始１３０４と整合させる位置で、カテーテルハブ受容空間５０４内からのカテーテルハブ４０４の引き出しを止める。

【０１１０】

予想外なことに、患者の同意とともに、頭痛を緩和するために、先進プロトタイプカテーテルが効果的に使用されている。これらの手技の結果が記録されており、有望である。７４例の手技後に、わずか４人の患者が、手技の忍容性を「不良」または「妥当」のいずれか一方として評価した。残りの患者のうち、２４人が忍容性を「良好」として評価し、４６人が「優良」と評価した。この忍容性は、以下の表１で要約されるように、患者が鼻腔内麻酔薬で前処置されたときに改善した。

【０１１１】

記録された７４例の処置のうち、いかなる有害事象も介入を必要としなかった。５例において、鼻粘膜にわずかに血液が滲んだことが着目されたが、明らかな鼻出血は起こらなかった。２例の手技が、頭痛の悪化をもたらしたが、両方の患者は、さらなる発症を伴わずに次の日に基準頭痛に戻った。これら２人の患者を除いて、全ての患者が、必要であれば、該手技を再び受けるであろうと答えた。

【０１１２】

ＳＰＧＢが行われた日に、患者の５８％が、頭痛の完全解消とともに診療室を去った一方で、７４％は、視覚的アナログ尺度（ＶＡＳ）によって査定されるように、有意な臨床改善を経験した。一部の患者が追跡調査失敗になっているが、頭痛の重症度の有意な改善が１ヶ月に患者の３分の１で持続した。これらの結果は、臨床転帰ならびにデバイスおよび手順の両方の予想有効性の両方に関して、期待基準に反する。同様に、手技の直示的な患者容認および忍容性も予想外である。手技および患者満足度の成果の性質を考慮して、最も技能が高く経験豊富な熟練外科医以外による、この手技の実施は、この場合、神経科医または神経外科医であると示唆される、当業者による、予想外の一連の結果に基づくような科学の進歩および有用な技術を構成すると考えられる。

【０１１３】

【表１】

表1 ：

VASにおける低減	退院時 (N=74)
80-100%	43 (58%)
50-79%	12 (16%)
20-49%	3 (4%)
<19%	16 (23%)

【実施例】

【０１１４】

ＢＣは、１０年近く前にスノーモービル事故で頭部損傷を受け、それ以来、頭痛がない日を思い出すことができなかった。治療、標準薬剤、麻酔剤さえも彼に緩和を与えることができなかった。毎日が８／１０の頭痛で終わった。彼は、ＳＰＧＢ後に頭痛の１００％解消を経験し、１年以上頭痛がない状態のままである。

【０１１５】

ハイウェイパトロール警官のＡＤは、何年も事実上毎日、８／１０の頭痛に苦しんでいた。彼は、ＳＰＧＢ後の２ヶ月間、頭痛がない状態のままであった。この２ヶ月間に頭痛がないとどれほど生活が良好であり得るかを思い出して、彼は、頭痛が再発したとき、再手技を涙ながらに要求した。現在、彼は、短期間の無痛隔月手技を受け、頭痛がない状態で生活している。

【０１１６】

同様に、ある種類の頭痛は、神経機能障害の結果であり、機能不全回路を乱すことが、リセットの役割を果たすことができ、正常な神経機能が戻ることを可能にする。この理由により、ＳＰＧＢの有益性は、局所麻酔薬の効果をはるかに超えて、不確定期間にわたって持続し得る。したがって、手技が繰り返されたときに、多くの患者が有益性の向上を経験することが分かっている。

【０１１７】

従来の教示は、そのような結果を示唆することができない。例えば、１９９６年にＪｏｕｒｎａｌ ｏｆ ｔｈｅ Ａｍｅｒｉｃａｎ Ｍｅｄｉｃａｌ Ａｓｓｏｃｉａｔｉｏｎで発表された無作為化二重盲対照試験は、頭痛患者の鼻孔の中へ局所リドカインを点滴注入したときの患者の５５％で片頭痛の急速な緩和を説明した。応答した患者のうち、４２％が、通常は、１時間以内に頭痛の再発を経験した。留意すべきこととして、彼らは「頭痛が３日より長く持続した、または重度の頭痛の頻度が週に１回より多い場合」の患者を除外した。

【０１１８】

我々の患者は、慢性の日常的な頭痛に苦しみ、多くの患者に、まさにこの研究によって排除された種類の頭痛があった。数種類の頭痛に対するＳＰＧＢの背後に良好な科学的理論があるため、および手技の潜在的な有害影響が非常に少なく、かつ非常に軽度であるため、我々は、ＳＰＧＢの使用において、はるかに包括的であるというアプローチを取り、期待よりも良好な結果を経験している。

【０１１９】

２００６年のトマス・ジェファーソン大学（Ｔｈｏｍａｓ Ｊｅｆｆｅｒｓｏｎ Ｕｎｉｖｅｒｓｉｔｙ）でのレトロスペクティブカルテ審査は、１２人に日常的な持続性頭痛があり、１５人に「他の頭痛診断」がある、４１人の患者を含む、我々の患者により類似した難治性慢性頭痛母集団を調べた。彼らは、「２５．４％に完全応答があり、５７．１％に部分応答があり、３．２％が悪化し、１４．３％に変化がなかった」と報告した。しかしながら、彼らのリドカイン投薬計画は、２～１５日間の心臓監視ユニットでの静脈内リドカインであった。

【０１２０】
ＳｐｈｅｎｏＣａｔｈ™ブランドの医療機器は、単に、より精密かつ一貫して薬剤を所望の場所に送達するため、全てではないにしても大抵の発表された研究結果を凌ぐ可能性があると考えられる。直接蛍光透視法が、輸液を標的に送達するＳｐｈｅｎｏＣａｔｈ™ブランドの医療機器の能力を立証している。さらに、ＳｐｈｅｎｏＣａｔｈ™ブランドの医療機器は、少数の疼痛専門医から診療室の施術者まで、ＳＰＧＢの機会を拡張し、手技への患者アクセスを指数関数的に増加させる。

【０１２１】
ある実施形態では、シース４２０の導入端５０５における頂点５０８は、球状先端領域１３１０の丸みを帯びた側壁１３１４によって、患者の鼻腔１０４内の繊細な組織から保護される。他の実施形態では、シース４２０の外径１３１６は、球状先端領域が、患者の鼻腔１０４内の繊細な組織への潜在的な引っ掛かりまたは他の損傷からシース４２０の導入端５０５を保護するように、球状先端領域１３１０の外径１３１８よりも実質的に小さくあり得る。そのような実施形態では、導入端５０５は、描写した実施形態で図示されるように、傾斜よりもむしろ、角がとられるか、または丸みを帯びてもよい。

【０１２２】
当業者であれば、頭頸部癌、複合性局所疼痛症候群、反射性交感神経性ジストロフィ、血管運動神経性鼻炎、口腔および顎顔面手術における術前および術後感覚脱失、群発性頭痛、頭痛、頸部けいれん、任意のレベルの椎間板疾患またはヘルニア、腰痛、腰仙部けいれん、梨状筋けいれん症候群、痙性（けいれん性）斜頸、ＳＰＧ神経痛（スルダー症候群）、三叉神経痛（疼痛性チック）、帯状疱疹後神経痛、自律神経痛、非定型顔面痛、椎間板膨隆、腰仙椎間板、カウザルギー、反射性交感神経性ジストロフィ（ＲＳＤ）、頚椎症、片頭痛、副鼻洞性頭痛、脳脊髄液（ＣＳＦ）漏出頭痛、慢性副鼻腔炎、緊張性頭痛、筋筋膜疼痛症候群、圧迫神経、坐骨神経痛、椎間板脱出、副鼻腔痛、顎関節症候群（ＴＭＪ）、むち打ち、アレルギー性鼻炎、血管運動神経性鼻炎、喘息、ベル麻痺（顔面神経麻痺）、骨痛、癌疼痛、気管支けいれん、慢性気管支炎、月経困難症、子宮内膜症、線維筋痛症、けいれんを伴う多発性硬化症、末梢神経障害（神経障害性疼痛）、レイノー現象、関節リウマチ（発赤）、帯状疱疹（帯状ヘルペス）、脊髄狭窄、慢性疲労症候群、慢性吃逆、糖尿病性神経障害、多汗症、脳圧低下頭痛、幻肢／歯痛、感覚異常、反復性ストレス損傷、および耳鳴（低頻度）のうちの少なくとも１つである、適応症に対する本発明の使用を容易に理解するであろう。

【０１２３】
本主題は、その精神または本質的な特性から逸脱することなく、他の具体的形態で具現化されてもよい。説明された実施形態は、あらゆる点において、制限的ではなく例証的にすぎないと見なされるものである。したがって、本主題の範囲は、前述の説明よりもむしろ、添付の請求項によって示される。請求項の同等物の意味および範囲内に入る全ての変更は、それらの範囲内に包含されるものである。

【０１２４】
本方法および装置は、最も実用的であると現在見なされているものに関して説明されているが、本開示は、開示された実装に限定される必要がないことを理解されたい。請求項の精神および範囲内に含まれる、種々の修正および類似配列を対象とすることが意図され、その範囲は、全てのそのような修正および類似構造を包含するよう、最も広い解釈を受けるべきである。本開示はまた、以下の請求項のありとあらゆる実装も含む。

【０１２５】
また、本開示の本質から逸脱することなく、種々の変更が行われてもよいことも理解されたい。そのような変更もまた、暗示的に説明に含まれる。それらは依然として、本開示の範囲内に入る。本開示は、方法および装置モードの両方において、独立して、および全体的なシステムとしての両方で、本発明の多数の側面を対象とする特許をもたらすことを目的としていると理解されたい。

【０１２６】

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IPR2025-01125

さらに、本開示および請求項の種々の要素のそれぞれはまた、種々の様式で達成されてもよい。本開示は、任意の装置実装のうちの実装の変形例、方法またはプロセス実装、あるいはさらに、単にこれらのうちの任意の要素の変形例であれ、それぞれのそのような変形例を包含すると理解されるべきである。

【０１２７】

具体的には、本開示が本発明の要素に関するため、たとえ機能または結果のみが同一であっても、各要素に対する言葉は、同等の装置の用語または方法の用語によって表されてもよいことを理解されたい。

【０１２８】

そのような同等の、より広い、またはさらに一般的な用語は、各要素または措置の説明に包含されると見なされるべきである。そのような用語は、本発明が享有できる暗示的に広い範囲を明示的にすることが所望される場合に、代用することができる。

【０１２９】

全ての措置は、その措置を講じるための手段として、またはその措置を引き起こす要素として表されてもよいことを理解されたい。

【０１３０】

同様に、開示される各物理的要素は、その物理的要素が促進する措置の開示を包含すると理解されるべきである。

【０１３１】

特許のために本願で記述される任意の特許、出版物、または他の参考文献は、参照することにより本明細書に組み込まれる。加えて、使用される各用語に関して、本願でのその利用がそのような解釈と矛盾しない限り、一般的な辞書の定義が、各用語について組み込まれるように理解されるべきであり、熟練者によって認識される標準専門辞典およびＲａｎｄｏｍ Ｈｏｕｓｅ Ｗｅｂｓｔｅｒ’ｓ Ｕｎａｂｒｉｄｇｅｄ Ｄｉｃｔｉｏｎａｒｙの最新版のうちの少なくとも１つに含有されるような全ての定義、代替用語、および同義語が、参照することにより本明細書に組み込まれることを理解されたい。

【０１３２】

最後に、本願とともに出願される情報開示陳述書または他の情報文書に記載される全ての参考文献は、参照することにより本明細書に組み込まれるが、上記のそれぞれに関して、参照することにより組み込まれる、そのような情報または文書が、本発明／これらの発明の特許と矛盾すると見なされる場合がある限りでは、そのような文書は、出願者によって作製されたと明示的に見なされないものである。

【０１３３】

この点に関して、実用的な理由で、潜在的に何百もの請求項を追加することを回避するよう、本出願者は、最初の従属項を伴う請求項のみを提示していることを理解されたい。

【０１３４】

不十分な代替が行われる限りにおいて、本出願者が、任意の特定の例示的実装を文字通りに包含するよう、任意の請求項を実際に草稿しなかった限りにおいて、および別様に適用可能な程度に、本出願者が、単に全ての不測の事態を予測できなかった場合があるため、出願者は、いかようにもそのような範囲を放棄することを意図していた、または実際に放棄したと理解されるべきではない。当業者は、そのような代替的な例示的実装を文字通り包含したであろう請求項を草稿したと合理的に期待されるべきではない。

【０１３５】

さらに、「～を備える（ｃｏｍｐｒｉｓｉｎｇ）」という移行句の使用は、従来の請求項の解釈によれば、本明細書で「非制約的な」請求項を維持するために使用される。したがって、文脈が別様に要求しない限り、「備える（ｃｏｍｐｒｉｓｅ）」という用語、または「備える（ｃｏｍｐｒｉｓｅｓ）」または「～を備える（ｃｏｍｐｒｉｓｉｎｇ）」等の変形例は、任意の他の要素またはステップあるいは要素またはステップ群の除外ではなく、記述された要素またはステップあるいは要素またはステップ群の包含を暗示することを目的としていることを理解されたい。

【０１３６】
そのような用語は、法的に許容される最も広い範囲を本出願者に与えるよう、最も拡張的な形態で解釈されるべきである。

【図１】

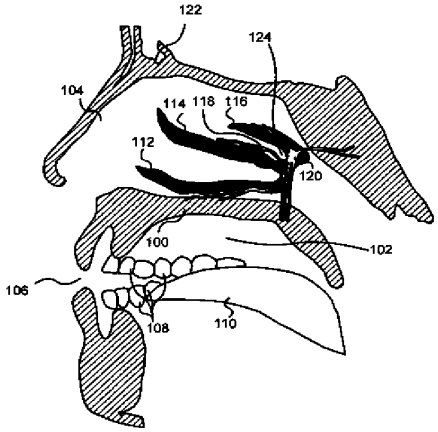


FIG. 1
（従来技術）

【図２】

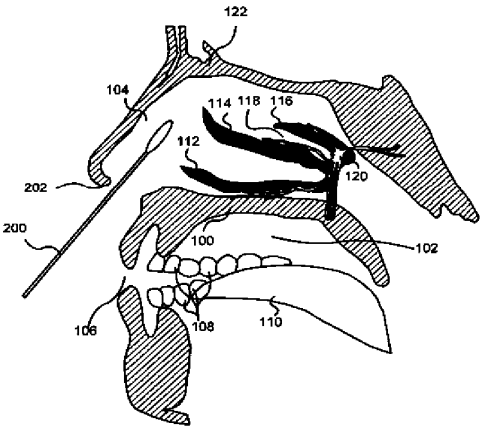


FIG. 2
（従来技術）

【図３】

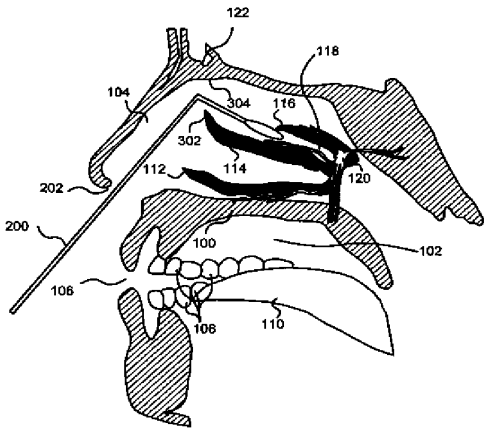


FIG. 3
（従来技術）

【図４Ａ】

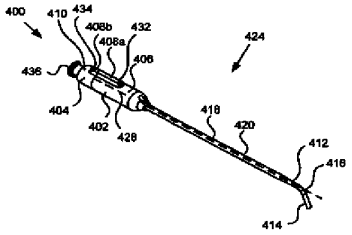


FIG. 4A

【図４Ｂ】

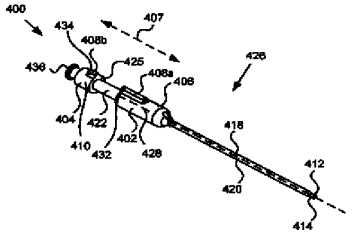


FIG. 4B

【図５Ａ】

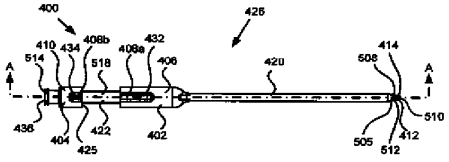


FIG. 5A

【図５Ｂ】

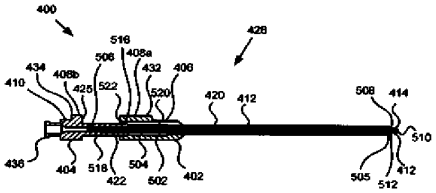


FIG. 5B

【図６Ａ】

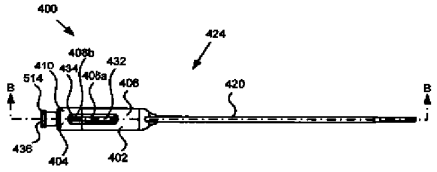


FIG. 6A

【図６Ｂ】

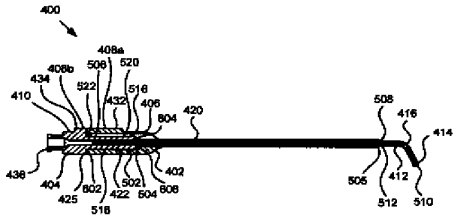


FIG. 6B

【図７】

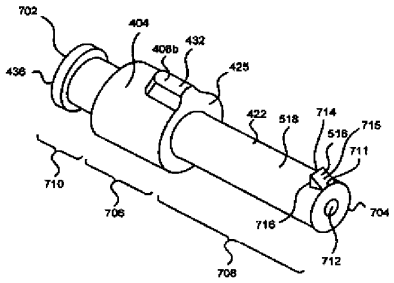


FIG. 7

【図８Ａ】

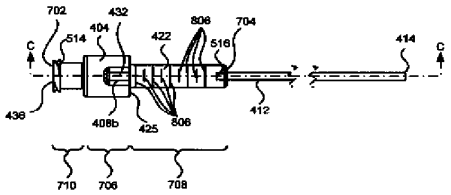


FIG. 8A

【図８Ｂ】

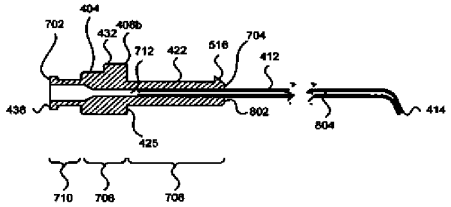


FIG. 8B

【図９Ａ】

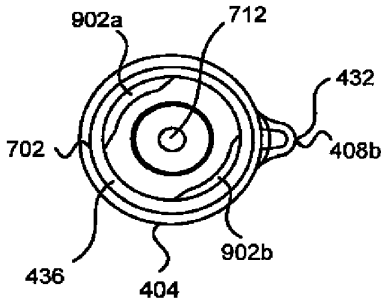


FIG. 9A

【図９Ｂ】

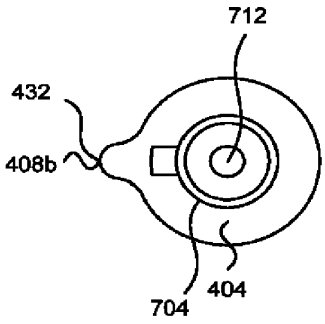


FIG. 9B

【図１０Ａ】

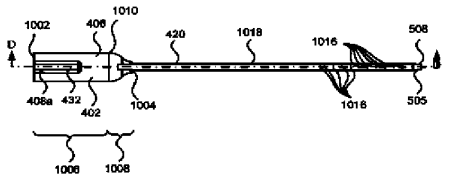


FIG. 10A

【図１０Ｂ】

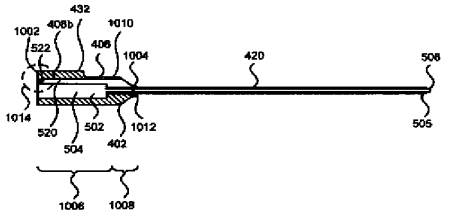


FIG. 10B

【図１１】

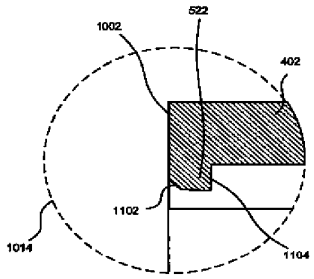


FIG. 11

【図１２】

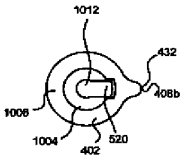


FIG. 12

【図１３Ａ】

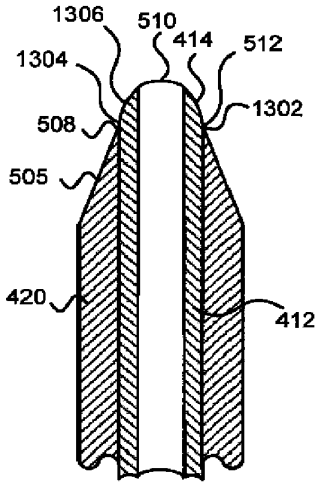


FIG. 13A

【図１３Ｂ】

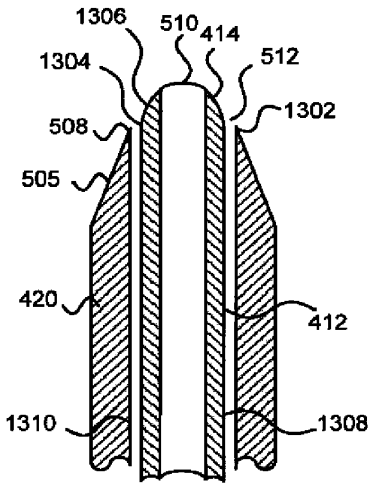


FIG. 13B

【図１３Ｃ】

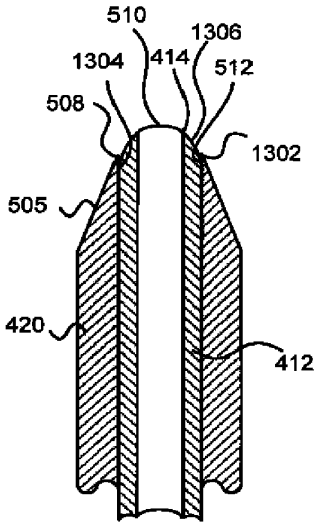


FIG. 13C

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/027138

A. CLASSIFICATION OF SUBJECT MATTER

A61B 17/24(2006.01)i, A61B 17/34(2006.01)i, A61M 25/01(2006.01)i, A61M 25/092(2006.01)i

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 17/24; A61M 19/00; A61F 2/00; A61M 5/00; A61M 11/00; A61M 25/00; A61M 5/178

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: sphenopalatine, pterygopalatine, catheter, hub

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 2010-0030187 A1 (XIA TIAN) 04 February 2010 See abstract; figs. 1-4; paragraphs 49-51; claims 1, 11.	1,11,19 2-10,12-18,20
A	US 2010-0057048 A1 (ELDREDGE STEPHEN) 04 March 2010 See abstract; figs. 4, 8; paragraphs 6-61; claims 4, 6, 12.	1-20
A	US 2007-0021648 A1 (JAY LENKER et al.) 25 January 2007 See abstract; fig. 3; paragraph 35; claims 1, 8.	1-20
A	US 05830189A A (CHANG, JOSEPH J.) 03 November 1998 See abstract; figs. 1, 2; column 4, lines 5-9; claims 1, 2.	1-20
A	US 20040015068 A1 (SHALEV, ALON et al.) 22 January 2004 See abstract; figs. 1, 2; paragraphs 30, 111-116; claims 2, 12, 13.	1-20
A	US 7632243 B2 (BIALECKI DENNIS M et al.) 15 December 2009 See abstract; figs 3A-3C, 6D; claim 1.	1-20

☐ 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 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 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
08 FEBRUARY 2013 (08.02.2013)	**08 FEBRUARY 2013 (08.02.2013)**
Name and mailing address of the ISA/KR Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon Metropolitan City, 302-701, Republic of Korea Facsimile No. 82-42-472-7140	Authorized officer CHO, Woo Yeon Telephone No. 82-42-481-5617

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2012/027138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Form PCT/ISA/210 (patent family annex) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2012/027138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Form PCT/ISA/210 (patent family annex) (July 2009)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/US2012/027138

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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Form PCT/ISA/210 (patent family annex) (July 2009)

フロントページの続き

(81)指定国 AP(BW,GH,GM,KE,LR,LS,MW,MZ,NA,RW,SD,SL,SZ,TZ,UG,ZM,ZW),EA(AM,AZ,BY,KG,KZ,MD,RU,TJ,TM),EP(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),OA(BF,BJ,CF,CG,CI,CM,GA,GN,GQ,GW,ML,MR,NE,SN,TD,TG),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,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

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(72)発明者 ピプキン, ウィリアム
アメリカ合衆国 ユタ ８４０９７, オレム, サウス ９００ イースト ３２８

Ｆターム(参考) 4C160 MM06 NN03 NN09 NN13 NN15

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
Schoen, Adam M.
BROWN RUDNICK LLP
One Financial Center
Boston, MA 02111
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference NEURE-003/01WO 3524	Date of mailing *(day/month/year)* 11 January 2021 (11-01-2021) **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/IB2020/000544	International filing date *(day/month/year)* 29 June 2020 (29-06-2020)
Applicant NEURENT MEDICAL LIMITED	

1. [X] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   How? Directly to the International Bureau preferably through ePCT, or on paper to:
   The International Bureau of WIPO, 34 chemin des Colombettes, 1211 Geneva 20, Switzerland

   For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 - 9.011.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   The applicant may **submit comments on an informal basis on the written opinion of the International Searching Authority** to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

   Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

   Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer ACQUAVIVA, Laure Tel: +49 (0)89 2399-5656

Form PCT/ISA/220 (revised January 2020)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
NEURE-003/01WO 3524		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB2020/000544	29 June 2020 (29-06-2020)	28 June 2019 (28-06-2019)
Applicant		
NEURENT MEDICAL LIMITED		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [X] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title**,
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. 2
      [ ] as suggested by the applicant
      [X] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

Aerin Exhibit 1011, Page 811 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2020/000544

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.: 11-33, 57-72, 86-98
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.:

1-10, 44-56

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.

Aerin Exhibit 1011, Page 812 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2020/000544

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/053 A61B18/14
ADD. A61B18/00 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)
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 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.
Y	US 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17) cited in the application the whole document	1-10, 44-56
Y	WO 2007/008954 A2 (ABLATION FRONTIERS [US]; WERNETH RANDELL L [US]) 18 January 2007 (2007-01-18) abstract paragraph [0002] - paragraph [0013] paragraph [0096] - paragraph [0099] claims 52-61	1-10, 44-56
A	US 2016/331459 A1 (TOWNLEY DAVID [IE] ET AL) 17 November 2016 (2016-11-17) cited in the application the whole document	1-10, 44-56

-/--

[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
8 October 2020	11/01/2021

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	Artikis, T

1

Form PCT/ISA/210 (second sheet) (April 2005)

Aerin Exhibit 1011, Page 813 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2020/000544

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2015/048806 A2 (NIDUS MEDICAL LLC [US]) 2 April 2015 (2015-04-02) abstract paragraph [0149]; figures 20A-20E	1-10, 44-56
A	US 2005/283148 A1 (JANSSEN WILLIAM M [US] ET AL) 22 December 2005 (2005-12-22) the whole document	1-10, 44-56

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

Aerin Exhibit 1011, Page 814 of 2183
Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2020/000544

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		US 2018317993 A1	08-11-2018
		US 2019083157 A1	21-03-2019
		US 2020054379 A1	20-02-2020
		WO 2015048806 A2	02-04-2015
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		CA 2570911 A1	26-01-2006
		CN 1981256 A	13-06-2007
		CR 8817 A	18-03-2008
		EP 1769320 A2	04-04-2007
		JP 2008503255 A	07-02-2008
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		US 2005283148 A1	22-12-2005
		US 2007060921 A1	15-03-2007
		US 2007167943 A1	19-07-2007
		US 2010114095 A1	06-05-2010
		US 2013046292 A1	21-02-2013

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2020/000544

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 2016066984 A1	10-03-2016
		WO 2006009705 A2	26-01-2006
		ZA 200610576 B	30-07-2008

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10, 44-56

Systems for treating a condition comprising: a device comprising an end effector including a plurality of electrodes; and a controller operably associated with the device and configured to: receive data from the device associated at least with presence and/or a depth/location of neural tissue at a position of each of the plurality of electrodes; and process the data to determine a level of energy to be delivered by each of the plurality of electrodes such that the energy delivered at each position by each of the plurality of electrodes is sufficient to ablate the neural tissue at each position and minimize and/or prevent damage to non-neural tissue including a blood vessel adjacent to the neural tissue at each position.

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2. claims: 34-43

A system for treating at least one of rhinitis, congestion, and rhinorrhea within a nasal cavity of a patient, the system comprising: a device comprising an end effector including a plurality of electrodes; a controller operably associated with the device and configured to: receive data from the device associated at least with presence and/or a depth/location of blood vessels associated with mucus producing and/or mucosal engorgement elements at a position of each of the plurality of electrodes within the nasal cavity; and process the data to determine a level of energy to be delivered by each of the plurality of electrodes such that the energy delivered at each position by each of the plurality of electrodes is sufficient to: cause thrombus formation within one or more blood vessels associated with the mucus producing and/or mucosal engorgement elements, resulting in local hypoxia of the mucus producing and/or mucosal engorgement elements, thereby decreasing production of mucus and/or mucosal engorgement.

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3. claims: 73-85

A system for diagnosing and/or treating a neurological condition of a patient, the system comprising: a device comprising an end effector including a plurality of electrodes; and a controller operably associated with the device and configured to: receive data from the device that is associated with neural tissue at a target site; process the data to determine a type of neural tissue at the target site; and determine energy output from the end effector based on the type of neural tissue at the target site.

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/IB2020/000544

TITLE: SYSTEMS AND METHODS FOR TARGETED THERAPEUTIC NASAL NEUROMODULATION

APPLICANT: NEURENT MEDICAL LIMITED

IPC CLASSIFICATION: A61B5/053, A61B18/14, A61B18/00, A61N1/05, A61N1/36

EXAMINER: Artikis, T

CONSULTED DATABASES: WPI, PRESEARCH, ANSERA, COMBI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B18/1492, A61B2018/00327, A61B2018/00434, A61N1/0546, A61N1/36014

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
Systems for treating a condition comprising: a device comprising an end effector including a plurality of electrodes; and a controller operably associated with the device and configured to: receive data from the device associated at least with presence and/or a depth/location of neural tissue at a position of each of the plurality of electrodes; and process the data to determine a level of energy to be delivered by each of the plurality of electrodes such that the energy delivered at each position by each of the plurality of electrodes is sufficient to ablate the neural tissue at each position and minimize and/or prevent damage to non-neural tissue including a blood vessel adjacent to the neural tissue at each position.

EPO FORM P0A42

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2020/000544	29.06.2020	28.06.2019

International Patent Classification (IPC) or both national classification and IPC
INV. A61B5/053 A61B18/14 ADD. A61B18/00 A61N1/05 A61N1/36

Applicant
NEURENT MEDICAL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Artikis, T Telephone No. +49 89 2399-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 11-43, 57-98

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 11-43, 57-98

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☒ See Supplemental Box for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-10, 44-56

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10, 44-56
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-10, 44-56
Industrial applicability (IA)	Yes:	Claims	1-10, 44-56
	No:	Claims	

2. Citations and explanations

   see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

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Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1 No examination will be carried out in respect of claims 11-43 and 57-98, because they have not been searched (see Art. 17(2)(a) or (3) PCT, Rule 66.1(e) PCT and the international search report).

Re Item IV

Lack of unity of invention

2 The present application lacks unity according to Rule 13.1 PCT, because the three inventions of claims I) 1-10 and 44-56, II) 34-43, and III) 73-85 are not linked by a single general inventive concept and no technical relationship in the sense of Rule 13.2 PCT exists between them.

Document US2018/133460 discloses (see fig. 3A and the corresponding description) the common subject-matter of independent claims 1 (or 44), 34 and 73, namely a system (300) comprising: a device comprising (302) an end effector (312) including a plurality of electrodes (344); and a controller (304, 318, 320) operably associated with the device (302) and configured (see par. 38) to receive data from the device (302), process the data and determine (see par. 46) energy output (activate the electrodes 344 or not) from the end effector (312) based on the processed data.

Furthermore, said independent claims do not share any corresponding special technical features in the sense of Rule 13.2 PCT, because the problems that they seek to solve are completely different, namely:

- how to select an energy delivery parameter for neural tissue ablation in order to minimise or prevent damage to a blood vessel adjacent to the neural tissue for claim 1 (or 44);
- how to select an energy delivery parameter in order to form thrombus within nasal blood vessels for claim 34; and
- how to determine energy output based on neural tissue type in order to diagnose and/or treat a neurological condition for claim 73.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3 Reference is made to the following documents:

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D1 US 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17) cited in the application

D2 WO 2007/008954 A2 (ABLATION FRONTIERS [US]; WERNETH RANDELL L [US]) 18 January 2007 (2007-01-18)

4 The present application does not meet the criteria of Article 33(3) PCT, because the subject-matter of independent claims 1 and 44 does not involve an inventive step.

4.1 D1 is regarded as being the prior art closest to the subject-matter of claim and discloses (see the passages of said document cited under item IV above) a system (300) for treating a condition within a nasal cavity of a patient, the system comprising:
a device (302) comprising an end effector (312) including a plurality of electrodes (344); and
a controller (304, 318, 320) operably associated with the device (302) and configured to:
receive data from the device (302) associated at least with presence and/or a depth/location of neural tissue at a position of each of the plurality of electrodes within the nasal cavity; and
process the data to determine (see par. 100) a parameter (frequency) of energy to be delivered by each of the plurality of electrodes such that the energy delivered at each position by each of the plurality of electrodes is sufficient to modulate/ablate the neural tissue at each position and minimize and/or prevent damage to an artery or arterial wall adjacent to the neural tissue at each position.
The subject-matter of claim 1 therefore differs from this known system in that the level of energy is determined and is therefore new (Art. 33(2) PCT).
The problem to be solved by the present invention may therefore be regarded as how to select an energy delivery parameter for neural tissue ablation in order to minimise or prevent said damage.
The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT), because D2 discloses (see claims 52-61) that the energy level is an alternative to the frequency for targeted tissue ablation. Therefore, it appears obvious to the skilled person to substitute energy level as disclosed in D2 for the frequency disclosed in D1, thereby arriving at the subject-matter of claim 1 without the exercise of an inventive step (Art. 33(3) PCT).

4.2 The argumentation of the previous point can be applied in an analogous manner to the subject-matter of independent claim 44.

5 Dependent claims 2-10 and 45-56 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step (Art. 33(3) PCT), because said additional features are already disclosed in D1 or D2 as explained below:
Claims 2-9, 45-52, 54-55: see the aforementioned passages of D1;
Claims 10, 53, 56: see D2, par. 96-99.

Re Item VII

Certain defects in the international application

6 The independent claims are not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art, namely D1, being placed in the preamble (Rule 6.3(b)(i) PCT) and the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

7 The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

The following points should be considered when filing amendments:

A) Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply and not be incorporated into the application (Article 34(2)(b) PCT).

B) In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT). If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

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Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO/ISA)

General information

For all international applications, the competent International Searching Authority **(ISA)** will establish an international search report **(ISR)** accompanied by a written opinion of the International Searching Authority **(WO/ISA)**. The **WO/ISA** may be responded to by

- filing informal comments with the **International Bureau of WIPO (IB)** (where no demand for international preliminary examination **(demand)** is filed)
- filing amendments under Art. 19 PCT (this can be done whether or not a **demand** is filed)
- filing amendments under Art. 34 PCT and/or formal observations in response to objections raised in the **WO/ISA** (where a **demand** *is* actually filed)

This document explains these possibilities.

Filing informal comments

After receipt of the **ISR and WO/ISA**, the applicant may file informal comments on the **WO/ISA, directly with the IB** (see International Search and Preliminary Examination Guidelines 2.15). These will be communicated to the designated/elected Offices, together with the International Preliminary Report on Patentability **(IPRP)** at 30 months from the priority date.

Amending claims under Art. 19 PCT

The applicant may file **amended claims** under Art. 19 PCT, **directly with the IB** by the later of the following dates:

- 2 months from the date of mailing of the **ISR** and the **WO/ISA**
- 16 months from the priority date

However, any such amendment received by the **IB** after the expiration of the applicable time limit shall be **considered to have been received on time** by the **IB**, if it reaches it **before** the technical preparations for international publication have been completed (the 15th day prior to the date of publication, see PCT Applicant's Guide, International Phase, 9.013).

For further information, please see Rule 46 PCT as well as form PCT/ISA/220.

Please also note that, when filing amended claims under Art. 19 PCT, such amendments shall be **accompanied by a letter** identifying the amendments made and also the basis for the amendments in the application as originally filed (Rule 46.5(b) PCT). Where a **demand** is filed, failure to comply with this requirement may result in the amendments being ignored in the International Preliminary Examination Report **(IPER)**, see Rule 70.2(*c-bis*) PCT.

BNSDOCID: <XS_____20070401GK_1_>

Filing a demand for international preliminary examination

In principle, the **WO/ISA** will be considered to be the written opinion of the International Preliminary Examining Authority (**IPEA**). Where the **WO/ISA** issued by the **EPO** as **ISA** gives a positive opinion on the international application and the invention to which it relates, filing a **demand** with the **EPO** as **IPEA** would normally be unnecessary, since a positive IPRP would anyway be established by the IB based on the WO/ISA (see also further below).

If the applicant wishes to file a **demand** (for example, to allow him to argue his case in international preliminary examination with regard to objections raised in a negative **WO/ISA** before the **IPEA** issues an **IPER**), this must be done before expiration of **3 months after the date of mailing of the ISR and WO/ISA** or **22 months after priority date**, whichever expires later (Rule 54*bis* PCT). Amendments under Art. 34 PCT can be filed with the IPEA, normally at the same time as filing the demand (Rule 66.1(b) PCT) or within the time limit set for reply to any written opinion issued during international preliminary examination by the **IPEA**.

If a **demand** is filed at the **EPO** as **IPEA** and no comments/amendments have been received by the time the **EPO** starts drawing up the **IPER** (Rule 66.4*bis* PCT), the **WO/ISA** will be transformed by the **IPEA** into an **IPER** (also called the **IPRP (Chapter II)** which would merely reflect the content of the **WO/ISA** (OJ 10/2011, 532). The **demand** can still be withdrawn (Art. 37 PCT).

Please also note that, when filing amendments under Art. 34 PCT, such amendments shall be accompanied by a letter which identifies the amendments made and also the basis for the amendments in the application as originally filed (Rule 66.8(a) PCT). Failure to comply with this requirement may result in the amendments being ignored in the **IPER (IPRP (Chapter II))**, see Rule 70.2(c-*bis*) PCT.

Filing a request for supplementary international search

The applicant may, with the IB, file a request for **supplementary international search** under Rule 45*bis*.1 PCT. The present **ISR** and **WO/ISA** may also be taken into account in the execution of that supplementary international search, provided that these are available to the Authority charged with this task before it starts the supplementary search (Rule 45*bis*.5 PCT).

This kind of request **cannot be filed specifying the ISA** who did the **international search**.

More information on this topic can be found in the **PCT Applicant's Guide**, Chapter 8 (http://www.wipo.int/pct/en/guide/ip08.html).

End of the international phase

Where no **demand** is filed, at the end of the international phase, the **IB** will transform the **WO/ISA** into the IPRP (PCT Chapter I) (Rule 44*bis* PCT), which will then be transmitted together with possible informal comments to the designated Offices. Where a demand is filed, the **WO/ISA** is not transformed into an **IPRP (Chapter I)** by the **IB**, but rather the **IPEA** will establish an **IPER**, (the IPER is the same as the IPRP (PCT Chapter II), see Rule 70.15 PCT).

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PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
Schoen, Adam M.
BROWN RUDNICK LLP
One Financial Center
Boston, MA 02111
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference NEURE-009/01WO 35242/70	Date of mailing *(day/month/year)* 25 August 2021 (25-08-2021) **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/IB2021/000243	International filing date *(day/month/year)* 8 April 2021 (08-04-2021)
Applicant NEURENT MEDICAL LIMITED	

1. [X] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   How? Directly to the International Bureau preferably through ePCT, or on paper to:
   The International Bureau of WIPO, 34 chemin des Colombettes, 1211 Geneva 20, Switzerland

   For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 - 9.011.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   The applicant may **submit comments on an informal basis on the written opinion of the International Searching Authority** to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

   Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

   Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer OBLINGER, Sabine Tel: +49 (0)89 2399-7714

Form PCT/ISA/220 (revised January 2020)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
NEURE-009/01WO 35242/70		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB2021/000243	8 April 2021 (08-04-2021)	9 April 2020 (09-04-2020)
Applicant		
NEURENT MEDICAL LIMITED		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of:
      [X] the international application in the language in which it was filed
      [ ] a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. [ ] This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box No. II)

3. [ ] **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant
   [ ] the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. 9A
      [ ] as suggested by the applicant
      [X] as selected by this Authority, because the applicant failed to suggest a figure
      [ ] as selected by this Authority, because this figure better characterizes the invention
   b. [ ] none of the figures is to be published with the abstract

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000243

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.: 1-22
because they relate to subject matter not required to be searched by this Authority, namely:

The subject-matter of claims 1-22 refers to a surgical and therapeutic treatment.According to the PCT neither search (Rule 39.1(iv) PCT) nor examination (Rule 67.1(iv) PCT) is required for such subject-matter.

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.

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000243

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/12
ADD. A61B18/00 A61B18/14

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

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, BIOSIS, COMPENDEX, INSPEC, 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 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17) cited in the application paragraphs [0002] - [0003], [0031], [0053] - [0055], [0071], [0119]; figure 3A	23-44
X	WO 2016/183337 A2 (NAT UNIV IRELAND GALWAY [IE]; QI ZHAN MICHELE [US]) 17 November 2016 (2016-11-17)	23-30, 34,35, 37-44
A	paragraphs [0002], [0038] - [0044], [0093] - [0096], [0111]; figure 2	31-33,36

☐ 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 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
17 August 2021	25/08/2021

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	Aronsson, Fredrik

1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000243

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2018133460 A1	17-05-2018	AU 2017357869 A1	06-06-2019
		CA 3041440 A1	17-05-2018
		CN 110191674 A	30-08-2019
		EP 3537954 A1	18-09-2019
		JP 2019535386 A	12-12-2019
		US 2018133460 A1	17-05-2018
		US 2020086112 A1	19-03-2020
		US 2020101283 A1	02-04-2020
		US 2020171302 A1	04-06-2020
		WO 2018087601 A1	17-05-2018
WO 2016183337 A2	17-11-2016	AU 2016262085 A1	04-01-2018
		AU 2021200322 A1	18-03-2021
		CA 2984207 A1	17-11-2016
		CN 107835705 A	23-03-2018
		EP 3294410 A2	21-03-2018
		HK 1252823 A1	06-06-2019
		JP 6854015 B2	07-04-2021
		JP 2018515314 A	14-06-2018
		JP 2021087861 A	10-06-2021
		US 2016331459 A1	17-11-2016
		US 2019231429 A1	01-08-2019
		US 2019239953 A1	08-08-2019
		US 2019239954 A1	08-08-2019
		US 2019239955 A1	08-08-2019
		US 2019239956 A1	08-08-2019
		US 2019239957 A1	08-08-2019
		US 2020100838 A1	02-04-2020
		US 2020107882 A1	09-04-2020
		WO 2016183337 A2	17-11-2016

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Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/IB2021/000243

TITLE: SYSTEMS AND METHODS FOR IDENTIFYING AND CHARACTERIZING TISSUE AND PROVIDING TARGETED TREATMENT THEREOF

APPLICANT: NEURENT MEDICAL LIMITED

IPC CLASSIFICATION: A61B18/12, A61B18/00, A61B18/14

EXAMINER: Aronsson, Fredrik

CONSULTED DATABASES: BIOSIS, COMPDX, EPODOC, INSPEC, KIME, MEDLINE, NPL, WPI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B18/1206, A61B2018/00839, A61B2018/00875, A61B2018/00904, A61B2018/00732, A61B2018/00577, A61B2018/00351, A61B2018/00327, A61B2018/00434, A61B2018/00267, A61B2018/0016, A61B18/1485, A61B18/1492, A61B2018/00791, A61B2018/00642, A61B2018/00648, A61B2018/00708, A61B2018/00672, A61B2018/00678, A61B2018/00886

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
Receiving bioelectric data, identifying tissue types and relaxation patterns for each identified tissue type and determining an ablation pattern based on identified relaxation patterns

EPO FORM P0A442

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2021/000243	08.04.2021	09.04.2020

International Patent Classification (IPC) or both national classification and IPC
INV. A61B18/12 ADD. A61B18/00 A61B18/14

Applicant
NEURENT MEDICAL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Fax: +49 89 2399 - 4465	see form PCT/ISA/210	Aronsson, Fredrik Telephone No. +49 89 2399-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-22

because:

☒ the said international application, or the said claims Nos. 1-22 relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 1-22

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☒ See Supplemental Box for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	30, 36
	No:	Claims	23-29, 31-35, 37-44
Inventive step (IS)	Yes:	Claims	
	No:	Claims	23-44
Industrial applicability (IA)	Yes:	Claims	23-44
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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IPR2025-01125

1 **Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The subject-matter of claims 1-22 refers to a surgical and therapeutic treatment.

According to the PCT neither search (Rule 39.1(iv) PCT) nor examination (Rule 67.1(iv) PCT) is required for such subject-matter.

2 **Re Item V**

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2.1 Reference is made to the following documents:

D1 US 2018/133460 A1 (TOWNLEY DAVID [IE] ET AL) 17 May 2018 (2018-05-17)cited in the application

D2 WO 2016/183337 A2 (NAT UNIV IRELAND GALWAY [IE]; QI ZHAN MICHELE [US]) 17 November 2016 (2016-11-17)

2.2 D1 discloses:

A system (300) for treating a condition [0002], the system comprising:

a device (302) comprising an end effector (312) including a plurality of electrodes (344); and

a controller (318) operably associated with the device (fig. 3A) and configured to:

receive data from the device associated with bioelectric properties of one or more tissues at the target site [0053];

process the data to identify a type of each of the one or more tissues at the target site and further identify a relaxation pattern(s) for each of the one or more identified tissue types [0053]-[0054]; and

determine an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified relaxation patterns ([0055]: frequency attuned to target tissue),

wherein ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site [0071].

Thus, the subject-matter of claim 23 is not new (Article 33(2) PCT).

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Dependent claims 24-44 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step over D1, see:

claims 24-26: [0053]-[0054]; claims 27-33: [0055]; claims 34-35, 37: [0003]; claim 36: [0119]; claim 38-44: [0031].

2.3 D2 discloses:

A system (200) for treating a condition [0002], the system comprising:

a device (202) comprising an end effector (212) including a plurality of electrodes (214) [0043]; and

a controller (218) operably associated with the device (fig. 2) and configured to:

receive data from the device associated with bioelectric properties of one or more tissues at the target site [0044];

process the data to identify a type of each of the one or more tissues at the target site [0096] and further identify a relaxation pattern(s) for each of the one or more identified tissue types ([0093]: impedance mapping at different frequencies); and

determine an ablation pattern to be delivered by one or more of the plurality of electrodes of the end effector based on identified relaxation patterns ([0094]: electrode configuration),

wherein ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site [00111].

Thus, the subject-matter of claim 23 is not new (Article 33(2) PCT).

Dependent claims 24-30, 34-35 and 37-44 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step over D2, see:

claims 24-26, 29: [0094]; claims 27-28, 30: [0096]; claims 34-35, 37-38: [0002]; claims 39-44: [0038]-[0040].

3 **Re Item VII**

Certain defects in the international application

3.1 The independent claim is not in the two-part form in accordance with Rule 6.3(b) PCT.

3.2 The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).

3.3 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in D2 is not mentioned in the description, nor is this document identified therein.

4 **Re Item VIII**

Certain observations on the international application

4.1 In claim 23 the last feature "wherein ablation energy associated with the ablation pattern is at a level sufficient to ablate a targeted tissue and minimize and/or prevent collateral damage to surrounding or adjacent non-targeted tissue at the target site" merely states the desired result rather than the technical features of the system that are actually responsible for the effect. This renders the subject-matter of claim 23 unclear (Article 6 PCT).

Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO/ISA)

General information

For all international applications, the competent International Searching Authority **(ISA)** will establish an international search report **(ISR)** accompanied by a written opinion of the International Searching Authority **(WO/ISA)**. The **WO/ISA** may be responded to by

- filing informal comments with the **International Bureau of WIPO (IB)** (where no demand for international preliminary examination **(demand)** is filed)
- filing amendments under Art. 19 PCT (this can be done whether or not a **demand** is filed)
- filing amendments under Art. 34 PCT and/or formal observations in response to objections raised in the **WO/ISA** (where a **demand** *is* actually filed)

This document explains these possibilities.

Filing informal comments

After receipt of the **ISR and WO/ISA**, the applicant may file informal comments on the **WO/ISA, directly with the IB** (see International Search and Preliminary Examination Guidelines 2.15). These will be communicated to the designated/elected Offices, together with the International Preliminary Report on Patentability **(IPRP)** at 30 months from the priority date.

Amending claims under Art. 19 PCT

The applicant may file **amended claims** under Art. 19 PCT, **directly with the IB** by the later of the following dates:

- 2 months from the date of mailing of the **ISR** and the **WO/ISA**
- 16 months from the priority date

However, any such amendment received by the **IB** after the expiration of the applicable time limit shall be **considered to have been received on time** by the **IB**, if it reaches it **before** the technical preparations for international publication have been completed (the 15th day prior to the date of publication, see PCT Applicant's Guide, International Phase, 9.013).

For further information, please see Rule 46 PCT as well as form PCT/ISA/220.

Please also note that, when filing amended claims under Art. 19 PCT, such amendments shall be **accompanied by a letter** identifying the amendments made and also the basis for the amendments in the application as originally filed (Rule 46.5(b) PCT). Where a **demand** is filed, failure to comply with this requirement may result in the amendments being ignored in the International Preliminary Examination Report **(IPER)**, see Rule 70.2(c-*bis*) PCT.

ENSDOCID: <XS_____20070401OCK_I_>

Filing a demand for international preliminary examination

In principle, the **WO/ISA** will be considered to be the written opinion of the International Preliminary Examining Authority (**IPEA**). Where the **WO/ISA** issued by the **EPO** as **ISA** gives a positive opinion on the international application and the invention to which it relates, filing a **demand** with the **EPO** as **IPEA** would normally be unnecessary, since a positive IPRP would anyway be established by the IB based on the WO/ISA (see also further below).

If the applicant wishes to file a **demand** (for example, to allow him to argue his case in international preliminary examination with regard to objections raised in a negative **WO/ISA** before the **IPEA** issues an **IPER**), this must be done before expiration of **3 months after the date of mailing of the ISR and WO/ISA** or **22 months after priority date,** whichever expires later (Rule 54*bis* PCT). Amendments under Art. 34 PCT can be filed with the IPEA, normally at the same time as filing the demand (Rule 66.1(b) PCT) or within the time limit set for reply to any written opinion issued during international preliminary examination by the **IPEA**.

If a **demand** is filed at the **EPO** as **IPEA** and no comments/amendments have been received by the time the **EPO** starts drawing up the **IPER** (Rule 66.4*bis* PCT), the **WO/ISA** will be transformed by the **IPEA** into an **IPER** (also called the **IPRP (Chapter II)** which would merely reflect the content of the **WO/ISA** (OJ 10/2011, 532). The **demand** can still be withdrawn (Art. 37 PCT).

Please also note that, when filing amendments under Art. 34 PCT, such amendments shall be accompanied by a letter which identifies the amendments made and also the basis for the amendments in the application as originally filed (Rule 66.8(a) PCT). Failure to comply with this requirement may result in the amendments being ignored in the **IPER (IPRP (Chapter II))**, see Rule 70.2(c-*bis*) PCT.

Filing a request for supplementary international search

The applicant may, with the **IB**, file a request for **supplementary international search** under Rule 45*bis*.1 PCT. The present **ISR** and **WO/ISA** may also be taken into account in the execution of that supplementary international search, provided that these are available to the Authority charged with this task before it starts the supplementary search (Rule 45*bis*.5 PCT).

This kind of request **cannot be filed specifying the ISA** who did the **international search**.

More information on this topic can be found in the **PCT Applicant's Guide**, Chapter 8 (http://www.wipo.int/pct/en/guide/ip08.html).

End of the international phase

Where no **demand** is filed, at the end of the international phase, the **IB** will transform the **WO/ISA** into the IPRP (PCT Chapter I) (Rule 44*bis* PCT), which will then be transmitted together with possible informal comments to the designated Offices. Where a demand is filed, the **WO/ISA** is not transformed into an **IPRP (Chapter I)** by the **IB**, but rather the **IPEA** will establish an **IPER**, (the IPER is the same as the IPRP (PCT Chapter II), see Rule 70.15 PCT).

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
Schoen, Adam M.
BROWN RUDNICK LLP
One Financial Center
Boston, MA 02111
ETATS-UNIS D'AMERIQUE

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference NEURE-011/01WO 35242/85	Date of mailing *(day/month/year)* 4 April 2022 (04-04-2022) **FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/IB2021/000700	International filing date *(day/month/year)* 6 October 2021 (06-10-2021)
Applicant NEURENT MEDICAL LIMITED	

1. [X] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   How? Directly to the International Bureau preferably through ePCT, or on paper to:
   The International Bureau of WIPO, 34 chemin des Colombettes, 1211 Geneva 20, Switzerland

   For more detailed instructions, see the *PCT Applicant's Guide*, International Phase, paragraphs 9.004 - 9.011.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to any protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with any request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   The applicant may **submit comments on an informal basis on the written opinion of the International Searching Authority** to the International Bureau. These comments will be made available to the public after international publication. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established.

   Shortly after the expiration of **18 months from the priority date, the international application will be published** by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau before the completion of the technical preparations for international publication (Rules 90*bis*.1 and 90*bis*.3).

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for **entry into the national phase** before those designated Offices. In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months. For details about the applicable time limits, Office by Office, see www.wipo.int/pct/en/texts/time_limits.html and the *PCT Applicant's Guide*, National Chapters.

   Within **22 months from the priority date, the applicant may request that a supplementary international search be carried out** by a different International Searching Authority that offers this service (Rule 45*bis*.1). The procedure for requesting supplementary international search is described in the *PCT Applicant's Guide*, International Phase, paragraphs 8.006-8.032.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040 Fax: (+31-70) 340-3016	Authorized officer WACH, Patrick Tel: +31 (0)70 340-3325

Form PCT/ISA/220 (revised January 2020)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
NEURE-011/01WO 35242/85		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IB2021/000700	6 October 2021 (06-10-2021)	6 October 2020 (06-10-2020)
Applicant		
NEURENT MEDICAL LIMITED		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))

b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).

c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box No. II)

3. ☒ **Unity of invention is lacking** (see Box No III)

4. With regard to the **title,**

☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regard to the **drawings,**

a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant

☐ as selected by this Authority, because the applicant failed to suggest a figure

☐ as selected by this Authority, because this figure better characterizes the invention

b. ☒ none of the figures is to be published with the abstract

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2021/000700

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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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. ☒ 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.:
1-20

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.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000700

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B18/12 A61B18/14 A61B90/90 A61B18/00 A61B90/00
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)
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 2020/129223 A1 (ANGELES MICHAEL [CA] ET AL) 30 April 2020 (2020-04-30) paragraphs [0003], [0028], [0033] - [0040]; figures 1, 4,5	1-8, 11-18 1-20
Y	US 2020/078134 A1 (LOYD RODNEY B [US] ET AL) 12 March 2020 (2020-03-12) paragraphs [0002], [0026], [0029] - [0035], [0039], [0043], [0046] - [0049]; figures 1-4	1-20
Y A	WO 01/17450 A1 (CURON MEDICAL INC [US]) 15 March 2001 (2001-03-15) page 13, line 24 - page 14, line 21; figures 7,8,12 page 20, lines 6-19	8-10,19, 20 2-7, 11-18

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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 :

"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
1 February 2022	04/04/2022

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	Husselin, Stephane

1

Form PCT/ISA/210 (second sheet) (April 2005)

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IPR2025-01125

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2021/000700

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94/10921 A1 (EP TECHNOLOGIES [US]) 26 May 1994 (1994-05-26) pages 12-18; figures 4,5	1-7, 11-18

1

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2021/000700

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2020129223 A1	30-04-2020	NONE	
US 2020078134 A1	12-03-2020	EP 3847663 A1	14-07-2021
		US 10350025 B1	16-07-2019
		US 2020078134 A1	12-03-2020
		WO 2020051279 A1	12-03-2020
WO 0117450 A1	15-03-2001	AU 7118000 A	10-04-2001
		CA 2384410 A1	15-03-2001
		EP 1211998 A1	12-06-2002
		JP 2003525659 A	02-09-2003
		US 6464689 B1	15-10-2002
		WO 0117450 A1	15-03-2001
WO 9410921 A1	26-05-1994	CA 2148714 A1	26-05-1994
		EP 0746249 A1	11-12-1996
		JP H08506738 A	23-07-1996
		US 5383874 A	24-01-1995
		US 5651780 A	29-07-1997
		WO 9410921 A1	26-05-1994

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20

A system for treating a condition within a sino-nasal cavity of a patient, comprising a console unit configured to be operably associated with a treatment device. The system being configured to determine authenticity of the treatment device.

---

2. claims: 21-40

A system for treating a condition within a sino-nasal cavity of a patient, comprising a treatment device including an end effector comprising one or more electrodes. The system being configured to determined availability of the one or electrodes based on impedance assessment.

---

3. claims: 41-60

A system for treating a condition within a sino-nasal cavity of a patient, the system comprising a treatment device including a multi-segment end effector comprising a plurality of sets of support structures. The system being configured to determine a status of each of the plurality of support structures with respect to the treatment pattern.

---

4. claims: 61-95

A system for treating a condition within a sino-nasal cavity of a patient, the system comprising a treatment device. The system being configured to provide, via an interactive interface associated with the console unit, one or more post-procedure inputs for controlling subsequent use of the end effector.

Information on Search Strategy - Pilot phase (see OJ 2015, A86)
The type of information contained in this sheet may change during the pilot for improving the usefulness of this new service.

Application Number
PCT/IB2021/000700

TITLE: SYSTEMS AND METHODS FOR THERAPEUTIC NASAL TREATMENT

APPLICANT: NEURENT MEDICAL LIMITED

IPC CLASSIFICATION: A61B18/12, A61B18/14, A61B90/90, A61B18/00, A61B90/00

EXAMINER: Husselin, Stephane

CONSULTED DATABASES: WPI

CLASSIFICATION SYMBOLS DEFINING EXTENT OF THE SEARCH:

IPC:

CPC: A61B2018/00327, A61B2018/00577, A61B2018/00595, A61B18/12, A61B18/1485, A61B2018/00267, A61B2018/1475, A61B2090/0803, A61B2090/0808, A61B2090/0814, A61B90/90, A61B2560/028, A61B2560/0285

FI/F-TERMS:

KEYWORDS OR OTHER ELEMENTS FEATURING THE INVENTION:
IDENTIFICATION
EAR, NOSE, THROAT
RETRACTABLE ELECTRODES
BASKET SHAPE
COUNT USE
INDICATING CORRECT ASSEMBLING
PREVENTING RE-USE
ID?, identif+, authenti+
(pr[é,e]vent+, avoid+, emp#ch+, #vite+) 5d (use?, r[é,e]_use+)
display+, indicat+, affich+, GUI?, screen?, #cran?
(nose, nasal, sino-nasal, nez, Sinus) 5d (micro_debrid+, d#brid+)
(alert+, info+, messag+, signal+, suggest+, indicat+) 5d (user?, utilisateur?, physician?, op#rateur?,op#rator?, surg+, chirug+)

EPO FORM P04A42

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2021/000700	06.10.2021	06.10.2020

International Patent Classification (IPC) or both national classification and IPC
INV. A61B18/12 A61B18/14 A61B90/90 A61B18/00 A61B90/00

Applicant
NEURENT MEDICAL LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Husselin, Stephane Telephone No. +31 70 340-0

Form PCT/ISA/237 (Cover Sheet) (January 2015)

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 21-95

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international search *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 21-95

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a) or (b).

☐ See Supplemental Box for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-20

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9, 10, 19, 20
	No:	Claims	1-8, 11-18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-20
Industrial applicability (IA)	Yes:	Claims	1-20
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item IV

Lack of unity of invention

This Authority considers that the application does not meet the requirements of unity of invention and that there are four inventions. The following separate inventions are not so linked as to form a single general inventive concept:

I. Claims: 1-20

A system for treating a condition within a sino-nasal cavity of a patient, comprising a console unit configured to be operably associated with a treatment device. The system being configured to determine authenticity of the treatment device.

II. Claims: 21-40

A system for treating a condition within a sino-nasal cavity of a patient, comprising a treatment device including an end effector comprising one or more electrodes. The system being configured to determined availability of the one or electrodes based on impedance assessment.

III. Claims: 41-60

A system for treating a condition within a sino-nasal cavity of a patient, the system comprising a treatment device including a multi-segment end effector comprising a plurality of sets of support structures. The system being configured to determine a status of each of the plurality of support structures with respect to the treatment pattern.

IV. Claims: 61-95

A system for treating a condition within a sino-nasal cavity of a patient, the system comprising a treatment device. The system being configured to provide, via an interactive interface associated with the console unit, one or more post-procedure inputs for controlling subsequent use of the end effector.

The reasons, for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The common matter linking together the independent claims 1, 21, 41 and 61 is "*A system for treating a condition within a sino-nasal cavity of a patient, the system comprising: a console unit configured to be operably associated with a treatment device and control operation thereof*". This common matter does not comprise a single general

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

inventive concept, based on same or corresponding special technical features within the meaning of Rule 13.2 PCT, because at least documents D1 and D2 anticipate the common matter, see D1 (FIG.1 and [0003]) and D2 (FIG.1, [0002]).

Additional features of claim 1, representing the difference over the non-inventive common matter, provide the technical effect of determining the authenticity of the treatment device and solve the objective technical problem of preventing the use of non-authorized treatment devices.

Additional features of claim 21, representing the difference over the non-inventive common matter, provide the technical effect of determining the availability of the one or more electrodes of the treatment device and solve the objective technical problem of providing the user with an indication as to when the device is primed and ready to perform treatment in the selected location.

Additional features of claim 41, representing the difference over the non-inventive common matter, provide the technical effect of determining a status of each of the plurality of support structures with respect to a treatment pattern and solve the objective technical problem of ensuring successful ablation/modulation of the targeted tissue while minimizing and/or preventing collateral damage to surrounding or adjacent non-targeted tissue at the target site.

Additional features of claim 61, representing the difference over the non-inventive common matter, provide the technical effect of providing, via an interactive interface associated with the console unit, one or more post-procedure inputs for controlling subsequent use of the end effector and solve the objective technical problem of ensuring that the overall procedure (i.e., treatment of rhinosinusitis) is completed by ensuring that all portions of targeted tissue undergo treatment.

The above mentioned features representing the difference over the non-inventive common matter are therefore not corresponding because they solve different problems.

Hence, the claims comprise neither the same, nor corresponding special technical features, so the technical relationship between the subject matter of the claims required by Rule 13.2 PCT is lacking and the claims are not so linked as to form a single general inventive concept as required by Rule 13.1 PCT.

Consequently the application does not meet the requirement for unity of invention.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

Reference is made to the following documents:

D1 US 2020/129223 A1 (ANGELES MICHAEL [CA] ET AL) 30 April 2020 (2020-04-30)

D2 US 2020/078134 A1 (LOYD RODNEY B [US] ET AL) 12 March 2020 (2020-03-12)

D3 WO 01/17450 A1 (CURON MEDICAL INC [US]) 15 March 2001 (2001-03-15)

D4 WO 94/10921 A1 (EP TECHNOLOGIES [US]) 26 May 1994 (1994-05-26)

1 Independent claim 1 not new

The present application does not meet the criteria of Article 33(2) PCT, because the subject-matter of independent claim 1 is not new.

Document D1 discloses:

A system (FIG.1) *for treating a condition within a sino-nasal cavity of a patient* (see [0003]: "the treatments may address any of a wide variety of conditions, just two examples of which are nasal valve insufficiency (which may cause difficulty breathing through the nose) and chronic rhinitis (runny nose)"), *the system comprising:*

a console unit (102) *configured to be operably associated with a treatment device* (104) *and control operation thereof, the console unit configured to:*

analyze identifying data associated with a treatment device upon connection of the treatment device to the console unit (see [0028]: "In some embodiments, electronics inside the console 102 may include a stylus identification safety feature that identifies the stylus 104 when it is plugged into the stylus connection port 110");

determine authenticity of the treatment device based on the analysis of the identifying data (see [0028]: "The stylus connection port 110 can be configured to accept only the connection end of the stylus 104 and can be configured to not accept or work with counterfeit or other devices"); *and*

output, via an interactive interface associated with the console unit, an alert to a user indicating at least the authenticity determination (see "the stylus type indicator 506" in FIG.5 and [0040]: "If such an alternative type of stylus 104 is inserted, the console 102 will identify the stylus type and

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

indicate the type via the stylus type indicator 506". See also [0037]: "FIG. 5 shows the default image 500 displayed on the display 108 of the console 102, once a valid stylus 104 is connected.").

Subject-matter of claim 1 is therefore known from D1.

2 Independent claim 1 not inventive

The present application does not meet the criteria of Article 33(3) PCT, because the subject-matter of independent claim 1 does not involve an inventive step.

Document D2 discloses:

A system (FIG.1) *for treating a condition within a sino-nasal cavity of a patient* (see [0002], [0043]: "The device unit 200 may be a microdebrider or a sinus debrider [...]"), *the system comprising:*

a console unit (100) *configured to be operably associated with a treatment device* (200) *and control operation thereof, the console unit configured to:*

analyze identifying data associated with a treatment device upon connection of the treatment device to the console unit (see [0031]: "In certain embodiments, the query is a request or software command to the device unit 200 to respond with a message containing, for example, device unit 200 identifying information and device status information");

determine authenticity of the treatment device based on the analysis of the identifying data (see [0031]: "The identifying information can be information such as a unique and serialized device ID number such that no other connected device (either the same or a different model of the connected device) can have the same device ID number"); *and*

The subject-matter of claim 1 therefore differs from this known system in that the console unit is further configured to *output, via an interactive interface associated with the console unit, an alert to a user indicating at least the authenticity determination*

The problem to be solved by the present invention may therefore be regarded as to ensure that the user is made aware of the result of the authenticity determination. A skilled person in the art would consider documents D1 or D4 that provide user interfaces which are used for outputting messages related to the identification of a treatment device upon connection to a console (see in D1 "the stylus type indicator 506" in FIG.5 and [0040]: "If such an alternative type of stylus 104 is inserted, the console 102 will identify the stylus type and indicate the type via the stylus type indicator 506" . See also D4 79 or 84 in FIG.4: "[...] the first control signal 78 preferably generates a confirming,

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Aerin Medical Inc. v. Neurent Medical Ltd.
IPR2025-01125

user discernible "Use Permitted" message 79." and "the second control signal 80 generates a user discernible "Use Not Permitted" alarm message 84 [...]"). By applying the teachings of either D1 or D4 to the system of D2, the skilled person would arrive at the invention, without the exercise of inventive skills.

The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT).

3 Dependent claims

Dependent claims do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

Claims 2-4	See D1 ([0028], [0033-0034]). See also D2 ("unique and serialized device ID number" in [0029], [0031]); D3 ("identification codes") or D4 ("catheter identification means 88 [...] programmed with a digital value representing the catheter identification code").
Claims 5-7	See D1 ([0028]: "Such a safety feature may, for example, automatically shut down (or disable powering on) the console 102, if a user tries to plug in a device other than the stylus 104."). See also D2 ([0035]: " In certain embodiments, the unlocking circuit 201 may be a locking or unlocking mechanism or circuit which may comprise an electronically controllable component that has the capability to prevent or allow the transmission of power or drive signals to the motor unit in a way that prevents operation of the drive unit 202"); D3 (FIG.8 and p.13, ln.24 - p.14, ln.21) or D4 (p.12, ln.19 - p.13, ln.19).
Claim 8	See D1 ("the stylus type indicator 506" in FIG.5 and [0040]: "If such an alternative type of stylus 104 is inserted, the console 102 will identify the stylus type and indicate the type via the stylus type indicator 506").

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See also D3 (FIG.12 and p.20, ln 6-19) or D4 (79 or 84 in FIG.4: "[...] the first control signal 78 preferably generates a confirming, user discernible "Use Permitted" message 79." and "the second control signal 80 generates a user discernible "Use Not Permitted" alarm message 84 [...]").

Adding an audible alert to the visual alert is not considered inventive.

Claims 9, 10, 19, 20

The GUI in D3 provides one or more suggested actions (see p.20, ln 6-19: "When the identification code 214 is not valid, the REGISTRATION function 514 commands the display microprocessor 474 to generate an EXCHANGE prompt 516 on the graphics display monitor 420. Fig. 12 shows a representative EXCHANGE prompt 516. When graphically implemented, as shown in Fig. 12, the EXCHANGE prompt 516 leads the operator in a step-wise fashion through the tasks of replacing the previously used device 26 and its key card 202 with a new device 26 and its associated key card 202.").

Claims 11-18

See D1 ([0033-0034]: " In some embodiments, the console 102 may permanently deactivate the stylus 104 when it has reached its maximum number of uses.").

See also D2 ([FIG.2-4 and [0032]: "The MCU 103 is also configured to process the message received from the query command by, for example, analyzing the usage status of the device unit 200 to determine if the device unit 200 has been used previously, and then accordingly whether the device unit 200 should be locked or unlocked."); D3 (p.13, ln.24 - p.14, ln.21: "The presence of a match between the instant identification code and any registered identification code indicates the usage key card 202 has been previously read by the module 48, which reflects a prior use of the device 26 or another device not packaged with the card 202.") or D4 (FIG.5 and p.17, ln.20: "As Fig. 5 shows, the identification means 76 can also serve to monitor the use of the catheter 14.").

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Possible steps after receipt of the international search report (ISR) and written opinion of the International Searching Authority (WO/ISA)

General information

For all international applications, the competent International Searching Authority **(ISA)** will establish an international search report **(ISR)** accompanied by a written opinion of the International Searching Authority **(WO/ISA)**. The **WO/ISA** may be responded to by

- filing informal comments with the **International Bureau of WIPO (IB)** (where no demand for international preliminary examination **(demand)** is filed)
- filing amendments under Art. 19 PCT (this can be done whether or not a **demand** is filed)
- filing amendments under Art. 34 PCT and/or formal observations in response to objections raised in the **WO/ISA** (where a **demand** *is* actually filed)

This document explains these possibilities.

Filing informal comments

After receipt of the **ISR and WO/ISA**, the applicant may file informal comments on the **WO/ISA, directly with the IB** (see International Search and Preliminary Examination Guidelines 2.15). These will be communicated to the designated/elected Offices, together with the International Preliminary Report on Patentability **(IPRP)** at 30 months from the priority date.

Amending claims under Art. 19 PCT

The applicant may file **amended claims** under Art. 19 PCT, **directly with the IB** by the later of the following dates:

- 2 months from the date of mailing of the **ISR** and the **WO/ISA**
- 16 months from the priority date

However, any such amendment received by the **IB** after the expiration of the applicable time limit shall be **considered to have been received on time** by the **IB**, if it reaches it **before** the technical preparations for international publication have been completed (the 15th day prior to the date of publication, see PCT Applicant's Guide, International Phase, 9.013).

For further information, please see Rule 46 PCT as well as form PCT/ISA/220.

Please also note that, when filing amended claims under Art. 19 PCT, such amendments shall be **accompanied by a letter** identifying the amendments made and also the basis for the amendments in the application as originally filed (Rule 46.5(b) PCT). Where a **demand** is filed, failure to comply with this requirement may result in the amendments being ignored in the International Preliminary Examination Report **(IPER)**, see Rule 70.2(c-*bis*) PCT.

BNSDOCID: <XS_____2007040106CK_I_>

Filing a demand for international preliminary examination

In principle, the **WO/ISA** will be considered to be the written opinion of the International Preliminary Examining Authority (**IPEA**). Where the **WO/ISA** issued by the **EPO** as **ISA** gives a positive opinion on the international application and the invention to which it relates, filing a **demand** with the **EPO** as **IPEA** would normally be unnecessary, since a positive IPRP would anyway be established by the IB based on the WO/ISA (see also further below).

If the applicant wishes to file a **demand** (for example, to allow him to argue his case in international preliminary examination with regard to objections raised in a negative **WO/ISA** before the **IPEA** issues an **IPER**), this must be done before expiration of **3 months after the date of mailing of the ISR and WO/ISA** or **22 months after priority date,** whichever expires later (Rule 54*bis* PCT). Amendments under Art. 34 PCT can be filed with the IPEA, normally at the same time as filing the demand (Rule 66.1(b) PCT) or within the time limit set for reply to any written opinion issued during international preliminary examination by the **IPEA**.

If a **demand** is filed at the **EPO** as **IPEA** and no comments/amendments have been received by the time the **EPO** starts drawing up the **IPER** (Rule 66.4*bis* PCT), the **WO/ISA** will be transformed by the **IPEA** into an **IPER** (also called the **IPRP (Chapter II)** which would merely reflect the content of the **WO/ISA** (OJ 10/2011, 532). The **demand** can still be withdrawn (Art. 37 PCT).

Please also note that, when filing amendments under Art. 34 PCT, such amendments shall be accompanied by a letter which identifies the amendments made and also the basis for the amendments in the application as originally filed (Rule 66.8(a) PCT). Failure to comply with this requirement may result in the amendments being ignored in the **IPER (IPRP (Chapter II))**, see Rule 70.2(c-*bis*) PCT.

Filing a request for supplementary international search

The applicant may, with the **IB**, file a request for **supplementary international search** under Rule 45*bis*.1 PCT. The present **ISR** and **WO/ISA** may also be taken into account in the execution of that supplementary international search, provided that these are available to the Authority charged with this task before it starts the supplementary search (Rule 45*bis*.5 PCT).

This kind of request **cannot be filed specifying the ISA** who did the **international search**.

More information on this topic can be found in the **PCT Applicant's Guide**, Chapter 8 (http://www.wipo.int/pct/en/guide/ip08.html).

End of the international phase

Where no **demand** is filed, at the end of the international phase, the **IB** will transform the **WO/ISA** into the IPRP (PCT Chapter I) (Rule 44*bis* PCT), which will then be transmitted together with possible informal comments to the designated Offices. Where a demand is filed, the **WO/ISA** is not transformed into an **IPRP (Chapter I)** by the **IB**, but rather the **IPEA** will establish an **IPER**, (the IPER is the same as the IPRP (PCT Chapter II), see Rule 70.15 PCT).

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Espacenet

Bibliographic data: JP2001120565 (A) — 2001-05-08

HIGH FREQUENCY TREATMENT INGREDIENT

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Classification: **- international:*A61B17/24; A61B18/04; A61B18/12;***
(IPC1-7): A61B17/24; A61B18/04; A61B18/12
- cooperative:

Application number: JP19990301383 19991022

Priority number(s): JP19990301383 19991022

Abstract of JP2001120565 (A)

PROBLEM TO BE SOLVED: To provide a high frequency treatment ingredient which can uniformly cauterize lesion over an extensive range, and considerably shorten the treatment time. SOLUTION: In the high frequency treatment ingredient 1 comprising a hand piece 2, an insertion part 3 provided on the hand piece 2 and inserted in a body cavity and a treatment part 6 provided on the tip part of the insertion part 3, the treatment part 6 has a contact surface 7 in contact with the lesion, and a bipolar electrode 8 to cauterize the lesion by the high frequency wave is provided on the contact surface 7.

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DESCRIPTION JP2001120565A

[0001]

BACKGROUND OF THE INVENTION 1. Field of the Invention The present invention relates to a high-frequency treatment instrument used for excision of the inferior nasal turbinate mucosa on the nasal mucosa, for example, as a surgical treatment for allergic rhinitis.

[0002]

2. Description of the Related Art Hay fever is known to be caused by pollen adhering to the mucous membranes of the nose and causing an allergic reaction.

Therefore, inferior nasal turbinate mucosal resection, high-frequency electrocautery, and laser ablation are used as nasal mucosal removal methods that treat the mucous membrane to make it less likely to cause allergic reactions.

[0003]

Examples of high-frequency treatment instruments used in high-frequency electrocautery include US Pat. No. 5,733,282, US Pat. No. 5,823,197, and US Pat. No. 4,936,842. It has been known.

[0004]

U.S. Patent No. 5,733,282 has an electrode section bent at a right angle to the axial direction of the insertion section at the distal end of the insertion section to be inserted into the nasal cavity, and the insertion section is inserted into the nasal cavity. The electrode is then brought into contact with the affected area, and a high-frequency current is passed through the electrode to ablate the mucous membrane of the affected area.

[0005]

U.S. Patent No. 5,823,197 discloses that an energy probe is provided at the tip of a catheter to be inserted into the nasal cavity, the catheter is inserted into the nasal cavity, and energy is delivered inside the inferior nasal turbinate. It is designed to cauterize a part of the body.

[0006]

Further, U.S. Pat. No. 4,936,842 discloses an operating section that is held by the operator, a probe that is detachable from the operating section, and a probe that is provided at the tip of the probe and that can be selectively switched. The probe is inserted into the body cavity and the affected area is treated with electrical energy.

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[0007]

However, laser ablation requires an expensive laser device, and monopolar electrocautery has the problem that it is difficult to control the coagulated layer.

Furthermore, when attempting to remove the inferior nasal turbinate mucosa for the intranasal mucosa as a surgical treatment for allergic rhinitis, when the tip of the electrode is brought into contact with the affected area as in the past, only the contact area is cauterized at a high temperature. In order to uniformly cauterize the target area of the inferior nasal turbinate, it is a hassle to grasp the operation part, move the insertion part, and move the electrode part at the tip uniformly over the entire surface of the inferior nasal turbinate. operation is required.

[0008]

However, the shape and size of the inferior nasal turbinate varies from person to person, and skilled technique is required to cauterize the surface uniformly.

Furthermore, even if an attempt is made to cauterize the inferior nasal turbinate with a spatula-shaped probe having a wide area, the surface of the inferior nasal turbinate is uneven, so there is a problem in that the contact area is uneven, and as a result, it is not possible to cauterize uniformly.

[0009]

This invention was made in view of the above-mentioned circumstances, and its purpose is to provide a high-frequency treatment tool that can uniformly cauterize the affected area by contacting it with high-frequency waves and has excellent operability. be.

[0010]

[Means for Solving the Problems] In order to achieve the above object, the present invention includes a handpiece, an insertion section provided on the handpiece to be inserted into a body cavity, and a distal end portion of the insertion section provided with a handpiece. A high-frequency treatment instrument comprising a treatment section is characterized in that the treatment section has a contact surface that comes into contact with the affected area, and an electrode for high-frequency cauterization of the affected area is provided on this contact surface

[0011]

According to the configuration, the insertion section is inserted into the nasal cavity, for example, through the anterior nostril, and the contact surface of the treatment section is brought into contact with the intranasal mucous membrane.

By passing high-frequency current through the electrodes provided on the contact surface, the nasal mucosa can be uniformly cauterized over a wide area.

[0012]

DESCRIPTION OF THE PREFERRED EMBODIMENTS Embodiments of the present invention will be described below with reference to the drawings.

[0013]

1 and 2 show the first embodiment, FIG. 1 is a usage state diagram when the high-frequency treatment device is used for treating allergic rhinitis, and FIG. 2 is a front view and a side view of the treatment section of the high-frequency treatment device. be.

[0014]

As shown in FIGS. 1 and 2, the high-frequency treatment instrument 1 includes a hand piece 2 that is held by an operator, and a pipe-shaped insertion portion 3 that extends in the axial direction at the distal end of the hand piece 2.

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The grip part 4 of the hand piece 2 is provided with a connecting part 5 for removably connecting the insertion part 3, and this connecting part 5 has an angle θ1 with respect to the grip part 4. The connected insertion part 3 is inclined with respect to the grip part 4.

The upper surface of the grip portion 4 and the upper surface of the insertion portion 3 are formed on the same plane.

[0015]

Further, a treatment section 6 is provided at the distal end of the insertion section 3, and the treatment section 6 has an angle θ2 with respect to the axis of the insertion section 3 in the same direction as the angle of the insertion section 3 with respect to the grip section 4. ing.

Further, the treatment section 6 is formed of an insulating member, and has a flat contact surface 7 on one side thereof, and a rod-shaped bipolar electrode 8 is provided on the contact surface 7 in the front-rear direction.

This bipolar electrode 8 consists of an active electrode 8a and a return electrode 8b, and both electrodes 8a and 8b are electrically insulated.

[0016]

The bipolar electrode 8 is connected to a high frequency current supply source 10 via a high frequency cable 9 that passes through the insertion section 3 and the inside of the hand piece 2 and is connected to the hand piece 2. A switch 11 is provided that can be operated by the operator with his or her fingers while holding the grip portion 4.

[0017]

Therefore, as shown in FIG. 1, the insertion section 3 can be inserted into the nasal cavity 12 through the anterior nostril 12a by holding the handpiece 2, and the bipolar electrode 8 of the treatment section 6 can be brought into contact with the intranasal mucous membrane 13.

At this time, since the insertion part 3 has an angle θ1 with respect to the grip part 4, the grip part 4 and the fingers gripping the grip part 4 do not obstruct the field of view, and the treatment part 6 and the intranasal mucosa 13 are not obstructed. This can be visually confirmed and the intranasal mucosa 13 intended for the treatment area 6 can be easily approached.

In addition, since the treatment section 6 has an angle θ2 with respect to the axis of the insertion section 3, when the insertion section 3 is tilted, the contact surface 7 of the treatment section 6 becomes substantially upward and horizontal. It can be brought into surface contact with the intranasal mucosa 13.

[0018]

Therefore, when the operator turns on the switch 11, a high frequency current flows from the high frequency current supply source 10 to the bipolar electrode 8 of the treatment section 6 via the high frequency cable 9.

Specifically, a high frequency current flows from the active electrode 8a through the nasal mucosa 13 to the return electrode 8b, and the nasal mucosa 13 is cauterized.

Therefore, a wide range of the intranasal mucosa 13 can be uniformly cauterized by high-frequency current, and there is no need to change the position of the treatment section 6 with respect to the intranasal mucosa 13 many times, and the treatment can be performed in a short time.

[0019]

In addition, since the insertion section 3 is removable from the connection section 5 of the gripping section 4, it is possible to treat insertion sections 3 with different lengths, insertion sections 3 with different structures of the treatment section 6, or insertion sections 3. By preparing parts 6 with different angles, it is possible to use the optimal high-frequency treatment instrument 1 for the patient.

[0020]

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FIG. 3 shows a second embodiment, in which the same components as those in the first embodiment are given the same numbers and the description thereof will be omitted.

In this embodiment, two pairs of bipolar electrodes 8 are arranged in the longitudinal direction on the contact surface 7 of the treatment section 6, and high-frequency current can be applied to the two pairs of bipolar electrodes 8 simultaneously or selectively. can.

[0021]

FIG. 4 shows a third embodiment, in which the same components as those in the first embodiment are given the same numbers and the description thereof will be omitted.

In this embodiment, four pairs of bipolar electrodes 8 are arranged in the width direction on the contact surface 7 of the treatment section 6, and high-frequency current can be applied to the four pairs of bipolar electrodes 8 simultaneously or selectively. can.

[0022]

FIGS. 5 and 6 show a fourth embodiment, in which the same components as those in the first embodiment are given the same numbers and the description thereof will be omitted.

In this embodiment, an active electrode 8a and a return electrode 8b constituting a bipolar electrode 8 are disposed apart from each other in the longitudinal direction on the contact surface 7 of the treatment section 6, and the contact between the active electrode 8a and the return electrode 8b is A suction port 14 is provided on the surface 7.

[0023]

The suction port 14 is connected to a suction tube 16 via a suction path 15 communicating from the inside of the treatment section 6 to the inside of the insertion section 3, and this suction tube 16 is connected to a suction device (not shown).

[0024]

According to this embodiment, the liquid substance in the nasal mucosa 13 can be forcibly sucked through the suction port 14 before or during the high-frequency treatment of the nasal mucosa 13.

[0025]

FIGS. 7 to 9 show a fifth embodiment, in which the same components as those in the first embodiment are given the same numbers and the description thereof will be omitted.

This embodiment shows monopolar electrocautery, and the high-frequency treatment instrument 17 shown in FIG. The treatment section 20 is provided at an angle θ2 with respect to the axis of the insertion section 19.

An active electrode 22a is provided on the contact surface 21 of the treatment section 20, and the high frequency current supply source 10 is provided with a high frequency cable 9, a foot switch 23, and a return electrode 22b.

[0026]

Further, as shown in FIGS. 8(a) and 8(b), an active electrode 22a is provided at the middle part in the width direction of the contact surface 21 of the treatment section 20, and an active electrode 22a is provided in a substantially U-shape so as to surround this active electrode 22a. An insulating member 24 is provided that protrudes from the electrode 22a.

[0027]

According to this embodiment, even if the contact surface 21 of the treatment section 20 contacts the intranasal mucosa 13 with a high-frequency current flowing through the active electrode 22a, the insulating member 24 contacts the intranasal mucosa 13, and the active electrode Since the nasal cavity mucosa 22a and the nasal cavity mucosa 13 are not in contact with each other, the nasal cavity mucosa 13 is not cauterized.

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[0028]

However, as shown in FIG. 9, when a conductive jelly-like substance 25 exists between the nasal mucosa 13 and the active electrode 22a, a high-frequency current flows to the nasal mucosa 13 via this jelly-like substance 25. , it becomes possible to cauterize the intranasal mucosa 13.

The high-frequency current supply source 10 uses an active electrode 22a, a jelly-like substance 25, and the patient's impedance to detect whether or not the jelly-like substance 25 is applied to the affected area. A control circuit is provided for energizing after confirming that the inner mucosa 13 has been coated.

[0029]

Therefore, in this embodiment as well, the field of view is secured as in the first embodiment, the treatment section 20 can easily approach the target site, and the treatment section 20 can be brought into surface contact with the intranasal mucosa 13. .

[0030]

Note that, as shown in FIG. 10, the insertion section 19 is provided with a discharge port 26 that opens to the contact surface 21 of the treatment section 20 and a supply passage 27 that communicates with the discharge port 26, and the jelly-like substance 25 is supplied from the supply passage 27. The jelly-like substance 25 may be discharged from the discharge port 26 and applied to the nasal mucosa 13.

[0031]

11 to 13 show the sixth embodiment, FIG. 11 is a usage state diagram when the high-frequency treatment device is used for allergic rhinitis treatment, FIG. 12 shows the treatment part of the high-frequency treatment device, and (a) 13(b) is a rear view, FIG. 13(a) is a sectional view taken along the line AA in FIG. 12, and FIG. 13(b) is a sectional view taken along the line BB in FIG. 12.

[0032]

As shown in FIGS. 11 to 13, the high-frequency treatment instrument 31 includes a hand piece 32 that is held by the operator, and a pipe-shaped insertion portion 33 that extends in the axial direction of the hand piece 32 at the tip of the hand piece 32. has been done.

A treatment section 34 is rotatably provided at the distal end of the insertion section 33.

[0033]

That is, a pair of protruding pieces 35 are provided on the back surface of the treatment section 34, and a pivot pin 36 is provided on the protruding pieces 35 at the distal end of the inserting section 33, passing through the inserting section 33 in the radial direction.

Both ends of the pivot pin 36 are rotatably supported on the protruding piece 35, and the treatment section 34 is rotatable with respect to the insertion section 33.

[0034]

Further, on the front surface of the treatment section 34, an active electrode 37a and a return electrode 37b, which constitute a bipolar electrode 37, are provided in an insulated state.

In addition, two high-frequency cables 38a and 38b are inserted through the insertion section 33, and these high-frequency cables 38a and 38b are led out from the tip of the insertion section 33, penetrate the back surface of the treatment section 34, and connect the active electrode 37a and the return electrode. 37b, respectively

[0035]

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According to this embodiment, the handpiece 32 and the insertion section 33 are configured in a straight line, but the treatment section 34 at the distal end of the insertion section 33 is rotatable about the pivot pin 36 as a fulcrum.

[0036]

Therefore, as shown in FIG. 11, by holding the hand piece 32 and inserting the insertion section 33 into the nasal cavity 12 through the anterior nostril 12a, the bipolar electrode 37 of the treatment section 34 can be brought into contact with the intranasal mucous membrane 13.

At this time, the treatment section 34 is rotationally displaced with respect to the insertion section 33 using the pivot pin 36 as a fulcrum, and the front surface of the treatment section 34 can be brought into close contact with the intranasal mucosa 13.

[0037]

When a high-frequency current is passed from the high-frequency current supply source to the bipolar electrode 37 of the treatment section 34 via the high-frequency cables 38a and 38b, specifically, the high-frequency current flows from the active electrode 37a through the intranasal mucosa 13 to the return electrode 37b. flows, and the nasal mucosa 13 is cauterized.

Therefore, a wide range of the nasal mucosa 13 can be uniformly cauterized by the high-frequency current, and there is no need to change the position of the treatment section 34 with respect to the nasal mucosa 13 many times, and the treatment can be performed in a short time.

[0038]

FIGS. 14 to 16 show a seventh embodiment, and the same components as those in the sixth embodiment are given the same numbers and the description thereof will be omitted.

FIG. 14 is a usage state diagram when the high-frequency treatment instrument is used to treat allergic rhinitis, FIG. 15 is an exploded perspective view showing the treatment section of the high-frequency treatment instrument, and FIG. 16 is a longitudinal sectional front view of the treatment section.

[0039]

As shown in FIG. 14, the high-frequency treatment instrument 31 includes a hand piece 32 held by the operator, and a pipe-shaped insertion portion 33 having an angle 63 with respect to the axis of the hand piece 32 at the tip of the hand piece 32. It is configured.

A treatment section 34 is connected to the distal end of the insertion section 33 so as to be rotatable in any direction.

[0040]

That is, an opening 40 is provided on the back surface of the treatment section 34, and a cylindrical ball receiving section 41 is provided so as to surround this opening 40.

On the other hand, a ball 42 is integrally provided at the distal end of the insertion portion 33, and this ball 42 is fitted into the ball receiving portion 41 to form a ball joint 43.

Furthermore, the two high-frequency cables 38a and 38b inserted through the insertion section 33 are led out from the tip of the insertion section 33, penetrate the opening 40 of the treatment section 34, and supply electricity to the active electrode 37a and the return electrode 37b, respectively. connected.

[0041]

Therefore, as shown in FIG. 14, the insertion section 33 can be inserted into the nasal cavity 12 from the anterior nostril 12a by holding the handpiece 32, and the bipolar electrode 37 of the treatment section 34 can be brought into contact with the intranasal mucous membrane 13.

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At this time, since the insertion part 33 has an angle θ3 with respect to the axis of the handpiece 32, the handpiece 32 and the fingers gripping the handpiece 32 do not obstruct the field of view, and the treatment part 34 and the nasal mucosa are 13 can be visually confirmed, and the intranasal mucosa 13 intended for the treatment section 34 can be easily approached.

Furthermore, since the treatment section 34 can be oscillated three-dimensionally with respect to the insertion section 33 by the ball joint 43, the treatment section 34 can be brought into surface contact with the intranasal mucosa 13 regardless of the direction of the insertion section 33. Can be done.

[0042]

When a high-frequency current is passed from the high-frequency current supply source to the bipolar electrode 37 of the treatment section 34 via the high-frequency cables 38a and 38b, specifically, the high-frequency current flows from the active electrode 37a through the intranasal mucosa 13 to the return electrode 37b. flows, and the nasal mucosa 13 is cauterized.

Therefore, a wide range of the nasal mucosa 13 can be uniformly cauterized by the high-frequency current, and there is no need to change the position of the treatment section 34 with respect to the nasal mucosa 13 many times, and the treatment can be performed in a short time.

[0043]

According to each of the embodiments described above, the following configurations are obtained.

[0044]

(Additional Note 1) In a high-frequency treatment instrument consisting of a handpiece, an insertion section provided on the handpiece to be inserted into a body cavity, and a treatment section provided at the distal end of the insertion section, the treatment section is inserted into the affected area. A high-frequency treatment instrument characterized by having a contact surface that makes contact, and an electrode for high-frequency cauterization of the affected area is provided on the contact surface.

[0045]

(Supplementary Note 2) The high-frequency treatment instrument according to Supplementary Note 1, wherein the electrode is a bipolar electrode consisting of an active electrode and a return electrode.

[0046]

(Supplementary Note 3) The high-frequency treatment instrument according to Supplementary Note 1, wherein the electrode has an angle with respect to the axis of the insertion portion.

[0047]

(Supplementary Note 4) The high-frequency treatment instrument according to Supplementary Note 1, characterized in that a plurality of pairs of electrodes are provided in the treatment section.

[0048]

(Supplementary Note 5) The high-frequency treatment instrument according to Supplementary Note 1, wherein the insertion portion has an angle with respect to the axis of the handpiece.

[0049]

(Supplementary Note 6) The high-frequency treatment instrument according to Supplementary Note 1, wherein the treatment section has an angle with respect to the axis of the insertion section.

[0050]

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(Supplementary Note 7) The high-frequency treatment instrument according to Supplementary Note 1, wherein the treatment section is provided with a suction port for sucking a liquid substance.

[0051]

(Additional Note 8) The high-frequency treatment instrument according to Addendum 1, wherein the treatment section is provided with an ejection port for projecting a jelly-like substance.

[0052]

(Supplementary Note 9) The high-frequency treatment instrument according to Supplementary Note 1, wherein the treatment section is rotatably supported with respect to the insertion section.

[0053]

(Supplementary Note 10) The high-frequency treatment instrument according to Supplementary Note 1, wherein the treatment section is provided with a ball joint so as to be swingable three-dimensionally with respect to the insertion section.

[0054]

[Effects of the Invention] As explained above, the present invention provides a treatment section provided at the distal end of the insertion section with a contact surface for contacting the affected area, and an electrode for high-frequency cauterization of the affected area on this contact surface it is characterized by

Therefore, by inserting the insertion part into the nasal cavity through the nostrils, bringing the contact surface of the treatment part into contact with the intranasal mucosa, and passing a high-frequency current through the electrode provided on the contact surface, the intranasal mucosa can be spread over a wide area. It has the effect of being able to cauterize in many different ways and significantly shortening the treatment time.

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1.

In a high-frequency treatment instrument consisting of a handpiece, an insertion section provided on the handpiece to be inserted into a body cavity, and a treatment section provided at the distal end of the insertion section, the treatment section includes a contact surface that contacts the affected area. A high-frequency treatment instrument characterized in that the contact surface is provided with an electrode for high-frequency cauterization of the affected area.

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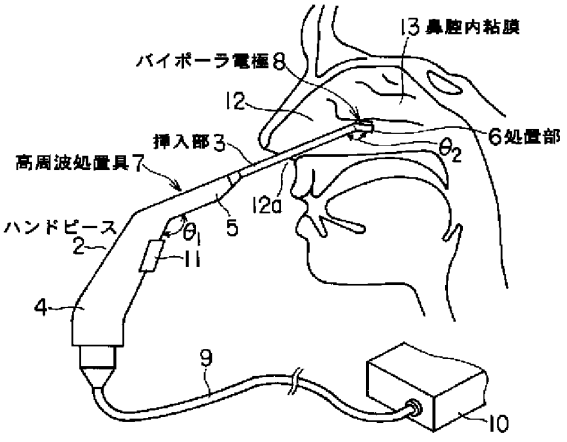
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最終頁に続く

(54)【発明の名称】　高周波処置具

(57)【要約】
【課題】患部を広範囲に亘って一様に焼灼でき、処置時間を大幅に短縮できる高周波処置具を提供することにある。
【解決手段】ハンドピース２と，このハンドピース２に設けられ体腔内に挿入する挿入部３と，この挿入部３の先端部に設けられた処置部６とからなる高周波処置具１において，前記処置部６は，患部に接触する接触面７を有し，この接触面７に患部を高周波焼灼するバイポーラ電極８を設けたことを特徴とする。



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【特許請求の範囲】
【請求項１】　ハンドピースと，このハンドピースに設けられ体腔内に挿入する挿入部と，この挿入部の先端部に設けられた処置部とからなる高周波処置具において，前記処置部は，患部に接触する接触面を有し，この接触面に患部を高周波焼灼する電極を設けたことを特徴とする高周波処置具。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】この発明は、例えば、アレルギー性鼻炎の手術的治療として、鼻内粘膜に対する下鼻甲介粘膜切除等に用いられる高周波処置具に関する。
【０００２】
【従来の技術】花粉症は、花粉が鼻の粘膜に付着してアレルギー反応を起こすために現れることが知られている。そこで、粘膜に処置を施してアレルギー反応を起こしにくい粘膜にする鼻腔粘膜除去法として、下鼻甲介粘膜切除術、高周波電気焼灼術、レーザー焼灼術が施行されている。
【０００３】高周波電気焼灼術に用いられる高周波処置具として、例えば，米国特許第５，７３３，２８２号明細書、米国特許第５，８２３，１９７号明細書及び米国特許第４，９３６，８４２号明細書等が知られている。
【０００４】米国特許第５，７３３，２８２号明細書は、鼻腔内に挿入する挿入部の先端部に，挿入部の軸方向に対して直角に屈曲した電極部を有し，挿入部を鼻腔内に挿入して電極部を患部に接触するとともに，電極部に高周波電流を流して患部の粘膜を切除するようになっている。
【０００５】米国特許第５，８２３，１９７号明細書は、鼻腔内に挿入するカテーテルの先端部にエネルギープローブを設け，カテーテルを鼻腔内に挿入し，下鼻甲介の内側でエネルギーを送出して下鼻甲介の一部を焼灼するようになっている。
【０００６】また、米国特許第４，９３６，８４２号明細書は、術者が把持する操作部と、この操作部に対して着脱可能なプローブと，このプローブの先端部に設けられ選択的に切替えられる２種の電極部とからなり，プローブを体腔内に挿入し、患部を電気エネルギーによって処置するようになっている。
【０００７】
【発明が解決しようとする課題】しかしながら、レーザ焼灼術は、高価なレーザ装置を必要とし，またモノポーラ電気焼灼術では凝固層の制御が難しいという問題がある。さらに、アレルギー性鼻炎の手術的治療として、鼻内粘膜に対する下鼻甲介粘膜切除を行おうとした場合，従来のように、電極部の先端部を患部に接触させると、接触部位のみが高温に焼灼されてしまい、目的部位の下鼻甲介を一様に焼灼するためには、操作部を把持して挿入部を移動させ，先端部の電極部を下鼻甲介全面に対して一様に動かす面倒な操作が必要となる。
【０００８】しかし，下鼻甲介は人によってその形状・大きさは様々であり，表面を一様に焼灼するためには熟練した技術が求められる。また、面積の広いヘラ状のプローブで下鼻甲介を焼灼しようとしても、下鼻甲介の表面は凹凸であるため，接触部位にムラが生じ，結果的に一様に焼灼できないという問題がある。
【０００９】この発明は、前記事情に着目してなされたもので、その目的とするところは、患部に接触して患部を一様に高周波焼灼でき，また操作性に優れた高周波処置具を提供することにある。
【００１０】
【課題を解決するための手段】この発明は、前記目的を達成するために、ハンドピースと，このハンドピースに設けられ体腔内に挿入する挿入部と，この挿入部の先端部に設けられた処置部とからなる高周波処置具において，前記処置部は，患部に接触する接触面を有し，この接触面に患部を高周波焼灼する電極を設けたことを特徴とする。
【００１１】前記構成によれば，挿入部を例えば前鼻孔から鼻腔内に挿入し、処置部の接触面を鼻腔内粘膜に接触させる。接触面に設けた電極に高周波電流を流すことにより，鼻腔内粘膜を広範囲に亘って一様に焼灼できる。
【００１２】
【発明の実施の形態】以下、この発明の各実施の形態を図面に基づいて説明する。
【００１３】図１及び図２は第１の実施形態を示し、図１は高周波処置具をアレルギー性鼻炎治療に用いた場合の使用状態図，図２は高周波処置具の処置部の正面図及び側面図である。
【００１４】図１及び図２に示すように，高周波処置具１は、術者が把持するハンドピース２と、このハンドピース２の先端に軸方向に延びるパイプ状の挿入部３とから構成されている。ハンドピース２の把持部４には挿入部３を着脱可能に連結するための連結部５が設けられ，この連結部５は把持部４に対して角度θ_1　を有しており，連結部５に連結された挿入部３は把持部４に対して傾斜している。そして、把持部４の上面と挿入部３の上面が同一面に形成されている。
【００１５】さらに，挿入部３の先端部には処置部６が設けられており，この処置部６は挿入部３の軸線に対し、把持部４に対する挿入部３の角度と同方向に角度θ_2　を有している。また、処置部６は絶縁部材によって形成され，その片面に平坦面からなる接触面７が設けられ，接触面７には前後方向に亘って棒状のバイポーラ電極８が設けられている。このバイポーラ電極８はアクティブ電極８ａとリターン電極８ｂとからなり、両電極８ａ，８ｂは電気的に絶縁されている。
【００１６】バイポーラ電極８は、挿入部３及びハンド

ピース２の内部を通ってハンドピース２に接続された高周波ケーブル９を介して高周波電流供給源１０に接続されており、ハンドピース２の把持部４には術者が把持部４を把持した状態で，手指で操作できるスイッチ１１が設けられている。

【００１７】従って，図１に示すように，ハンドピース２を持って挿入部３を前鼻孔１２ａから鼻腔１２に挿入し、処置部６のバイポーラ電極８を鼻腔内粘膜１３に接触させることができる。このとき，把持部４に対して挿入部３が角度θ_1　を有しているため、把持部４及び把持部４を把持した手指が視野を妨げることはなく，処置部６及び鼻腔内粘膜１３を目視で確認でき，処置部６を目的とする鼻腔内粘膜１３に容易にアプローチできる。しかも、処置部６は挿入部３の軸線に対して角度θ_2　を有しているため、挿入部３を傾斜したとき、処置部６の接触面７が略上向き水平となるため，接触面７を鼻腔内粘膜１３に面接触させることができる。

【００１８】そこで，術者がスイッチ１１をオンすると，高周波電流供給源１０から高周波ケーブル９を介して処置部６のバイポーラ電極８に高周波電流が流れる。具体的にはアクティブ電極８ａから鼻腔内粘膜１３を通ってリターン電極８ｂに高周波電流が流れ，鼻腔内粘膜１３が焼灼される。従って，鼻腔内粘膜１３の広い範囲を高周波電流によって均一に焼灼でき、鼻腔内粘膜１３に対して何度も処置部６の位置を変更する必要がなく，短時間に治療できる。

【００１９】また、把持部４の連結部５に対して挿入部３が着脱可能であるため，挿入部３の長さが異なるもの、処置部６の構造が異なる挿入部３あるいは挿入部３に対して処置部６の角度が異なるものを用意することにより，患者に対して最適な高周波処置具１を用いることができる。

【００２０】図３は第２の実施形態を示し、第１の実施形態と同一構成部分は同一番号を付して説明を省略する。本実施形態は、処置部６の接触面７に長手方向に２対のバイポーラ電極８を配置したものであり、２対のバイポーラ電極８に同時に高周波電流を流すことも，選択的に流すこともできる。

【００２１】図４は第３の実施形態を示し、第１の実施形態と同一構成部分は同一番号を付して説明を省略する。本実施形態は、処置部６の接触面７に幅方向に４対のバイポーラ電極８を配置したものであり、４対のバイポーラ電極８に同時に高周波電流を流すことも，選択的に流すこともできる。

【００２２】図５及び図６は第４の実施形態を示し、第１の実施形態と同一構成部分は同一番号を付して説明を省略する。本実施形態は、処置部６の接触面７に長手方向に離間してバイポーラ電極８を構成するアクティブ電極８ａとリターン電極８ｂとを配置するとともに，アクティブ電極８ａとリターン電極８ｂとの間の接触面７に吸引口１４を設けたものである。

【００２３】吸引口１４は処置部６の内部から挿入部３の内部に連通する吸引路１５を介して吸引チューブ１６に接続され、この吸引チューブ１６は吸引装置（図示しない）に接続されている。

【００２４】本実施形態によれば，鼻腔内粘膜１３を高周波処置する前または処置中に鼻腔内粘膜１３の液状物質を吸引口１４から強制的に吸引することができる。

【００２５】図７～図９は第５の実施形態を示し、第１の実施形態と同一構成部分は同一番号を付して説明を省略する。本実施形態は、モノポーラ電気焼灼術を示し，図７に示す，高周波処置具１７は、ハンドピース１８とこのハンドピース１８に対して挿入部１９が角度θ_1を有し、また挿入部１９に対して処置部２０が挿入部１９の軸線に対して角度θ_2　を有して設けられている。この処置部２０の接触面２１にはアクティブ電極２２ａが設けられ，高周波電流供給源１０には高周波ケーブル９とともに，フットスイッチ２３とリターン電極２２ｂが設けられている。

【００２６】また、図８（ａ）（ｂ）に示すように，処置部２０の接触面２１の幅方向中間部にはアクティブ電極２２ａが設けられ，このアクティブ電極２２ａを囲むように略Ｕ字状にアクティブ電極２２ａより突出した絶縁部材２４が設けられている。

【００２７】本実施形態によれば，アクティブ電極２２ａに高周波電流を流した状態で，処置部２０の接触面２１を鼻腔内粘膜１３に接触しても絶縁部材２４が鼻腔内粘膜１３に接触し，アクティブ電極２２ａと鼻腔内粘膜１３とは非接触となるため、鼻腔内粘膜１３が焼灼されることはない。

【００２８】しかし、図９に示すように，鼻腔内粘膜１３とアクティブ電極２２ａとの間に導電性のゼリー状物質２５が存在するとき，このゼリー状物質２５を介して鼻腔内粘膜１３に高周波電流が流れ、鼻腔内粘膜１３の焼灼が可能となる。なお、高周波電流供給源１０にはアクティブ電極２２ａとゼリー状物質２５と患者のインピーダンスを検知することにより、ゼリー状物質２５が患部に塗布されているか否かを検知し，ゼリー状物質２５が鼻腔内粘膜１３に塗布されていることを確認してから通電するための制御回路が設けられている。

【００２９】従って，本実施形態においても、第１の実施形態と同様に視野が確保され，目的部位に処置部２０を容易にアプローチでき，処置部２０を鼻腔内粘膜１３に対して面接触させることができる。

【００３０】なお、図１０に示すように，処置部２０の接触面２１に開口する吐出口２６及び吐出口２６と連通する供給通路２７を挿入部１９に設け，供給通路２７からゼリー状物質２５を供給して吐出口２６からゼリー状物質２５を吐出して鼻腔内粘膜１３に塗布するようにしてもよい。

【００３１】図１１～図１３は第６の実施形態を示し、図１１は高周波処置具をアレルギー性鼻炎治療に用いた場合の使用状態図，図１２は高周波処置具の処置部を示し，（ａ）は正面図、（ｂ）は背面図、図１３（ａ）は図１２のＡ－Ａ線に沿う断面図，（ｂ）は図１２のＢ－Ｂ線に沿う断面図である。

【００３２】図１１～図１３に示すように，高周波処置具３１は、術者が把持するハンドピース３２と、このハンドピース３２の先端にハンドピース３２の軸方向に延びるパイプ状の挿入部３３とから構成されている。挿入部３３の先端部には処置部３４が回動自在に設けられている。

【００３３】すなわち，処置部３４の背面には一対の突出片３５が設けられ，これら突出片３５には挿入部３３の先端部において挿入部３３の径方向に貫通する枢支ピン３６が設けられている。そして，枢支ピン３６の両端部は突出片３５に対して回動自在に枢支され，挿入部３３に対して処置部３４が回動自在になっている。

【００３４】さらに，処置部３４の前面にはバイポーラ電極３７を構成するアクティブ電極３７ａとリターン電極３７ｂとが絶縁状態で設けられている。また、挿入部３３には２本の高周波ケーブル３８ａ，３８ｂが挿通され、これら高周波ケーブル３８ａ，３８ｂは挿入部３３の先端から導出し、処置部３４の背面を貫通してアクティブ電極３７ａとリターン電極３７ｂとのそれぞれに電気的に接続されている。

【００３５】本実施形態によれば，ハンドピース３２と挿入部３３が一直線状に構成されているが，挿入部３３の先端部の処置部３４は枢支ピン３６を支点として回動自在である。

【００３６】従って，図１１に示すように，ハンドピース３２を持って挿入部３３を前鼻孔１２ａから鼻腔１２に挿入し、処置部３４のバイポーラ電極３７を鼻腔内粘膜１３に接触させることができる。このとき，挿入部３３に対して処置部３４が枢支ピン３６を支点として回動変位し，処置部３４の前面を鼻腔内粘膜１３に対して密着させることができる。

【００３７】そして、高周波電流供給源から高周波ケーブル３８ａ，３８ｂを介して処置部３４のバイポーラ電極３７に高周波電流を流すと，具体的にはアクティブ電極３７ａから鼻腔内粘膜１３を通ってリターン電極３７ｂに高周波電流が流れ，鼻腔内粘膜１３が焼灼される。従って，鼻腔内粘膜１３の広い範囲を高周波電流によって均一に焼灼でき、鼻腔内粘膜１３に対して何度も処置部３４の位置を変更する必要がなく，短時間に治療できる。

【００３８】図１４～図１６は第７の実施形態を示し、第６の実施形態と同一構成部分は同一番号を付して説明を省略する。図１４は高周波処置具をアレルギー性鼻炎治療に用いた場合の使用状態図，図１５は高周波処置具の処置部を示す分解斜視図，図１６は処置部の縦断正面図である。

【００３９】図１４に示すように，高周波処置具３１は、術者が把持するハンドピース３２と、このハンドピース３２の先端にハンドピース３２の軸線に対して角度θ_3を有するパイプ状の挿入部３３とから構成されている。挿入部３３の先端部には処置部３４が任意の方向に回動自在に連結されている。

【００４０】すなわち，処置部３４の背面には開口部４０が設けられ，この開口部４０を囲繞するように筒状のボール受け部４１が設けられている。一方，挿入部３３の先端部にはボール４２が一体に設けられ，このボール４２はボール受け部４１に対して嵌合され，ボールジョイント４３が構成されている。また、挿入部３３に挿通された２本の高周波ケーブル３８ａ，３８ｂは挿入部３３の先端から導出し、処置部３４の開口部４０を貫通してアクティブ電極３７ａとリターン電極３７ｂとのそれぞれに電気的に接続されている。

【００４１】従って，図１４に示すように，ハンドピース３２を持って挿入部３３を前鼻孔１２ａから鼻腔１２に挿入し、処置部３４のバイポーラ電極３７を鼻腔内粘膜１３に接触させることができる。このとき，ハンドピース３２の軸線に対して挿入部３３が角度θ_3　を有しているため、ハンドピース３２及びハンドピース３２を把持した手指が視野を妨げることはなく，処置部３４及び鼻腔内粘膜１３を目視で確認でき，処置部３４を目的とする鼻腔内粘膜１３に容易にアプローチできる。さらに、挿入部３３に対して処置部３４がボールジョイント４３によって３次元的に首振り運動可能であるため，挿入部３３の方向に関係なく，処置部３４を鼻腔内粘膜１３に面接触させることができる。

【００４２】そして、高周波電流供給源から高周波ケーブル３８ａ，３８ｂを介して処置部３４のバイポーラ電極３７に高周波電流を流すと，具体的にはアクティブ電極３７ａから鼻腔内粘膜１３を通ってリターン電極３７ｂに高周波電流が流れ，鼻腔内粘膜１３が焼灼される。従って，鼻腔内粘膜１３の広い範囲を高周波電流によって均一に焼灼でき、鼻腔内粘膜１３に対して何度も処置部３４の位置を変更する必要がなく，短時間に治療できる。

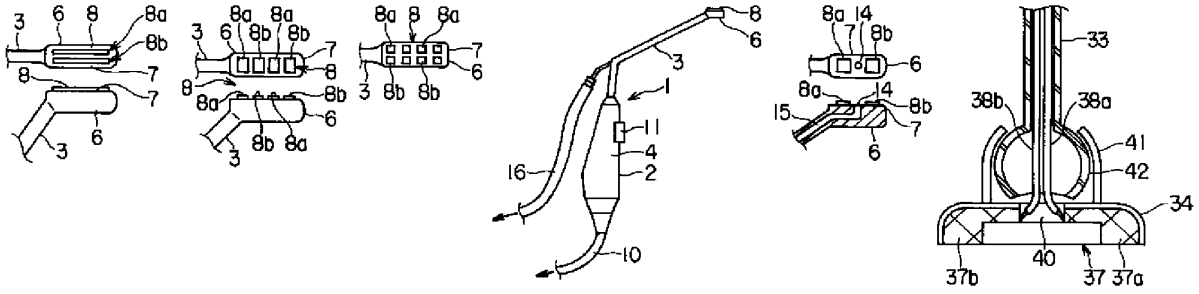
【００４３】前記各実施形態によれば、次のような構成が得られる。

【００４４】（付記１）ハンドピースと，このハンドピースに設けられ体腔内に挿入する挿入部と，この挿入部の先端部に設けられた処置部とからなる高周波処置具において，前記処置部は，患部に接触する接触面を有し，この接触面に患部を高周波焼灼する電極を設けたことを特徴とする高周波処置具。

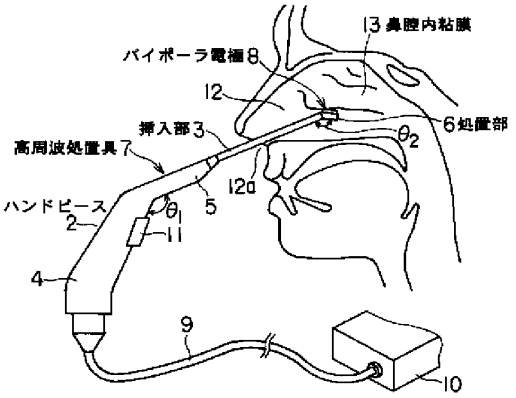
【００４５】（付記２）付記１における、電極は，アクティブ電極とリターン電極とからなるバイポーラ電極で

あることを特徴とする高周波処置具。
【００４６】（付記３）付記１における、電極は，挿入部の軸線に対して角度を持っていることを特徴とする高周波処置具。
【００４７】（付記４）付記１における、電極は，処置部に複数対設けられていることを特徴とする高周波処置具。
【００４８】（付記５）付記１における、挿入部は，ハンドピースの軸線に対して角度を持っていることを特徴とする高周波処置具。
【００４９】（付記６）付記１における、処置部は，挿入部の軸線に対して角度を持っていることを特徴とする高周波処置具。
【００５０】（付記７）付記１における、処置部は，液状物質を吸引する吸引口が設けられていることを特徴とする高周波処置具。
【００５１】（付記８）付記１における、処置部は，ゼリー状物質を突出する吐出口が設けられていることを特徴とする高周波処置具。
【００５２】（付記９）付記１における、処置部は，挿入部に対して回動自在に枢支されていることを特徴とする高周波処置具。
【００５３】（付記１０）付記１における、処置部は，挿入部に対してボールジョイントによって３次元的に首振り自在に設けられていることを特徴とする高周波処置具。
【００５４】
【発明の効果】以上説明したように、この発明は、挿入部の先端部に設けられた処置部に，患部に接触する接触面を設け，この接触面に患部を高周波焼灼する電極を設けたことを特徴とする。従って，挿入部を例えば鼻孔から鼻腔内に挿入し、処置部の接触面を鼻腔内粘膜に接触させ、接触面に設けた電極に高周波電流を流すことにより，鼻腔内粘膜を広範囲に亘って一様に焼灼でき、処置時間を大幅に短縮できるという効果がある。
【図面の簡単な説明】
【図１】この発明の第１の実施形態を示す高周波処置具の使用状態図。
【図２】同実施形態の処置部の正面図及び側面図。
【図３】この発明の第２の実施形態の処置部を示す正面図及び側面図。
【図４】この発明の第３の実施形態の処置部を示す正面図。
【図５】この発明の第４の実施形態を示す高周波処置具の側面図。
【図６】同実施形態の処置部を示す正面図及び縦断側面図。
【図７】この発明の第５の実施形態を示す高周波処置具の使用状態図。
【図８】同実施形態の処置部を示し，（ａ）は断面図，（ｂ）は正面図。
【図９】同実施形態の処置部をゼリー状物質を介して患部に接触した状態の側面図。
【図１０】同実施形態の変形例を示し，処置部をゼリー状物質を介して患部に接触した状態の側面図。
【図１１】この発明の第６の実施形態を示す高周波処置具の使用状態図。
【図１２】同実施形態の処置部を示し，（ａ）は正面図，（ｂ）は正面図。
【図１３】同実施形態の処置部を示し，（ａ）は図１２のＡ－Ａ線に沿う断面図，（ｂ）は図１２のＢ－Ｂ線に沿う断面図。
【図１４】この発明の第７の実施形態を示す高周波処置具の使用状態図。
【図１５】同実施形態の処置部の分解斜視図。
【図１６】同実施形態の処置部の断面図。
【符号の説明】
１…高周波処置具
２…ハンドピース
３…挿入部
６…処置部
７…接触面
８…バイポーラ電極

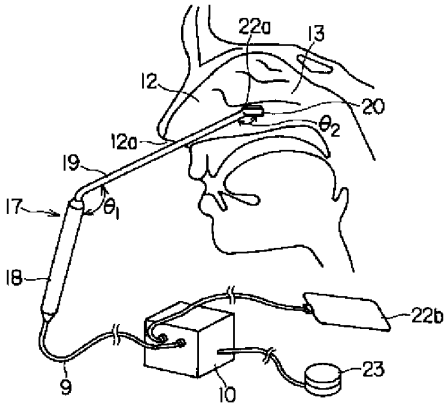
【図２】 【図３】 【図４】 【図５】 【図６】 【図１６】



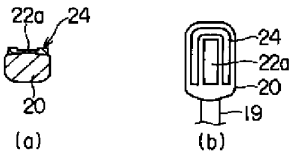
【図１】



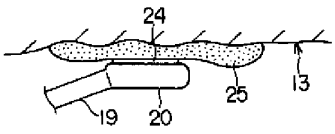
【図７】



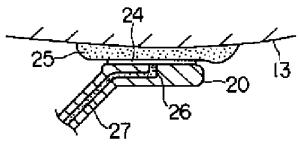
【図８】



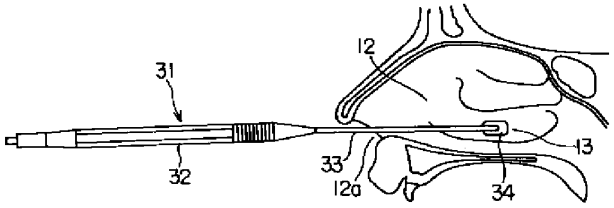
【図９】



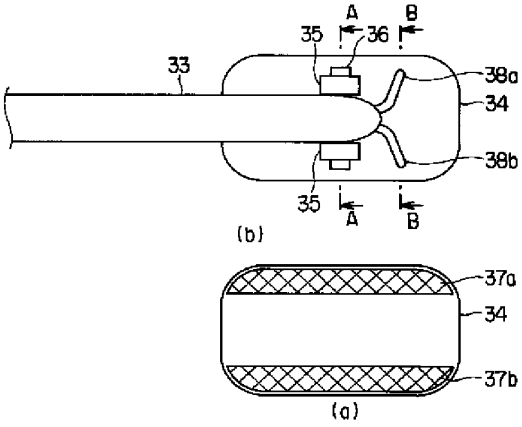
【図１０】



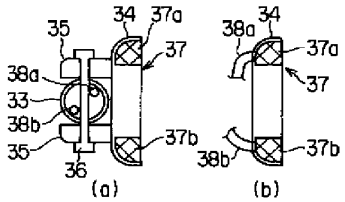
【図１１】



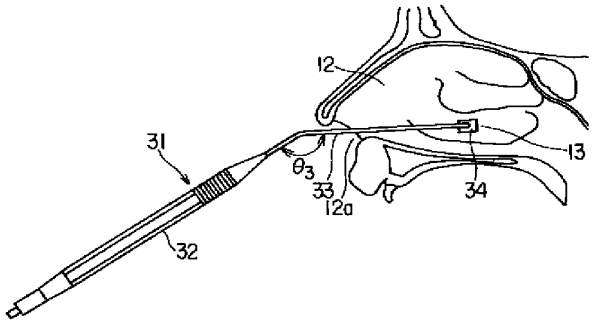
【図１２】



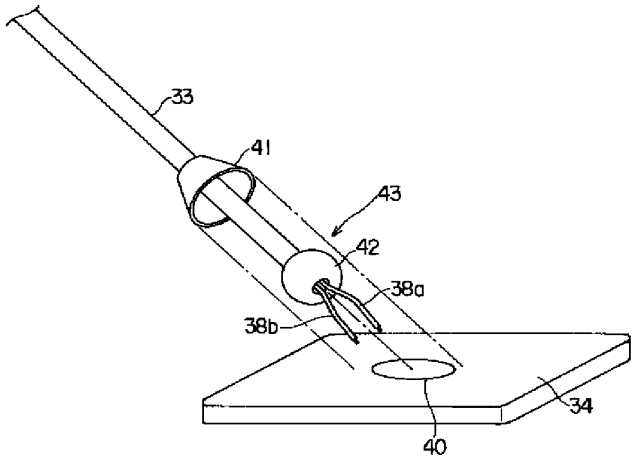
【図１３】



【図１４】



【図１５】



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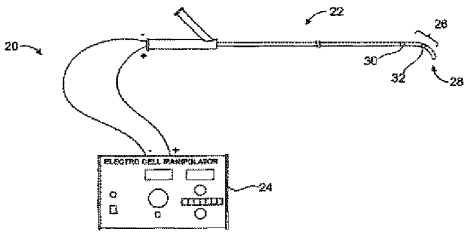
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最終頁に続く

(54)【発明の名称】鼻腔への毒素送達のための装置、方法、およびシステム

(57)【要約】
毒素および毒素フラグメントを患者の鼻腔に送達するための装置、方法およびシステムは、毒素の放出と、毒素の取込みを増強するために標的細胞を選択的に穿孔するエネルギーの送達との両方を提供する。エネルギーを介した送達の使用は、細胞結合能力を欠く軽鎖フラグメント毒素に、特に有利である。本発明の一つの実施形態において、ハンドルと、アプリケータを介した毒素の送達を促進するために患者の鼻孔内に挿入し、患者の鼻道内に配置するために形状が定められた少なくとも一つのアプリケータ先端とを含む装置を使用して、ボツリヌス毒素等の毒素が、鼻腔の組織に投与される。



【特許請求の範囲】
【請求項1】
患者の鼻粘膜の炎症を治療するための装置であって、前記装置は、
近位セクションと、第一部材と第二部材とを含むハンドルであって、前記第一部材および第二部材が、前記近位セクションで接続される、ハンドルと；
前記第一部材に連結された第一アプリケータ先端と；
前記第二部材に連結された第二アプリケータ先端と；
を含み、
前記第一アプリケータ先端および第二アプリケータ先端は、前記患者の鼻孔内への挿入および前記患者の鼻道内の配置のために形状が定められ、各アプリケータ先端は、前記患者の前記鼻腔内の鼻腔組織の領域に毒素を送達するために形状が定められ、これにより前記炎症が治療される、装置。
【請求項2】
前記ハンドルが、バネ要素をさらに含む、請求項１に記載の装置。
【請求項3】
前記バネ要素が、ｖ形バネまたは閉ループバネである、請求項２に記載の装置。
【請求項4】
前記ハンドルが、前記アプリケータ先端を前記鼻道内に配置するための圧縮送達形態、および前記鼻腔組織の領域に毒素を送達するための拡張治療形態で配置されるように形状が定められる、請求項２に記載の装置。
【請求項5】
各アプリケータ先端が、スポンジを含む、請求項１に記載の装置。
【請求項6】
各アプリケータ先端が、前記鼻道内の配置のための低体積送達形態、および前記鼻腔組織の領域に毒素を送達するための拡張体積治療形態で配置されるように形状が定められる、請求項５に記載の装置。
【請求項7】
前記拡張体積治療形態における各アプリケータ先端が、前記患者の前記鼻腔内に実質的に嵌合するように適合される、請求項６に記載の装置。
【請求項8】
各アプリケータ先端が、バネ要素をさらに含む、請求項５に記載の装置。
【請求項9】
各アプリケータ先端が、前記鼻道内の配置のための圧縮送達形態、および前記鼻腔組織の領域に毒素を送達するための拡張治療形態で配置されるように形状が定められる、請求項８に記載の装置。
【請求項10】
各アプリケータ先端が、アクチュエータをさらに含み、前記アクチュエータが、係合位置および格納位置から移動するために形状が定められる、請求項９に記載の装置。
【請求項11】
前記アクチュエータが前記係合位置にある時に、前記アプリケータ先端が、前記圧縮送達形態である、請求項１０に記載の装置。
【請求項12】
前記アクチュエータが前記格納位置にある時に、前記アプリケータ先端が、前記拡張送達形態である、請求項１０に記載の装置。
【請求項13】
係合要素をさらに含み、前記係合要素が、両アクチュエータの前記移動を同時に制御するように形状が定められる、請求項１０に記載の装置。
【請求項14】
各アプリケータ先端が、不浸透性ライニングをさらに含む、請求項５に記載の装置。

【請求項15】
各アプリケータ先端が、粘膜付着性パッドをさらに含む、請求項１に記載の装置。
【請求項16】
前記毒素が、生体再吸収性コーティングにより担持される、請求項１に記載の装置。
【請求項17】
前記アプリケータ先端に前記毒素を送達するための注入チャネルをさらに含む、請求項１に記載の装置。
【請求項18】
アクセスポートをさらに含み、前記装置が、前記アクセスポートを介して毒素供給源と流体連通する、請求項１７に記載の装置。
【請求項19】
前記アプリケータ先端が、前記鼻道内に配置される前に、前記毒素を受け取るように形状が定められる、請求項１７に記載の装置。
【請求項20】
前記アプリケータ先端が、前記鼻道内に配置された後に、前記毒素を受け取るように形状が定められる、請求項１７に記載の装置。
【請求項21】
前記毒素が、液体、ゲル、フォーム、クリーム、ローション、および凍結乾燥化合物からなる群より選択される少なくとも一つを含む、請求項１に記載の装置。
【請求項22】
前記毒素が、ボツリヌス毒素を含む、請求項１に記載の装置。
【請求項23】
前記ボツリヌス毒素が、Ａ、Ｂ、Ｃ、Ｄ、Ｅ、ＦおよびＧからなるボツリヌス毒素の群より選択される、請求項２２に記載の装置。
【請求項24】
前記毒素が、ボツリヌス毒素のフラグメントである、請求項２２に記載の装置。
【請求項25】
前記フラグメントが、ボツリヌス毒素の軽鎖フラグメントである、請求項２４に記載の装置。
【請求項26】
前記鼻腔組織への前記毒素の送達を増強するために、前記鼻腔組織の領域にエネルギーを送達するために形状が定められた、エネルギー送達アプリケータをさらに含む、請求項２５に記載の装置。
【請求項27】
前記エネルギー送達アプリケータが、前記鼻腔組織の領域の少なくとも一つの細胞の穿孔を生じる条件下でエネルギーを送達するように適合される、請求項２６に記載の装置。
【請求項28】
前記エネルギー送達アプリケータが、電気パルスを送達するのに適する、請求項２６に記載の装置。
【請求項29】
前記電気パルスが、ＲＦ信号である、請求項２８に記載の装置。
【請求項30】
前記エネルギー送達が、マイクロ波、超音波およびＸ線からなる群より選択されるエネルギーを送達するように適合される、請求項２６に記載の装置。
【請求項31】
鼻炎、鼻漏、枯草熱およびそれらの組み合わせからなる群より選択される、患者の鼻粘膜の炎症と関連した状態を治療するための装置であって、前記装置は、
（ａ）前記患者の鼻孔内に挿入し、（ｂ）前記患者の鼻道内に配置し、（ｃ）治療有効量の毒素を、前記患者の前記鼻腔内の鼻腔組織の領域に送達するために形状が定められたアプリケータ

を含み、
前記アプリケータは、内側部材および外側部材を含む、装置。
【請求項32】
前記アプリケータが、前記内側部材と外側部材とを隔てるために形状が定められた、不浸透性ライニングをさらに含む、請求項３１に記載の装置。
【請求項33】
前記アプリケータが、前記鼻道内の配置のための低体積形態、および前記鼻腔組織に前記毒素を送達するための拡張体積形態で配置されるように形状が定められる、請求項３１に記載の装置。
【請求項34】
前記内側部材が、バルーンを含む、請求項３３に記載の装置。
【請求項35】
前記内側部材が、スポンジを含む、請求項３３に記載の装置。
【請求項36】
前記内側部材が、バネ要素をさらに含む、請求項３５に記載の装置。
【請求項37】
前記外側部材が、スポンジ、メッシュパッド、有孔バルーン、多孔ポリマー、生体再吸収性コーティング、粘膜付着性表面、およびこれらの組み合わせからなる群より選択される一つを含む、請求項３１に記載の装置。
【請求項38】
前記外側部材が、バルーンおよびスポンジを含む、請求項３１に記載の装置。
【請求項39】
前記内側部材が、拡張するように形状が定められる、請求項３１に記載の装置。
【請求項40】
前記内側部材の拡張が、前記鼻腔組織への前記毒素の送達を促進する、請求項３９に記載の装置。
【請求項41】
鼻炎、鼻漏、枯草熱およびそれらの組み合わせからなる群より選択される、患者の鼻粘膜の炎症と関連した状態を治療するための装置であって、前記装置が、
第一遠位端および第二遠位端を含むハンドルと；
前記第一遠位端に連結された第一アプリケータ先端と；
前記第二遠位端に連結された第二アプリケータ先端と；
を含み、
前記第一アプリケータ先端および第二アプリケータ先端の各々が、前記患者の鼻孔内への挿入および前記患者の鼻道内の配置のために形状が定められ、各アプリケータ先端が、治療有効量の毒素を前記患者の鼻腔内の鼻腔組織の領域に送達するために形状が定められ、これにより前記状態が治療される、装置。
【請求項42】
バネ要素をさらに含み、前記アプリケータ先端が前記鼻道内に配置された時に、前記バネ要素が、前記アプリケータ先端に外向きの付勢を提供するように形状が定められる、請求項４１に記載の装置。
【請求項43】
前記外向きの付勢が、前記鼻腔内の鼻甲介に対して、各アプリケータ先端を押し付ける、請求項４２に記載の装置。
【請求項44】
患者の鼻粘膜の標的細胞に毒素を送達するための方法であって、前記方法が、
前記標的細胞に近接する領域に毒素を導入するステップと；
前記細胞への前記毒素の送達を増強するために、前記標的細胞にエネルギーを印加するステップ
を含む、方法。

【請求項45】
前記領域が、少なくとも一つの副鼻腔、主鼻道または鼻甲介を含む、請求項４４に記載の方法。
【請求項46】
前記領域が、鼻腔全体を実質的に含む、請求項４４に記載の方法。
【請求項47】
前記領域が、鼻咽頭を含む、請求項４４に記載の方法。
【請求項48】
前記標的細胞が、上皮または胚細胞を含む、請求項４４に記載の方法。
【請求項49】
前記エネルギーが、毒素が導入されている前記領域内の標的細胞に選択的に印加される、請求項４４に記載の方法。
【請求項50】
前記エネルギーが、毒素が導入されている領域内に非選択的に印加される、請求項４４に記載の方法。
【請求項51】
前記患者が、鼻漏を患うか、患う危険性がある、請求項４４に記載の方法。
【請求項52】
前記患者が、副鼻腔炎による頭痛を患うか、患う危険性がある、請求項４４に記載の方法。
【請求項53】
前記患者が、片頭痛を患うか、患う危険性がある、請求項４４に記載の方法。
【請求項54】
前記毒素が、ボツリヌス毒素を含む、請求項４４に記載の方法。
【請求項55】
前記毒素が、ボツリヌス毒素のフラグメントである、請求項５４に記載の方法。
【請求項56】
前記フラグメントが、ボツリヌス毒素の軽鎖フラグメントである、請求項５５に記載の方法。
【請求項57】
前記軽鎖フラグメントが、ボツリヌス毒素Ａ、Ｂ、Ｃ、Ｄ、Ｅ、ＦおよびＧの少なくとも一つから得られる、請求項５６に記載の方法。
【請求項58】
前記標的領域に印加される前記エネルギーが、電気パルスである、請求項４４に記載の方法。
【請求項59】
前記電気パルスが、１Ｖ～５００Ｖの間で印加される、請求項５８に記載の方法。
【請求項60】
前記電気パルスが、ＲＦ信号である、請求項５８に記載の方法。
【請求項61】
前記電気パルスが、５マイクロ秒～１００ミリ秒の間パルス化される、請求項５８に記載の方法。
【請求項62】
前記電気パルスが、ＤＣ電源により生成される、請求項５８に記載の方法。
【請求項63】
前記電気パルスが、ＡＣ電源により生成される、請求項５８に記載の方法。
【請求項64】
前記標的領域に印加される前記エネルギーが、超音波である、請求項４４に記載の方法。
【請求項65】

前記標的領域に印加されるエネルギーが、Ｘ線ビームである、請求項４４に記載の方法。
【請求項66】
前記標的領域に印加されるエネルギーが、集束超音波である、請求項４４に記載の方法。
【請求項67】
前記標的領域に印加されるエネルギーが、マイクロ波である、請求項４４に記載の方法。
【請求項68】
前記毒素が、カテーテルを通して前記標的領域に導入される、請求項４４に記載の方法。
【請求項69】
前記毒素が、前記カテーテル上のバルーンを通して導入される、請求項６８に記載の方法。
【請求項70】
前記バルーンが多孔であり、前記毒素が前記バルーンを通して導入される、請求項６９に記載の方法。
【請求項71】
前記毒素が、前記カテーテル上の針を通して導入される、請求項６８に記載の方法。
【請求項72】
前記毒素が、前記カテーテルからエアロゾル散布される、請求項６８に記載の方法。
【請求項73】
前記カテーテル上の供給源から、エネルギーが印加される、請求項６８に記載の方法。
【請求項74】
前記カテーテル上のトランスデューサから、音波エネルギーが印加される、請求項７３に記載の方法。
【請求項75】
前記カテーテル上の電極から、電気エネルギーが印加される、請求項７３に記載の方法。
【請求項76】
前記エネルギーが、前記患者の外部の供給源から送達される、請求項４４に記載の方法。
【請求項77】
前記供給源が、音波エネルギートランスデューサである、請求項７６に記載の方法。
【請求項78】
前記音波エネルギートランスデューサが、集束超音波トランスデューサである、請求項７７に記載の方法。
【請求項79】
鼻粘膜における標的細胞に毒素を送達するためのシステムであって、前記システムが、
前記標的細胞に近接する領域に毒素を導入するために適合されたカテーテルと；
前記毒素の送達を増強するために、前記細胞膜の穿孔を生じる条件下で前記標的細胞にエネルギーを印加するために形状が定められた、エネルギーアプリケータと；
前記カテーテルからの導入に適切な毒素の供給源と
を含む、システム。
【請求項80】
前記エネルギーアプリケータが、毒素が導入されている領域内の標的細胞にエネルギーを選択的に印加するように適合される、請求項７９に記載のシステム。
【請求項81】
前記エネルギーアプリケータが、毒素が導入されている領域内にエネルギーを非選択的に印加するように適合される、請求項７９に記載のシステム。

【請求項82】
前記毒素が、ボツリヌス毒素を含む、請求項７９に記載のシステム。
【請求項83】
前記毒素が、ボツリヌス毒素のフラグメントである、請求項８２に記載のシステム。
【請求項84】
前記フラグメントが、ボツリヌス毒素の軽鎖フラグメントである、請求項８３に記載のシステム。
【請求項85】
前記軽鎖フラグメントが、ボツリヌス毒素Ａ、Ｂ、Ｃ、Ｄ、Ｅ、ＦおよびＧの少なくとも一つから得られる、請求項８４に記載のシステム。
【請求項86】
前記エネルギーアプリケータが、前記標的領域に１ｖ～５００Ｖの間の電気パルスを印加するように適合される、請求項４４に記載のシステム。
【請求項87】
前記電気パルスが、ＲＦ信号である、請求項８６に記載のシステム。
【請求項88】
前記電気パルスが、５マイクロ秒～１００ミリ秒の間パルス化される、請求項８６に記載のシステム。
【請求項89】
前記電気パルスが、ＤＣ電源により生成される、請求項８６に記載のシステム。
【請求項90】
前記電気パルスが、ＡＣ電源により生成される、請求項８６に記載のシステム。
【請求項91】
前記エネルギーアプリケータが、前記標的領域に超音波エネルギーを印加するように適合される、請求項４４に記載のシステム。
【請求項92】
前記エネルギーアプリケータが、前記標的領域にＸ線ビームを印加するように適合される、請求項７９に記載のシステム。
【請求項93】
前記エネルギーアプリケータが、前記標的領域に集束超音波を印加するように適合される、請求項７９に記載のシステム。
【請求項94】
前記エネルギーアプリケータが、前記標的領域にマイクロ波を印加するように適合される、請求項７９に記載のシステム。
【請求項95】
前記毒素が、前記カテーテル上のバルーンにより導入される、請求項７９に記載のシステム。
【請求項96】
前記バルーンが一つ以上の孔を含み、前記毒素が、前記バルーンの孔を通して導入される、請求項９５に記載のシステム。
【請求項97】
前記毒素が、前記カテーテル上の針を通して導入される、請求項７９に記載のシステム。
【請求項98】
前記毒素が、前記カテーテルからエアロゾル散布される、請求項９５に記載のシステム。
【請求項99】
エネルギーアプリケータが、前記カテーテル上にある、請求項７９に記載のシステム。
【請求項100】
エネルギーアプリケータが、前記カテーテル上のトランスデューサから、音波エネルギ

ーを印加する、請求項９９に記載のシステム。
【請求項101】
エネルギーアプリケータが、前記カテーテル上の電極から、電気エネルギーを印加する、請求項９９に記載のシステム。
【請求項102】
前記アプリケータが、前記患者の外部の供給源からエネルギーを印加する、請求項７９に記載のシステム。
【請求項103】
前記供給源が、音波エネルギートランスデューサをさらに含む、請求項１０２に記載のシステム。
【請求項104】
前記音波エネルギートランスデューサが、集束超音波トランスデューサをさらに含む、請求項１０２に記載のシステム。
【請求項105】
前記毒素が、前記カテーテル上の足場の上に支持された膜を通して導入される、請求項７９に記載のシステム。
【請求項106】
前記毒素が、針なしの注射器により導入される、請求項７９に記載のシステム。
【請求項107】
前記エネルギーアプリケータが、鼻道内に配置されるように形状が定められた導波路を含む、請求項７９に記載のシステム。
【請求項108】
前記バルーンが、鼻道内に配置されるように形状が定められる、請求項９５に記載のシステム。
【請求項109】
前記バルーンが、副鼻腔の外側に配置されるように形状が定められる、請求項９５に記載のシステム。
【請求項110】
前記標的細胞にエネルギーを印加するステップが、前記細胞膜の穿孔を生じる条件下で前記標的細胞にエネルギーを印加するステップをさらに含む、請求項４４に記載の方法。
【請求項111】
前記供給源が、マイクロ波アンテナをさらに含む、請求項１０２に記載のシステム。
【請求項112】
前記カテーテル上のアンテナから、マイクロ波エネルギーが印加される、請求項７３に記載のシステム。
【発明の詳細な説明】
【技術分野】
【0001】
（発明の分野）
本発明は、一般に、医療方法およびシステムに関する。特に、本発明は、ボツリヌス毒素軽鎖フラグメント等の毒素を、鼻腔の標的細胞に送達するための方法およびシステムに関する。
【背景技術】
【0002】
鼻漏の症状を含む鼻炎は、患者の鼻腔を覆う粘膜の炎症および腫れからくる状態である。鼻炎および／または鼻漏は、多くの状態から生じ、花粉、塵、季節的アレルゲンまたは他の空中物質に対するアレルギーの結果起こることが最も多いが、（副鼻腔炎の場合のように）閉塞等の解剖病理によっても起こりうる。症状には、くしゃみ、痒み、鼻閉および鼻水が含まれうる。
【0003】
鼻炎のための多く治療が長年にわたり提唱されているが、全患者または全病状に最適な

治療はない。最も一般的には、枯草熱および他の形の鼻炎は、炎症反応をブロックする抗ヒスタミン剤により治療される。多くの抗ヒスタミン剤は、効果的ではあるものの、眠気を生じ、効果継続時間が限られ、患者は薬物を継続的に購入する費用がかかる。

【0004】

近年では、鼻粘膜の粘液産生細胞による粘液産生をブロックするためのボツリヌス毒素（「ＢｏＮＴ」）の使用に依存する、より長期間の鼻炎治療が提唱されている。ボツリヌス毒素および他の神経毒素は、鼻腔膜における大半の粘液産生を担う上皮細胞または杯細胞を含むアドレナリン細胞の機能を失わせることができる。Ｉｒａ　Ｓａｎｄｅｒｓ博士は、イヌの鼻道に完全なボツリヌス毒素分子を導入することにより、粘液分泌を相当量減少させうることを示している。

【0005】

Ｓａｎｄｅｒｓ博士の実験研究は、長期的な鼻炎治療に有望である一方で、ヒトへの広汎な使用に適切となるまでには、多くの課題がある。特に、ボツリヌス毒素は、標的の鼻道以外に誤って放出された場合には患者に重大な負の効果を与えうる、神経毒素である。口腔咽頭、口、舌の筋肉またはその他の場所への毒素の過失による分散は、患者に重篤な合併症をもたらしうる。さらに、Ｓａｎｄｅｒｓ博士が示す、毒素を鼻腔に送達するためのボツリヌス毒素を吸わせたガーゼパッドの使用は、鼻咽頭の上皮細胞または杯細胞など、好ましい標的細胞を高濃度で有する領域に、ボツリヌス毒素を均一かつ選択的に送達する能力が限定される。

【0006】

これらの理由から、ボツリヌス毒素およびボツリヌス毒素の活性フラグメント等の毒素を、患者、特に副鼻腔炎による頭痛および片頭痛等、鼻の炎症および症状と関連した鼻炎またはその他の症状を患う患者の鼻粘膜に送達するための、改良された方法およびシステムを提供することが望ましい。方法およびシステムは、特定の副鼻腔、鼻咽頭、および場合によっては鼻腔のほぼ全体を含む鼻腔内の特定の標的領域への、選択的および反復可能な毒素の送達を提供できなければならない。システムおよび方法は、毒素の安全かつ有効な送達を提供すべきであり、特に、毒素が鼻腔以外の非標的組織に送達される危険性を低減または除去すべきである。これらの目的の少なくともいくつかは、本明細書の以下に記載される本発明により満たされる。

【0007】

（背景技術の説明）

Ｓａｎｄｅｒｓ等に対する特許文献１は、上に記載されている。非特許文献１も、特許文献１に記載されるＳａｎｄｅｒｓ博士の研究を記載する。非特許文献２は、アレルギー性鼻炎を患う患者の鼻甲介への、ボツリヌス毒素Ａの注入を記載する。特許文献２も参照せよ。ボツリヌス毒素軽鎖の精製および治療的使用の可能性が、特許文献３、特許文献４、および非特許文献３に記載される。エネルギーにより媒介される完全なボツリヌス毒素の経皮送達が、特許文献５および特許文献６に示唆される。エネルギーにより媒介されるボツリヌス毒素軽鎖の送達のための、カテーテルおよび他のデバイスの使用が、共同所有の同時係属中の米国特許仮出願第６０／７０２，０７７号（代理人整理番号０２０９７９－００３４００ＵＳ、２００５年７月２２日出願）に記載され、その全開示が先の参照により本明細書に組み込まれているものとする。

【図面の簡単な説明】

【0032】

【図1】軽鎖（ＬＣ）フラグメントまたは部分を含む、神経毒素ボツリヌス毒素Ａ型（ＢｏＮＴ／Ａ）の生成の概略である。

【図2A】細胞膜および細胞内マトリクスを含む、標的細胞の概略である。

【図2B】ＬＣ分子が導入されている、標的細胞の概略である。

【図3A】細胞膜の透過化または孔（Ｐ）を生じるためのエネルギー場（ＥＦ）の印加、およびそれを通したＬＣフラグメントの導入を示す、図２の標的細胞である。

【図3B】細胞膜の透過化または孔（Ｐ）を生じるためのエネルギー場（ＥＦ）の印加、お

よびそれを通したＬＣフラグメントの導入を示す、図２の標的細胞である。
【図4】エネルギー場が中断され、細胞の神経伝達が効果的に遮断されている、細胞の概略である。
【図5】複数のエネルギー伝達要素およびエネルギー伝達システムを利用した、本発明の送達デバイスの実施形態である。
【図5A】複数のエネルギー伝達要素およびエネルギー伝達システムを利用した、本発明の送達デバイスの実施形態である。
【図5B】複数のエネルギー伝達要素およびエネルギー伝達システムを利用した、本発明の送達デバイスの実施形態である。
【図5A】複数のエネルギー伝達要素およびエネルギー伝達システムを利用した、本発明の送達デバイスの実施形態である。
【図5B】複数のエネルギー伝達要素およびエネルギー伝達システムを利用した、本発明の送達デバイスの実施形態である。
【図6A】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図6B】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図6C】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図6D】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図6AA】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図6CC】エネルギーまたはエネルギーと治療薬を標的組織に送達するのに適した、電極カテーテル形態である。
【図7】カテーテルデバイス上の超音波要素を利用した、本発明の実施形態である。
【図8】エアロゾル化要素を利用した、本発明の実施形態である、
【図9】別個のナザルエアロゾライザから送達される毒素の細胞取込みを促進するための、外部ハンドヘルドトランスデューサの使用である。
【図10】鼻咽頭に毒素を送達するための、バルーンカテーテルの使用である。
【図11】鼻咽頭に毒素を送達するための、バルーンカテーテルの使用である。
【図12A】カテーテル上の自己拡張毒素送達構造体の使用である。
【図12B】カテーテル上の自己拡張毒素送達構造体の使用である。
【図12C】カテーテル上の自己拡張毒素送達構造体の使用である。
【図13】多孔送達バルーンを一部満たすことにより、毒素導入を制限するためのプロトコルである。
【図14】多孔送達バルーンを一部満たすことにより、毒素導入を制限するためのプロトコルである。
【図15】鼻腔に放出される毒素の分布を制御するための、送達バルーンの大きさ設定である。
【図16】嗅球を保護するための、送達バルーンの配置である。
【図17】鼻腔への選択的毒素送達のための、複数の小さなバルーンの使用である。
【図18】副鼻腔および鼻の上から配置された外部マスクを用いた、ソノポレーションである。
【図19】超音波トランスデューサの配置を示す、外部ソノポレーションマスクの正面図である。
【図20】経口的に導入された、閉塞カテーテルおよびエネルギーアプリケータシステムである。
【図21】経口的に導入された、閉塞カテーテルおよびエネルギーアプリケータシステムである。

【図22】鼻腔を閉塞し、穿孔エネルギーを選択的に送達するための、鼻プラグである。
【図23】鼻腔を閉塞し、穿孔エネルギーを選択的に送達するための、鼻プラグである。
【図24】鼻咽頭への毒素の標的送達のための、代替的閉塞カテーテルシステムである。
【図25】鼻咽頭への毒素の標的送達のための、代替的閉塞カテーテルシステムである。
【図26】側孔と、嗅球（ｏｌｅｆａｃｔｏｒｙ　ｂｕｌｂ）を隔離および保護するための遠位閉塞バルーンとを有する毒素送達カテーテルの使用である。
【図27】側孔と、嗅球（ｏｌｅｆａｃｔｏｒｙ　ｂｕｌｂ）を隔離および保護するための遠位閉塞バルーンとを有する毒素送達カテーテルの使用である。
【図28】副鼻腔へ開いた小孔から標的副鼻腔内に毒素をエアロゾル散布するための、成形された遠位端を有する、単純なカテーテルの使用である。
【図29】鼻内噴霧を用いた毒素送達と、フェースマスクを用いたエネルギー送達である。
【図30】副鼻腔へ開いた小孔から標的副鼻腔内に毒素をエアロゾル散布するための、成形された遠位端を有する、単純なカテーテルの使用である。
【図31】別個の注入構造体を標的副鼻腔内に配置するための、成形された遠位端を有するカテーテルの使用である。
【図32】別個の注入構造体を標的副鼻腔内に配置するための、成形された遠位端を有するカテーテルの使用である。
【図33】ハンドルと鼻道内に配置するための二つのアプリケータ先端とを有する、鼻腔に毒素を送達するための、アプリケータデバイスである。
【図34】図３３に示されるアプリケータデバイスの、上面図である。
【図35】鼻道内に配置された時の、図３３に示されるアプリケータデバイスである。
【図36】アプリケータ先端に溶液を注入するための注入チャネルとアクセスポートとを伴って形状が定められた、アプリケータデバイスである。
【図37A】等角図における、アプリケータデバイスのハンドルである。
【図37B】拡張状態の上面図における、アプリケータデバイスのハンドルである。
【図37C】圧縮状態の上面図における、アプリケータデバイスのハンドルである。
【図38】バネ要素を含むアプリケータデバイスである。
【図39A】乾燥した低体積形態におけるアプリケータデバイスの、スポンジアプリケータ先端である。
【図39B】湿った拡張形態におけるアプリケータデバイスの、スポンジアプリケータ先端である。
【図40A】拡張形態における、バネ要素を含むアプリケータ先端である。
【図40B】圧縮形態における、バネ要素を含むアプリケータ先端である。
【図41】ループバネ要素を含む、アプリケータデバイスである。
【図42】係合されたアクチュエータにより圧縮状態に保たれた、ばね式アプリケータ先端である。
【図43】両アプリケータ先端のアクチュエータが係合要素により係合された、アプリケータデバイスである。

【図1】

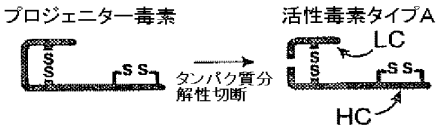


FIG. 1

【図2A】

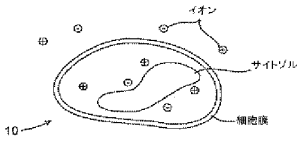


FIG. 2A

【図2B】

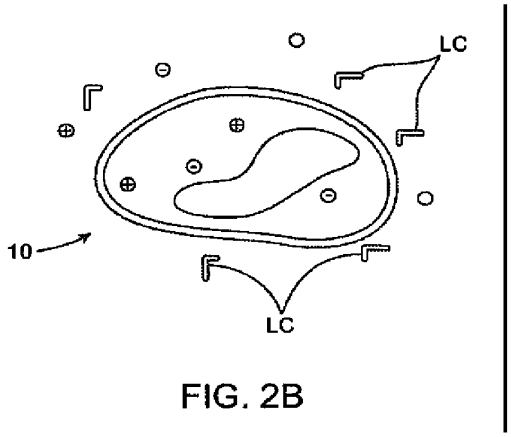


FIG. 2B

【図3A】

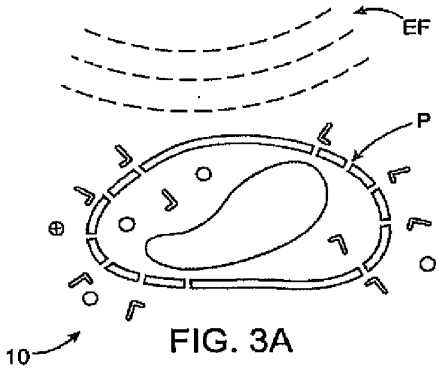


FIG. 3A

【図3B】

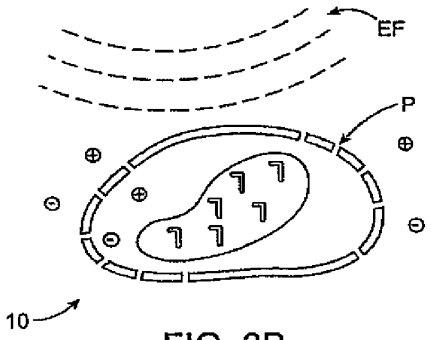


FIG. 3B

【図4】

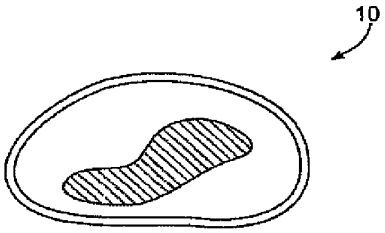


FIG. 4

【図5】

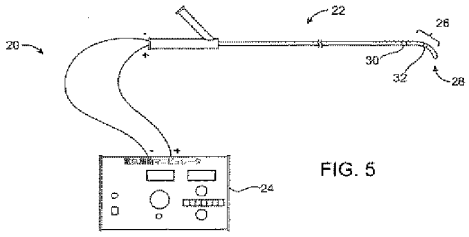


FIG. 5

【図5A】

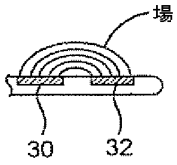


FIG. 5A

【図5B】

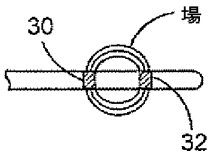


FIG. 5B

【図6A】

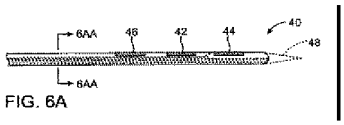


FIG. 6A

【図6AA】

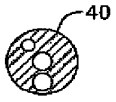


FIG. 6AA

【図6B】

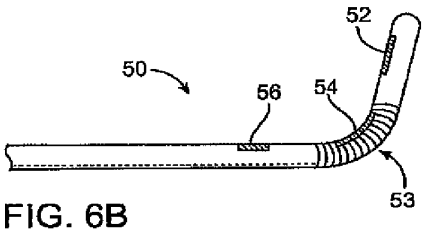


FIG. 6B

【図6C】

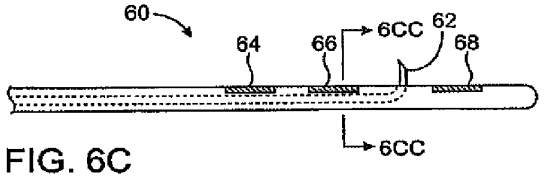


FIG. 6C

【図6CC】

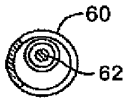


FIG. 6CC

【図6D】

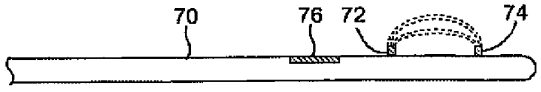


FIG. 6D

【図7】

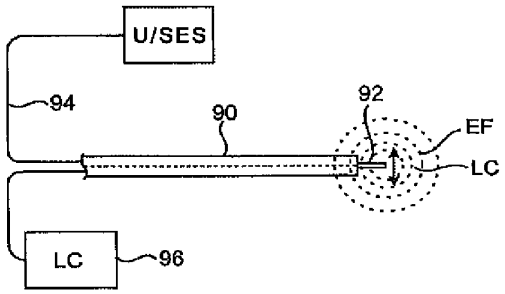


FIG. 7

【図8】

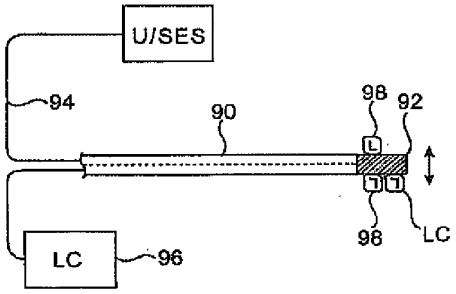


FIG. 8

【図9】

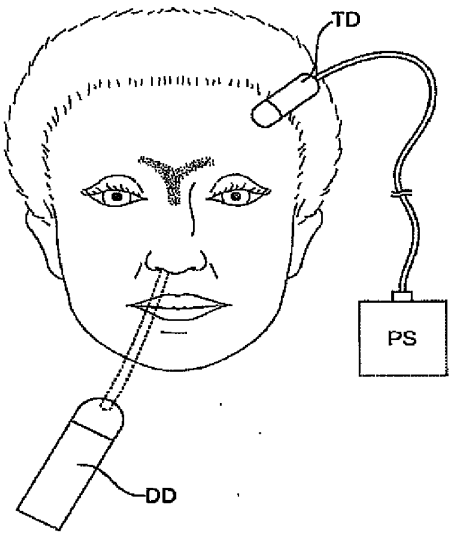


FIG. 9

【図10】

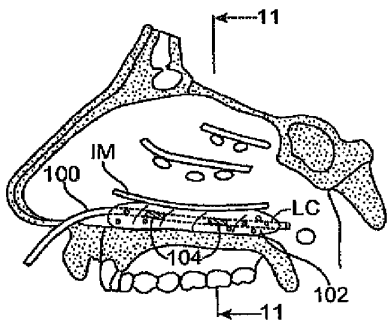


FIG. 10

【図11】

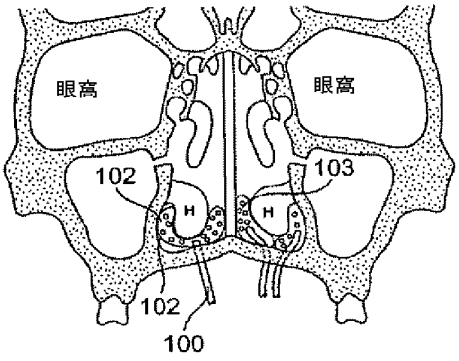


FIG. 11

【図12A】

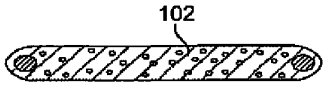


FIG. 12A

【図12B】【図12C】

【図14】

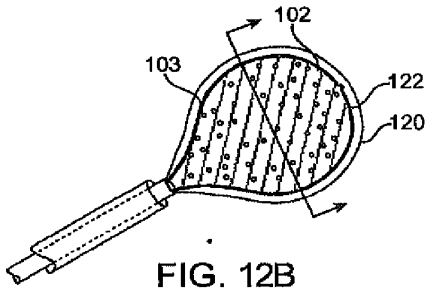


FIG. 12B

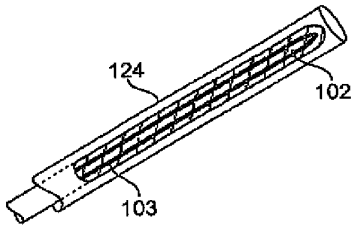


FIG. 12C

【図13】

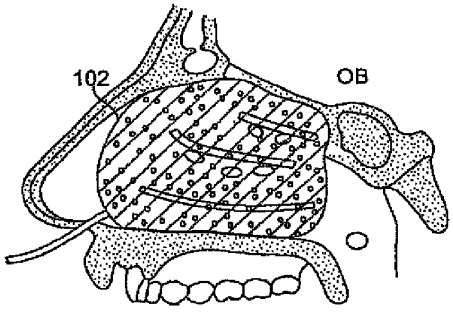


FIG. 13

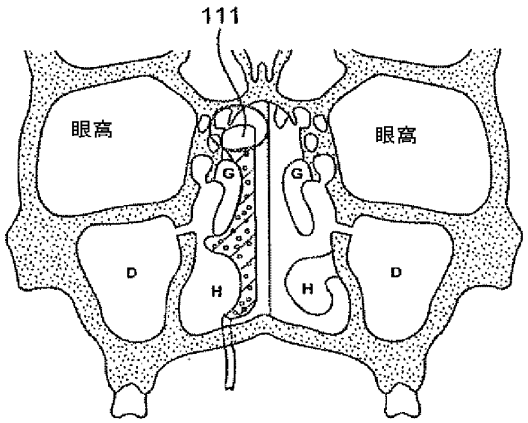


FIG. 14

【図15】

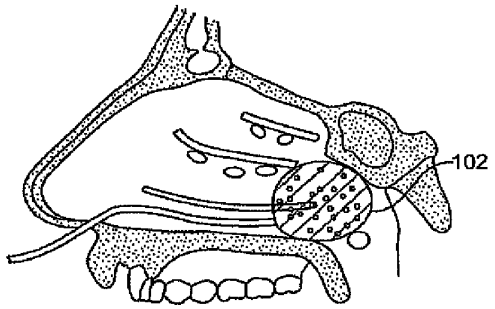


FIG. 15

【図16】

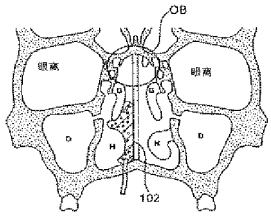


FIG. 16

【図17】

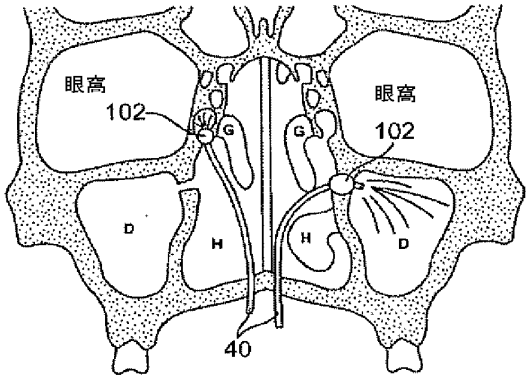


FIG. 17

【図18】

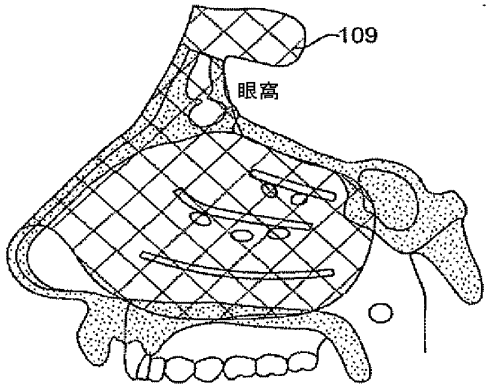


FIG. 18

【図19】

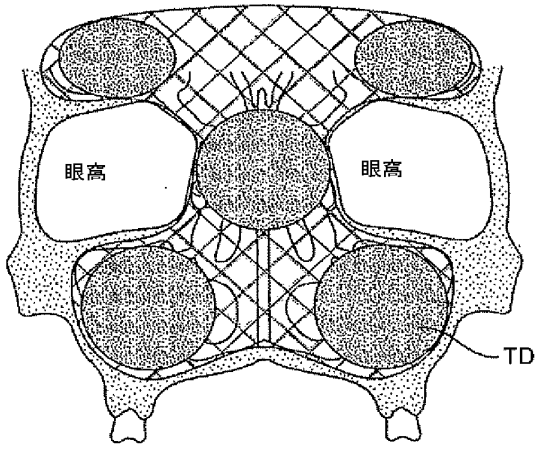


FIG. 19

【図20】

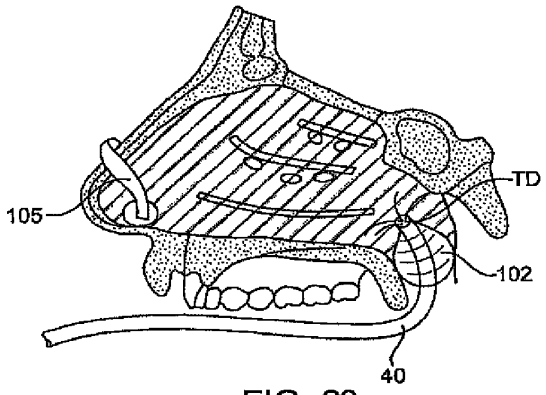


FIG. 20

【図22】

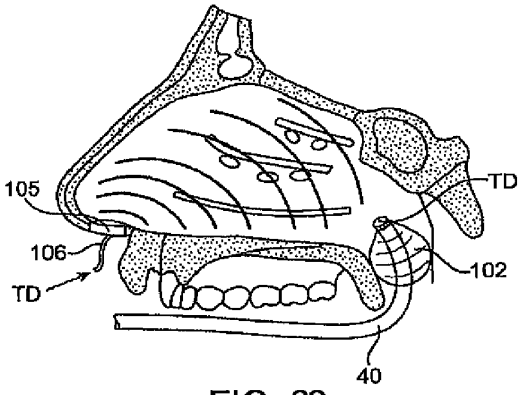


FIG. 22

【図21】

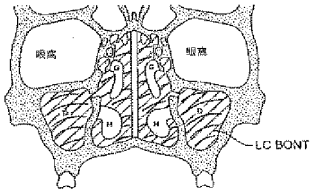


FIG. 21

【図23】

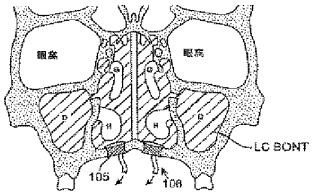


FIG. 23

【図24】

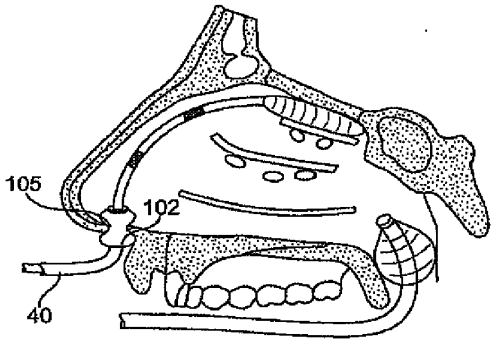


FIG. 24

【図25】

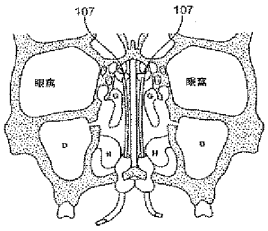


FIG. 25

【図26】

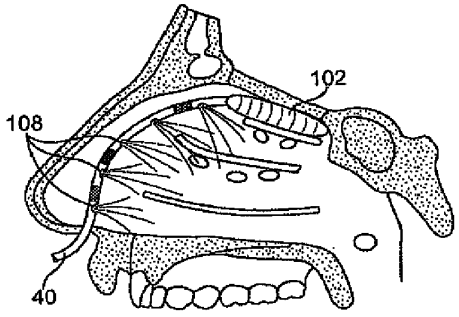


FIG. 26

【図27】

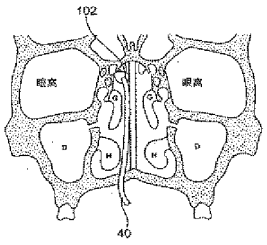


FIG. 27

【図28】

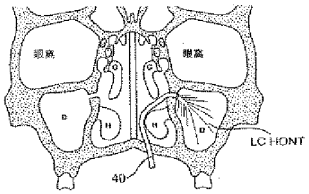


FIG. 28

【図29】

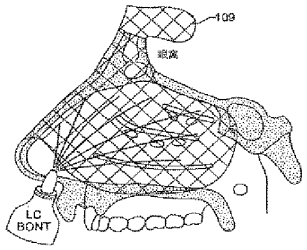


FIG. 29

【図30】

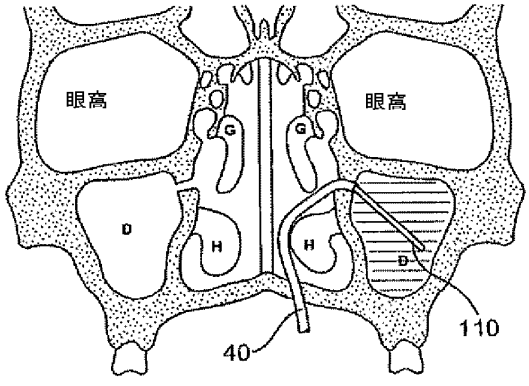


FIG. 30

【図31】

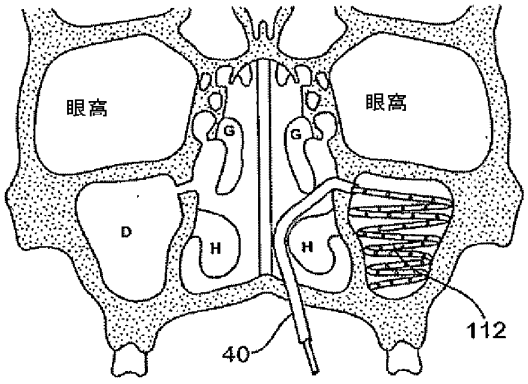


FIG. 31

【図32】

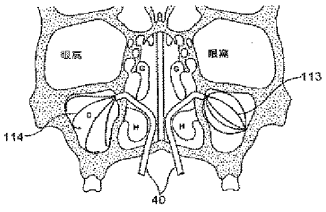


FIG. 32

【図33】

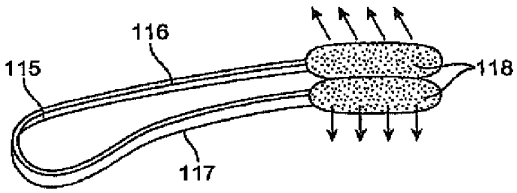


FIG. 33

【図34】

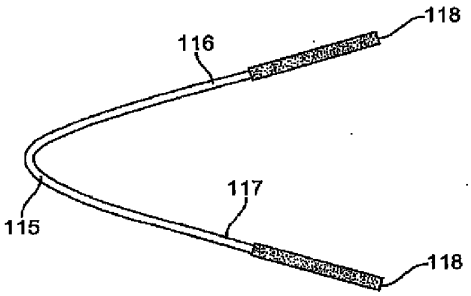


FIG. 34

【図35】

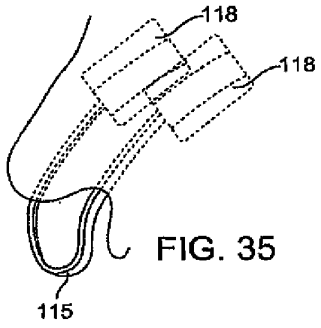


FIG. 35

【図36】

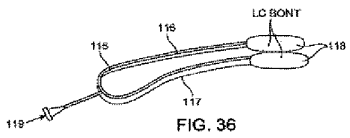


FIG. 36

【図37A】

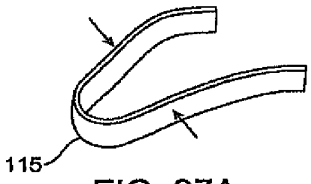


FIG. 37A

【図37B】

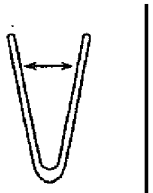


FIG. 37B

【図37C】

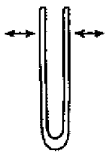


FIG. 37C

【図38】

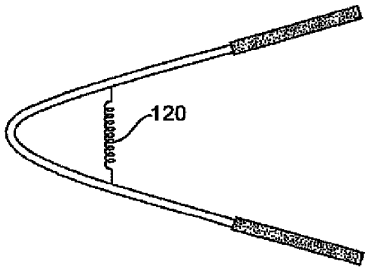


FIG. 38

【図39A】

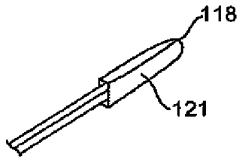


FIG. 39A

【図39B】

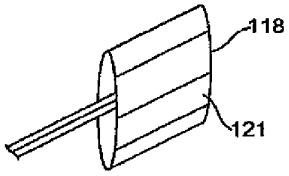


FIG. 39B

【図40A】

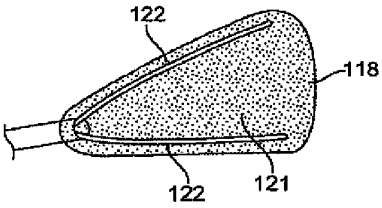


FIG. 40A

【図40B】

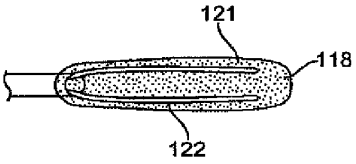


FIG. 40B

【図41】

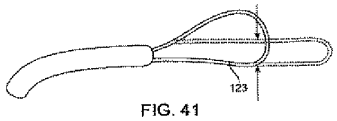


FIG. 41

【図42】

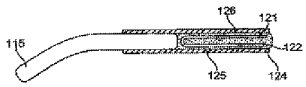


FIG. 42

【図43】

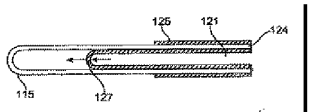


FIG. 43

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/69391

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61K 39/08 (2007.01)
USPC - 424/239.1; 514/8
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) - A61K 39/08 (2007.01)
USPC - 424/239.1; 514/8

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)
PubWEST(USPT,PGPB,EPAB,JPAB); Google Patents; Google Scholar
Search terms: botulinum, toxin, nasal cavity, deliver or administer or administration, rhinorrhea, headache, handle, first, second, spring, actuator, applicator, nostril, electric, ultrasound, x-ray, microwave, electromagnetic, poration, transdermal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2006/0106361 A1 (MUNI et al.) 18 May 2006 (18.05.2006) para [0010], [0014]-[0016], [0075], [0077], [0095], [0102], [0104], [0105], [0107] and [0161]	1-43, 68-78
Y	US 1,695,107 A (KAHL) 11 December 1928 (11.12.1928) col 1, ln 1-4, 22-35 and 49-55; col 2, ln 56-60 and 65-75	1-30, 41-43
Y	US 5,766,605 A (SANDERS et al.) 16 June 1998 (16.06.1998) col 2, ln 34-38 and 45; col 8, ln 29 and 33; col 10, ln 16-18	1-78
Y	US 2005/0152924 A1 (VOET) 14 July 2005 (14.07.2005) para [0013]-[0014], [0043], [0055], [0065] and [0074]	24-30, 52-53, 55-57
Y	US 2004/0009180 A1 (DONOVAN) 15 January 2004 (15.01.2004) para [0081]-[0083]	26-30, 44-78
Y	US 2005/0107853 A1 (KRESPI et al.) 19 May 2005 (19.05.2005) para [0037], [0060], [0108]-[0109] and [0115]	29, 59-67

☐ 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
30 December 2007 (30.12.2007)	03 MAR 2008

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PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/69391

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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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 extra 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 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.:
1-78

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.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2007)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 07/69391

Continuation of Box No. III - Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to from a single general inventive concept under PCT Rule 13.1.

Group I: claims 1-78 are directed to an apparatus for treating inflammation of a nasal membrane of a patient comprising: a handle comprising a proximal section, a first member and a second member, wherein the first member and second member are connected at the proximal section; a first applicator tip coupled to the first member; and a second applicator tip coupled to the second member; wherein the first applicator tip and second applicator tip are each configured for insertion into a nostril of the patient and placement within a nasal passageway of the patient and wherein each applicator tip is configured for delivering a toxin to a region of nasal tissue within the nasal cavity of the patient, thereby treating the inflammation.

Group II: claims 79-112 are directed to a system for delivering toxins to target cells in a nasal membrane, said system comprising: a catheter adapted to introduce a toxin to a region proximate the target cells; an energy applicator configured for applying energy to the target cells under conditions which cause portion of the cell membranes to enhance delivery of the toxin; and a source of toxin suitable for introduction from the catheter.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2 they lack the same or corresponding technical features for the following reasons:

Group II does not include the inventive concept of an applicator of the type as disclosed in claim 1 of Group I.

Group I does not include the inventive concept of an energy applicator configured for applying energy to the target cells as disclosed in Group II.

Neither of these technical features is common to the other group, nor do they correspond to a special technical feature in the other group. Therefore, unity of invention is lacking.

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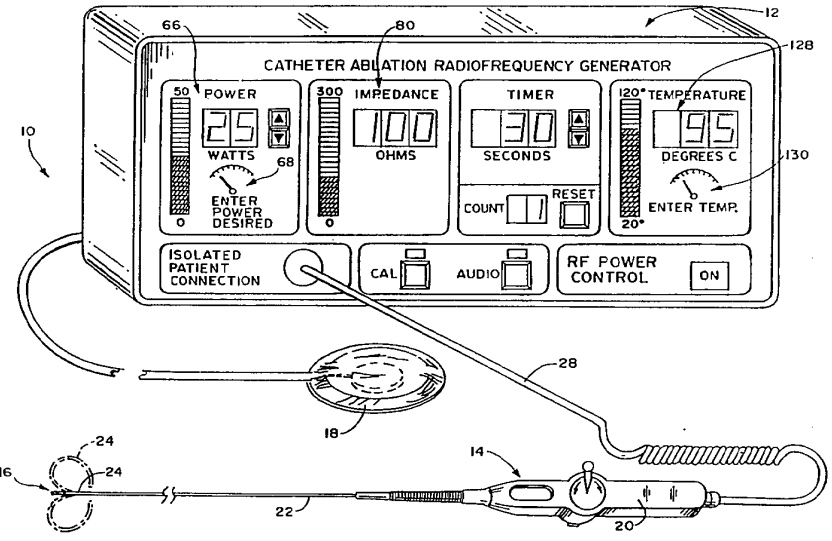
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(57) Abstract

A catheter (14) carries a functional component (16), like an ablating electrode, having a predetermined operating characteristic. The catheter (14) also electronically retains an identification code that uniquely identifies the predetermined characteristic. The catheter (14) is capable of transmitting the identification code to an external reader in response to a predetermined prompt. An associated apparatus, like an ablating energy source (12), reads the identification code and compares it to predetermined operating criteria. The apparatus (12) will not permit interaction with the functional catheter component (16) if the identification code indicates that the functional characteristics of the catheter (14) are not suited for the intended interaction. The catheter (14) can also store usage information to prevent reuse.

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SYSTEMS FOR IDENTIFYING CATHETERS AND MONITORING THEIR USE

Field of the Invention

The invention generally relates to catheters and associated power sources. In a more specific sense, the invention relates to ablation catheters and ablation methods that transmit energy to form lesions for therapeutic purposes.

Background of the Invention

Physicians make use of catheters today in medical procedures to gain access into interior regions of the body to ablate targeted tissue areas. It is important for the physician to control carefully and precisely the emission of energy within the body used to ablate the tissue.

The need for careful and precise control over the catheter is especially critical during procedures that ablate tissue within the heart. These procedures, called electrophysiological therapy, are becoming more widespread for treating cardiac rhythm disturbances.

During these procedures, a physician steers a catheter through a main vein or artery (which is typically the femoral vein or artery) into the interior region of the heart that is to be treated.

The physician then further manipulates a steering mechanism to place the electrode carried on the distal tip of the catheter into direct contact with the tissue that is to be ablated. The physician directs radio frequency energy from the electrode tip through tissue to an indifferent electrode to ablate the tissue and form a lesion.

Cardiac ablation especially requires the ability to precisely monitor and control the emission of energy from the ablation electrode.

Summary of the Invention

The invention provides systems and apparatus for identifying catheters and monitoring their use.

One aspect of the invention provides a catheter including a body carrying a functional component, like an ablating electrode, having a predetermined operating characteristic. The body also carries electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component. The electronic retaining means includes an output for transmitting the identification code to an external reader in response to a predetermined prompt.

Another aspect of the invention provides a catheter with a functional component, like an ablating electrode. In this aspect of the invention, the body also carries electronic means for retaining a code that represents the usage of the functional component. The electronic retaining means includes an output for generating the usage code in response to a predetermined prompt and an input for updating the usage code in response to use of the functional component.

Another aspect of the invention provides an apparatus for interacting with the functional component of the catheter. The apparatus includes a mechanism that prompts the electronic retaining means of the catheter to generate its identification code. The apparatus also stores predetermined criteria governing its interaction with the catheter. The apparatus compares the generated identification code to the predetermined interaction criteria. The apparatus generates a first control signal when the generated identification code meets the predetermined interaction criteria. The apparatus generates a second control signal, different than the first control signal, when the generated identification code does not meet the predetermined interaction criteria.

In one embodiment, the apparatus will not permit the intended interaction with the functional catheter component, if the identification code indicates that the catheter has been used too many times or if the functional characteristics of the catheter are not suited for the intended interaction.

In a preferred embodiment, the functional catheter component is an ablating electrode, and the apparatus is a source of ablating energy. In this embodiment, the apparatus sets the operating ablating power conditions depending upon the particular functional characteristics of the associated ablating electrode. In this way, the apparatus distinguishes among ablating electrodes of different functional characteristics and supplies ablating power accordingly.

The invention may be embodied in several forms without departing from its spirit or essential

characteristics. The scope of the invention is defined in the appended claims, rather than in the specific description preceding them. All embodiments that fall within the meaning and range of equivalency of the claims are therefore intended to be embraced by the claims.

Brief Description of the Drawings

Fig. 1 is a perspective view of a system for ablating tissue that embodies the features of the invention;

Fig. 2 is a schematic view of the generator and associated monitor and control circuits for the system;

Fig. 3 is a schematic view of the power monitor and control circuit for the system;

Fig. 4 is a schematic view of a catheter identification circuit that enables or prevents use of the catheter based upon functional and performance criteria; and

Fig. 5 is a schematic view of a catheter identification circuit that enables or prevents use of the catheter based upon prior use criteria.

Description of the Preferred Embodiments

Fig. 1 shows a system 10 for performing ablation on human tissue that embodies the features of the invention. The system 10 includes a radiofrequency generator 12 that delivers radiofrequency energy. The system 10 also includes a steerable catheter 14 carrying a radiofrequency emitting tip electrode 16.

In the illustrated embodiment, the system 10 operates in a monopolar mode. In this arrangement, the system 10 includes a skin patch electrode that serves as an indifferent second electrode 18. In use, the indifferent electrode 18

attaches to the patient's back or other exterior skin area.

Alternatively, the system 10 can be operated in a bipolar mode. In this mode, the catheter 14 carries both electrodes.

In the illustrated embodiment, the ablation electrode 16 and indifferent electrodes 18 are made of platinum.

The system 10 can be used in many different environments. This specification describes the system 10 when used to provide cardiac ablation therapy.

When used for this purpose, a physician steers the catheter 14 through a main vein or artery (typically the femoral vein or artery) into the interior region of the heart that is to be treated. The physician then further manipulates the catheter 14 to place the tip electrode 16 into contact with the tissue within the heart that is targeted for ablation. The user directs radio frequency energy from the generator 12 into the tip electrode 16 to form a lesion on the contacted tissue.

In the embodiment shown in Fig.1, the catheter 14 includes a handle 20, a guide tube 22, and a tip 24, which carries the tip electrode 16 (which also will be called the ablation electrode). The handle 20 encloses a steering mechanism 26 for the catheter tip 24. A cable 28 extending from the rear of the handle 20 has plugs (not shown). The plugs connect the catheter 14 to the generator 12 for conveying radiofrequency energy to the ablation electrode 16. The radiofrequency energy heats the tissue to form the lesion.

Left and right steering wires (not shown) extend through the guide tube 22 to interconnect the

steering mechanism 26 to the left and right sides of the tip 24. Rotating the steering mechanism 26 to the left pulls on the left steering wire, causing the tip 24 to bend to the left. Also, rotating the steering mechanism 26 to the right pulls on the right steering wire, causing the tip 24 to bend to the right. In this way, the physician steers the ablation electrode 16 into contact with the tissue to be ablated.

The generator 12 includes a radiofrequency power source 30 connected through a main isolation transformer 32 to first and second conducting lines 34 and 36.

In the illustrated environment, the power source 30 delivers up to 50 watts of power at a frequency of 500 kHz. The first conducting line 34 leads to the ablation electrode 16. The second conducting line 36 leads to the indifferent patch electrode 18.

As Figs. 2 and 3 show, the system 10 includes first monitoring means 38 for measuring the radiofrequency current and radiofrequency voltage delivered by the generator 12 to the patient. The first monitoring means 38 also derives control signals indicative of RMS (root mean squared) voltage (in volts), RMS current (in amps), and actual phase sensitive power (in watts) to support other control functions of the generator 12.

The first monitoring means 38 may be variously configured and constructed. In the illustrated embodiment, the first monitoring means 38 includes current monitoring means 40 for measuring the radiofrequency current passing from the first line 34 through the tissue to the second line 36 (i.e., from the ablation electrode 16 to the indif-

ferent patch electrode 18).

The first monitoring means 38 also includes voltage monitoring means 42. The voltage monitoring means 42 measures the radiofrequency voltage generated between the first and second conducting lines 34 and 36 (i.e., between the ablation electrode 16 and the indifferent patch electrode 18).

The first monitoring means 38 includes three control outputs 44, 46, and 48.

The first control output 44 carries a signal representative of RMS current conducted by the ablation electrode 16.

The second control output 46 carries a signal representative of the RMS voltage between the ablation electrode 16 and the indifferent patch electrode 18.

The third control output 48 carries a signal representative of actual phase sensitive power transmitted by the ablation electrode 16.

In the illustrated embodiment (as Figs. 2 and 3 show), the current monitoring means 40 includes an isolated current sensing transformer 50 connected in the second conducting line 36. In this arrangement, the current sensing transformer 50 directly measures the radiofrequency current passing through the ablation electrode 16 to the indifferent patch electrode 18.

The measured value is a radiofrequency signal varying at the selected rate, which in the illustrated embodiment is 500 kHz.

The current sensing transformer 50 is connected to the first control output 44, which derives RMS current. The first control output 44 includes an integrated circuit RMS converter 52 to do this

function. The RMS current converter first squares the radiofrequency current input signal from the current sensing transformer 50, and then averages the squared signal over a user prescribed period (which in the illustrated embodiment is about once every 0.01 second). The RMS current converter 52 then takes the square root of the average squared value. The resulting output represents RMS current.

The RMS current signal takes the form of a relatively slowly varying signal, compared with the rapidly varying radiofrequency current input signal.

As Figs. 2 and 3 show, the voltage monitoring means 42 includes an isolated voltage sensing transformer 54 that is connected between the first and second conducting lines. In this arrangement, the voltage sensing transformer 54 directly measures the radiofrequency voltage across the body tissue between the ablation electrode 16 and the indifferent patch electrode 18.

Like the value measured by the current sensing transformer 50, the measured voltage value is a radiofrequency signal varying at the selected 500 kHz rate.

The voltage sensing transformer 54 is connected to the second control output 46, which derives RMS voltage. The second control output 46 includes an integrated circuit RMS converter 56 to do this function. The RMS voltage converter 56 squares the radiofrequency voltage input signal and then averages it over the same user prescribed period used by the current converter 52. The RMS voltage converter 56 then takes the square root of the average squared voltage value.

The resulting RMS voltage signal (like the RMS current signal) takes the form of a relatively

slowly varying signal.

The voltage sensing transformer 54 is also connected to the third control output 48, which derives actual phase sensitive power. The third control output 48 includes an analog multiplier integrated circuit 58 to do this function. The multiplier circuit 58 receives as one input the radiofrequency input current signal directly from the current sensing transformer 50. The multiplier circuit 58 also receives as a second input the radiofrequency input voltage signal directly from the voltage sensing transformer 54.

The output of the multiplier circuit 58 is the product of these two inputs, which represents the actual radiofrequency power transmitted by the ablation electrode 16.

The power value is (like its component current and voltage inputs) a radiofrequency signal varying at a relatively high radiofrequency rate.

The third control output 48 also includes a low pass filter 60. In the illustrated embodiment, which operates with a radiofrequency rate of 500 kHz, the cut off frequency of the filter 60 selected is about 100 Hz. The rapidly varying measured input power value is low pass filtered by the filter 60 into a relatively slowly varying signal.

This signal represents the actual phase sensitive power signal of the radiofrequency energy that the ablation electrode 16 delivers to the targeted tissue.

The first, second, and third control outputs 44, 46, and 48 each includes appropriate inline scaling circuits 62. The scaling circuits 62 scale the RMS current signal, the RMS voltage signal, and

the actual phase sensitive power signal to a specified voltage range that can be usable by the remainder of generator 12 circuitry. In the illustrated embodiment, the scaled range is 0.0 to 5.0 volts.

The first monitoring means 38 also includes an analog to digital converter 64. The converter 64 digitizes a selected one or more of the analog RMS current output signal, RMS voltage output signal, and the actual phase sensitive power signal.

The digital output(s) of the converter 64 can be used to display measurement results. In the illustrated embodiment, the system 10 includes a first digital display 66 on the generator 12 to show the user the actual phase sensitive power signal.

The digital output(s) of the converter 64 also can be used to control operation of the generator 12. In the illustrated embodiment, the system 10 uses the digitized outputs in a feedback loop that maintains radiofrequency output voltage within a desired range or at a constant value to control radiofrequency power at the ablation electrode 16. By controlling the power delivered by the generator 12, the physician can reproducibly form lesions of the desired depth during an ablation procedure.

In this arrangement, the system 10 includes an input 68 for the user to enter an operating value desired for the actual phase sensitive power for the generator 12. The system 10 includes power control means 70 that includes comparator 71 to compare desired power with actual phase sensitive power. The output of the comparator varies the output voltage of radiofrequency power source 30 to maintain minimum error between the measured actual power and

the set point power.

In the illustrated embodiment, the power control means 70 also monitors phase differences between radiofrequency voltage and current. The power control means 70 does this function by computing apparent power and by comparing the computed apparent power to the actual phase sensitive power. If the radiofrequency voltage and current signals are exactly in phase, the apparent power and actual phase sensitive power will be the same. However, if there is a phase difference, actual phase sensitive power will differ from the apparent power by a factor that represents the cosine of the phase angle.

In the illustrated embodiment, the power control means 70 includes a multiplier circuit 72 that obtains the product of the RMS current and RMS voltage. The resulting output of the multiplier circuit 72 forms the apparent (i.e., not phase sensitive) power of the system 10. The power control means 70 includes a comparator 74 to compare the derived apparent power with the actual phase sensitive power. The magnitude of the output of the comparator 74 quantifies the amount of the phase shift.

If the output of the phase shift comparator 74 exceeds a preselected amount, the power control means 70 generates a warning signal to show that a phase shift between the radiofrequency voltage and current has occurred. The system 10 may include a flashing light and audible alarm (not shown) to warn the user.

The power control means 70 operates to maintain a constant set power when the output of the phase shift comparator 74 remains within an allowable range above the threshold amount. The power

control means 70 operates to reduce the output voltage of the source 30 when the output of the phase shift comparator 74 increases beyond this range. If the output of the phase shift comparator 74 shows a phase shift beyond a maximum threshold value, the power control means 70 generates a signal to shut off all power to the ablation electrode 16.

According to the invention, the system 10 also includes means 76 for identifying and monitoring the physical and/or functional characteristics of the catheter 14 that is connected to the radiofrequency generator 12.

The resulting control functions of the catheter identification means 76 can vary.

In one preferred arrangement (shown in Fig. 4), the identification means 76 assures that the catheter 14 and its intended use meet predetermined functional and therapeutic criteria.

In this embodiment, the identification means 76 senses the actual functional characteristics of the catheter 14 connected to the generator 12. The identification means compares these actual characteristics to the characteristics required for the intended use, based upon predetermined criteria. Based upon this comparison, the identification means 76 generates a variety of output control signals.

The control signals either actively control or passively monitor the operational characteristics of catheter 14 used in association with the power generator 12. The system 10 thereby guards against the use of a catheter 14 that does not meet the performance characteristics required.

More particularly, when the sensed physical and/or functional characteristics of the catheter 14 meet the predetermined use criteria, the output

control signal generated by the identification means 76 actively permits the intended use of the catheter 14. Alternatively, the output control signal generates a passive, user discernible "Use Permitted" message under this condition. Still alternatively, the output control signal can simultaneously permit use while generating a confirming, user discernible message.

Likewise, when the sensed physical and/or functional characteristics of the catheter 14 do not meet the predetermined use criteria, the output control signal generated by the identification means 76 actively intervenes to prevent the intended use of the catheter 14. Alternatively, the output control signal generates a passive, user discernible "Use Not Permitted" alarm under this condition. Still alternatively, the output control signal can simultaneously prevent use while generating a confirming, user discernible alarm.

In another preferred arrangement (shown in Fig. 5), the identification means 76 generates signals that track the use of the catheter 12. This aspect of the invention guards against the reuse or overuse of a given catheter 14.

The particular details of these arrangements will now be discussed.

Controlling/Monitoring the Catheter-Generator Interface

In Fig. 4, the identification means 76 senses the actual physical and/or functional characteristics of the attached catheter 14 and compares these to predetermined criteria.

As shown in Fig. 4, the identification means 76 includes means 88 carried within the

catheter handle 20 for automatically generating a uniquely coded identification signal 90 when the catheter 14 is attached to the system 10. The signal 90 is coded to uniquely identify the particular performance and/or physical characteristics of the catheter 14 and attached electrode 16.

The selected catheter characteristics identified by the code can vary. They may include electrode surface area, electrode configuration, electrode orientation, and electrode field dispersion properties. They also indicate the presence of a temperature sensor or thermistor and its associated resistance calibration value. They may simply identify catheter product numbers or other commercial designations.

The catheter identification means 88 carried within the handle can vary.

In one embodiment, the catheter identification means 88 can comprise a resistor having a prescribed ohm value, which varies according to the physical and/or performance characteristics of the catheter 14. The sensed ohm value then becomes the identification code for the catheter.

In an alternative and preferred embodiment, instead of the resistor, the catheter identification means 88 can comprise a solid state micro-chip, ROM, EEROM, EPROM, or non-volatile RAM carried within the handle 20. The micro-chip can be pre-programmed with a digital value representing the catheter identification code and other information. In this way, the catheter itself can be programmed to store information about its operational and functional characteristics.

The identification means 76 includes a register means 92 that latches the sensed catheter

identification code when the catheter 14 is attached to the generator 12.

The identification means 76 also includes a catheter criteria look-up table 86 in system ROM. The table 86 specifies the catheter types that are approved for use in association with the system 10, as well as those catheter types that are not approved for use. The selection criteria takes into account the performance and/or physical characteristics necessary for safe and efficacious therapeutic use, based upon empirical testing, governmental regulatory approval, and similar relevant considerations.

The approved catheter types in the look-up table 86 are coded to correspond with the identification codes the catheter 14 carries.

Preferably, the codes in the look up table 86 further classify the physical and/or performance characteristics of different catheters 14 at different set power conditions, as determined by empirical testing.

In this arrangement, the table 86 permits the identification means 76 to distinguish between acceptable and unacceptable catheter types on an interactive basis, taking into account the particular power condition set for the generator 12.

When the identification means 76 takes into account the selected power output of the generator 12, one catheter code may be acceptable for use at low selected power outputs, whereas the same catheter code may not be acceptable at selected higher power outputs.

The identification means 76 also includes a comparator 96. The comparator 96 looks to the input 68 to determine the set power condition and

compares the sensed catheter type (latched in the register means 92) with the catheter types listed in the catheter criteria table 86.

When the sensed physical and/or functional characteristics of the catheter 14 and the predetermined criteria at the set power condition match, the comparator 96 generates a first control signal 78. When the sensed physical and/or functional characteristics of the catheter 14 and the predetermined criteria at the set power condition do not match, the comparator 96 generates a second control signal 80.

The first control signal 78 enables the physician to operate the system 10 with the catheter 14 selected and at the set power condition. In addition, the first control signal 78 preferably generates a confirming, user discernible "Use Permitted" message 79.

The second control signal 80 disables or at least discourages operation of the system 10 at the set power condition. The particular operative effect of second control signal 80 can vary.

In a preferred embodiment, the second control signal 80 activates an interlock 82 that disables the power generator 12. The interlock 82 prevents operation of the system 10, thereby preventing the intended use of the catheter 14.

Alternatively, the second control signal 80 generates a user discernible "Use Not Permitted" alarm message 84 under this condition. Most preferably, the second control signal 80 simultaneously activates the interlock 82 while generating a confirming, user discernible alarm 84.

The identification means 76 also preferably serves as an information source for the physician.

In this mode, the identification means 76 includes a look-up table 87 that correlates the catheter identification codes with a user readable message that contains useful physical and performance information about the selected catheter 14. The message can list the manufacturer of the catheter, the surface area and other relevant characteristics of the ablating electrode, including the presence or absence of temperature sensing elements. The message can also list the set power conditions approved or recommended for the catheter.

In this embodiment, the identification means 76 includes a second comparator 97. The comparator reads the code latched in the register means 92 looks to the table 87 to obtain the corresponding message. The comparator 97 outputs the message to a display device 99 for the physician to read.

Monitoring Catheter Use

As Fig. 5 shows, the identification means 76 can also serve to monitor the use of the catheter 14.

In this preferred embodiment, the identification means 76 includes a use register 98 carried within the catheter handle 20. The use register 98 latches a digital value representing the number of times the catheter 14 has been used.

Preferably, the use register 98 comprises a solid state micro-chip having non-volatile RAM carried within the catheter handle 20.

The use register 98 is initially programmed by the manufacturer with a digital value of zero. The use register 98 includes an output 100 for generating this digital value. The use register 98 also includes an input 102 for incrementing the

digital value after each use.

The identification means 76 includes means 104 for incrementing by one the digital value carried by the use register 98 after each permitted use of the catheter 14.

The identification means 76 also includes means 106 for determining the digital value resident within the use register 98 before allowing use of the catheter 14 with the generator 12.

In this arrangement, the identification means 76 includes a comparator 108 that compares the resident digital value with a set value in a use criteria table 110, which represents the maximum number of uses allowed.

If the resident value is less than the set value, the comparator generates a signal 114 that permits continued use of the catheter 14 with the power generator 12.

If the resident value equals or exceeds the set value, the comparator 108 generates a signal 116 to activate the previously described power interlock 82. The interlock 82 prevents use of the catheter 14 with the generator 12.

Alternatively, the comparator 108 simply activates a display 112 to warn the physician, counseling against reuse of the chosen catheter 14. Of course, the identification means can both activate the interlock 82 and the display 112.

Various features of the invention are set forth in the following claims.

Claims

We Claim:

1. A catheter including a body carrying a functional component having a predetermined operating characteristic, the body also carrying electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component, the electronic retaining means including output means for transmitting the identification code to an external reader in response to a predetermined prompt.

2. A catheter according to claim 1 wherein the functional component includes an energy emitting electrode.

3. A catheter according to claim 1 wherein the body comprises a handle having an interior area, and wherein the electronic retaining means is carried within the interior area of the handle.

4. A catheter according to claim 3 wherein the functional component includes a guide body that carries an energy emitting electrode.

5. A catheter according to claim 1 wherein the electronic retaining means comprises a component having a predetermined resistance value that comprises the identification code.

6. A catheter according to claim 1 wherein the electronic retaining means includes a microchip holding the identification code as a digital value.

7. A catheter according to claim 1 wherein the electronic retaining means comprises non-volatile RAM.

8. A catheter according to claim 6 wherein the electronic retaining means comprises ROM.

9. A catheter according to claim 6 wherein the electronic retaining means comprises EPROM.

10. A system comprising

a catheter carrying a functional component having a predetermined operating characteristic, the catheter also carrying means for electronically retaining an identification code that uniquely identifies the predetermined operating characteristic of the functional component, the electronic retaining means including output means for generating the identification code in response to a predetermined prompt, and

apparatus means for interacting with the functional component of the catheter including

means for coupling the catheter to the device for interaction,

means operative, when coupled to the catheter, for prompting the electronic retaining means to generate the identification code,

means for registering the generated identification code,

means for storing predetermined criteria governing the interaction between the catheter and the apparatus means, and

means connected to the register means and the storage means for comparing the generated identification code to the predetermined interaction criteria and for generating a first control signal when the generated identification code meets the predetermined interaction criteria and for generating a second control signal, different than

the first control signal, when the generated identification code does not meet the predetermined interaction criteria.

11. A system according to claim 10 wherein the apparatus means includes control means for operating in a first interaction mode with the attached catheter in response to the first control signal and for operating in a second interaction mode with the attached catheter, different than the first interaction mode, in response to the second control signal.

12. A system according to claim 10 wherein the apparatus means includes interlock means for permitting interaction with the attached catheter in response to the first control signal and for preventing interaction with the attached catheter in response to the second control signal.

13. A system according to claim 10 wherein the apparatus means includes means for generating a first user discernible signal in response to the first control signal and for generating a second user discernible signal, different than the first user discernible signal, in response to the second control signal.

14. A catheter including a body carrying a functional component having a predetermined operating characteristic, the body also carrying electronic means for retaining a code that represents the usage of the functional component, the electronic retaining means including output means for generating the usage code response to a predetermined prompt and input means for updating the usage code in response to use of the functional component.

15. A catheter according to claim 14 wherein the functional component includes an energy emitting electrode.

16. A catheter according to claim 14 wherein the body comprises a handle having an interior area, and wherein the electronic retaining means is carried within the interior area of the handle.

17. A catheter according to claim 16 wherein the functional component includes a guide body that carries an energy emitting electrode.

18. A system comprising

a catheter carrying a functional component having a predetermined operating characteristic, the catheter also carrying means for electronically retaining a code representing the number of times the functional component has been used, the electronic retaining means including output means for generating the usage code in response to a predetermined prompt and input means for updating the usage code, and

apparatus means for interacting with the functional component of the catheter including

means for coupling the catheter to the device for interaction,

means operative, when coupled to the catheter, for prompting the electronic retaining means to generate the usage code,

means for registering the generated usage code,

means for storing a predetermined value representing the maximum number of times the functional component can be used, and

means connected to the register means

and the storage means for comparing the generated usage code to the predetermined usage value and for generating a first control signal when the generated usage code is less than the predetermined usage value and for generating a second control signal, different than the first control signal, when the generated usage code is equal to or exceeds the predetermined usage value.

19. A system according to claim 18 wherein the apparatus means includes control means for permitting operation in interaction with the attached catheter in response to the first control signal and for preventing the operation in interaction mode with the attached catheter in response to the second control signal.

20. A system according to claim 18 wherein the apparatus means includes means for generating a first user discernible signal in response to the first control signal and for generating a second user discernible signal, different than the first user discernible signal, in response to the second control signal.

21. A system according to claim 18 wherein the apparatus means include means for generating a signal to the input means of the electronic retaining means for updating the usage code after operation in interaction with the attached catheter.

22. A system comprising

a first catheter carrying a functional component having a first predetermined operating characteristic, the first catheter also carrying means for electronically retaining a first identification code that uniquely identifies the first predetermined operating characteristic of the

functional component, the storage means including output means for generating the first identification code in response to a predetermined prompt,

a second catheter carrying a functional component having a second predetermined operating characteristic different than the first predetermined operating characteristic, the second catheter also carrying means for electronically retaining a second identification code, different than the first identification code, that uniquely identifies the second predetermined operating characteristic of the functional component, the storage means including output means for generating the second identification code in response to a predetermined prompt, and

apparatus means for interacting with the functional component of either the first catheter or the second catheter including

means for coupling either the first or second catheter for interaction,

means for providing the predetermined prompt to generate the first or second identification code from the electronic retaining means of the attached catheter,

means for generating a first control signal when the first identification code is received and for generating a second control signal, different than the first control signal, when the second identification signal is received.

23. A tissue ablation catheter including a body carrying an ablating electrode having a predetermined operating characteristic, the body also carrying electronic means for retaining an identification code that uniquely identifies the predetermined operating characteristic of the

ablating electrode, the electronic retaining means including output means for transmitting the identification code to an external reader in response to a predetermined prompt.

24. A tissue ablation catheter including a body carrying an ablating electrode having a predetermined operating characteristic, the body also carrying electronic means for retaining a code that identifies the number of times the ablating electrode has been used, the electronic retaining means including output means for transmitting the usage code to an external reader in response to a predetermined prompt and input means for updating the usage code in response to use.

25. Apparatus for supplying energy to a tissue ablation electrode comprising

generating means for producing ablating energy for the electrode in a first power mode and in a second power mode different than the first power mode,

means for connecting an electrode to the generating means,

means for registering a first control condition when an ablating electrode having a first characteristic is connected to the generating means and for registering a second control condition when an ablating electrode having a second characteristic, different than the first characteristic, is connected to the generator means, and

control means responsive to the register means for operating the generating means in the first power mode when the first control condition is registered and for operating the generating means in the second power mode when the second control condition is registered.

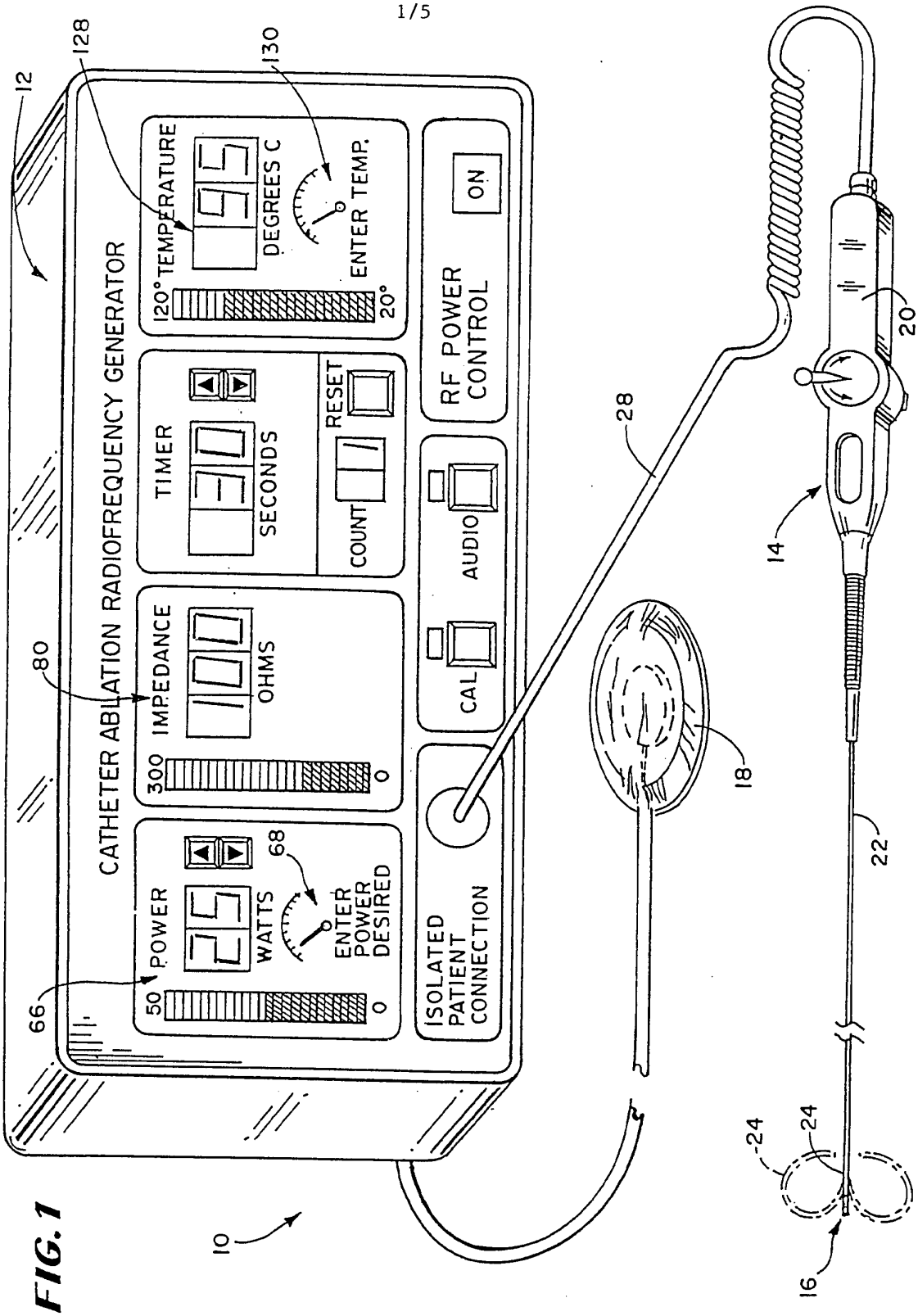


FIG. 1

SUBSTITUTE SHEET

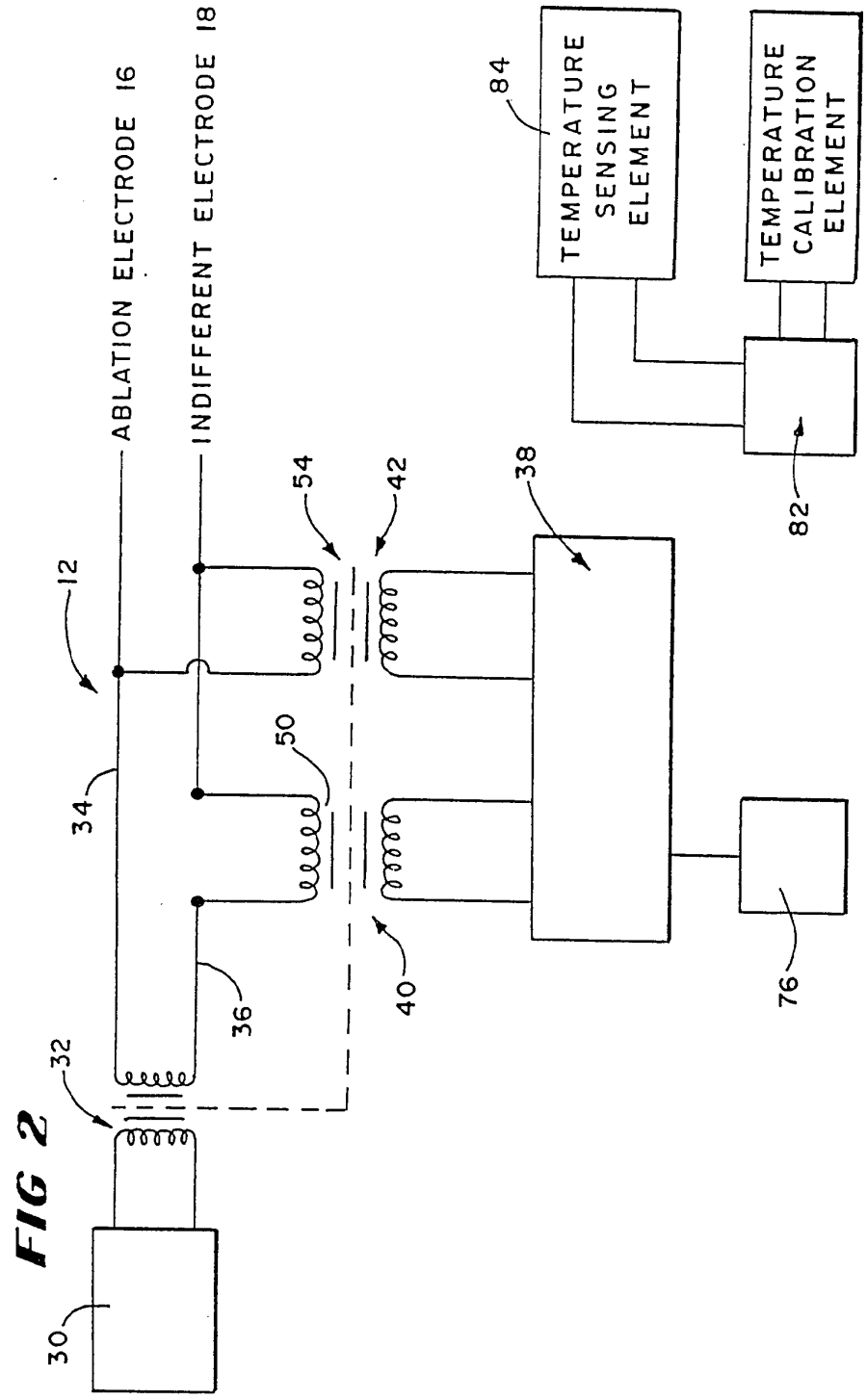


FIG 2

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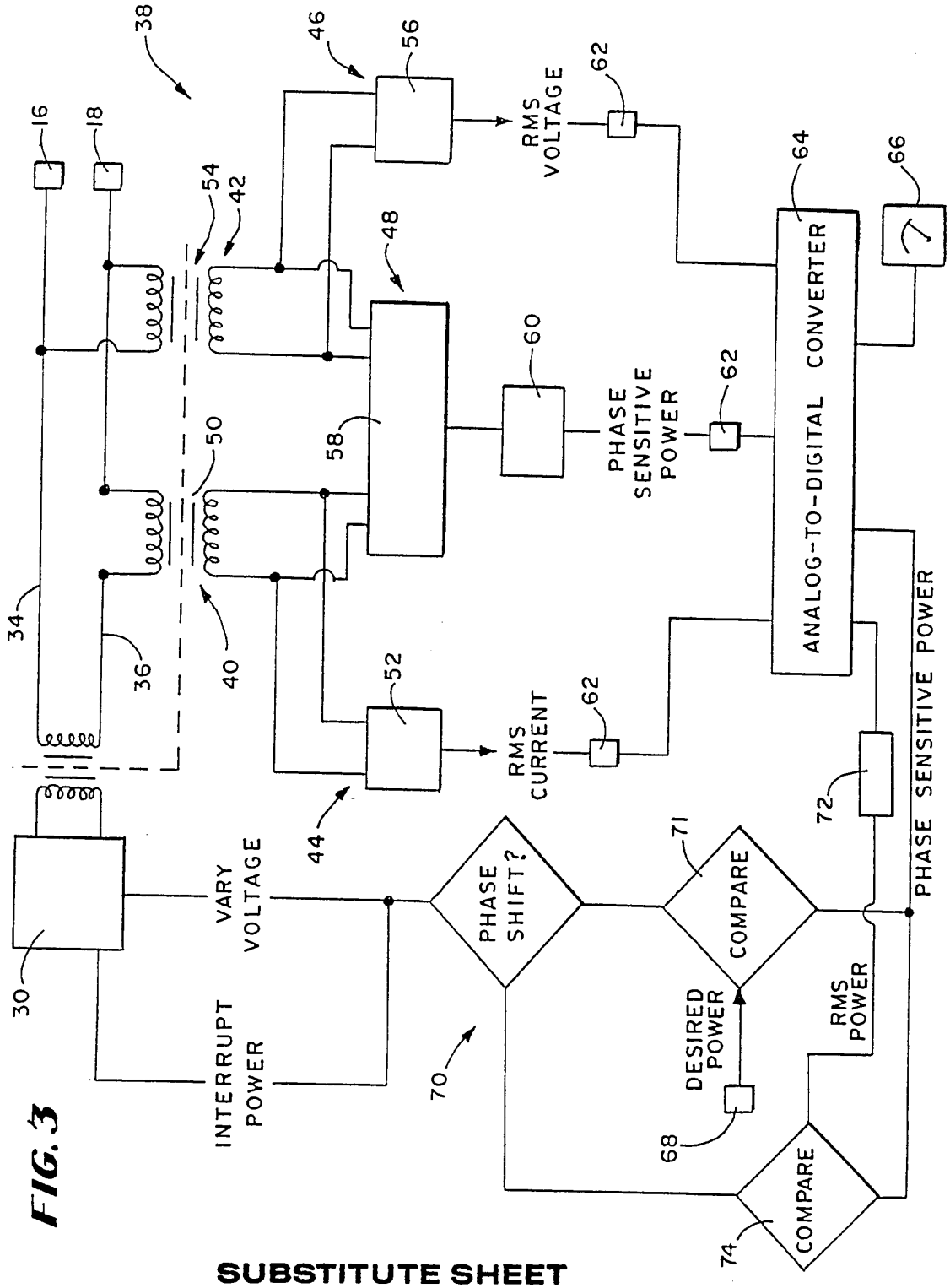
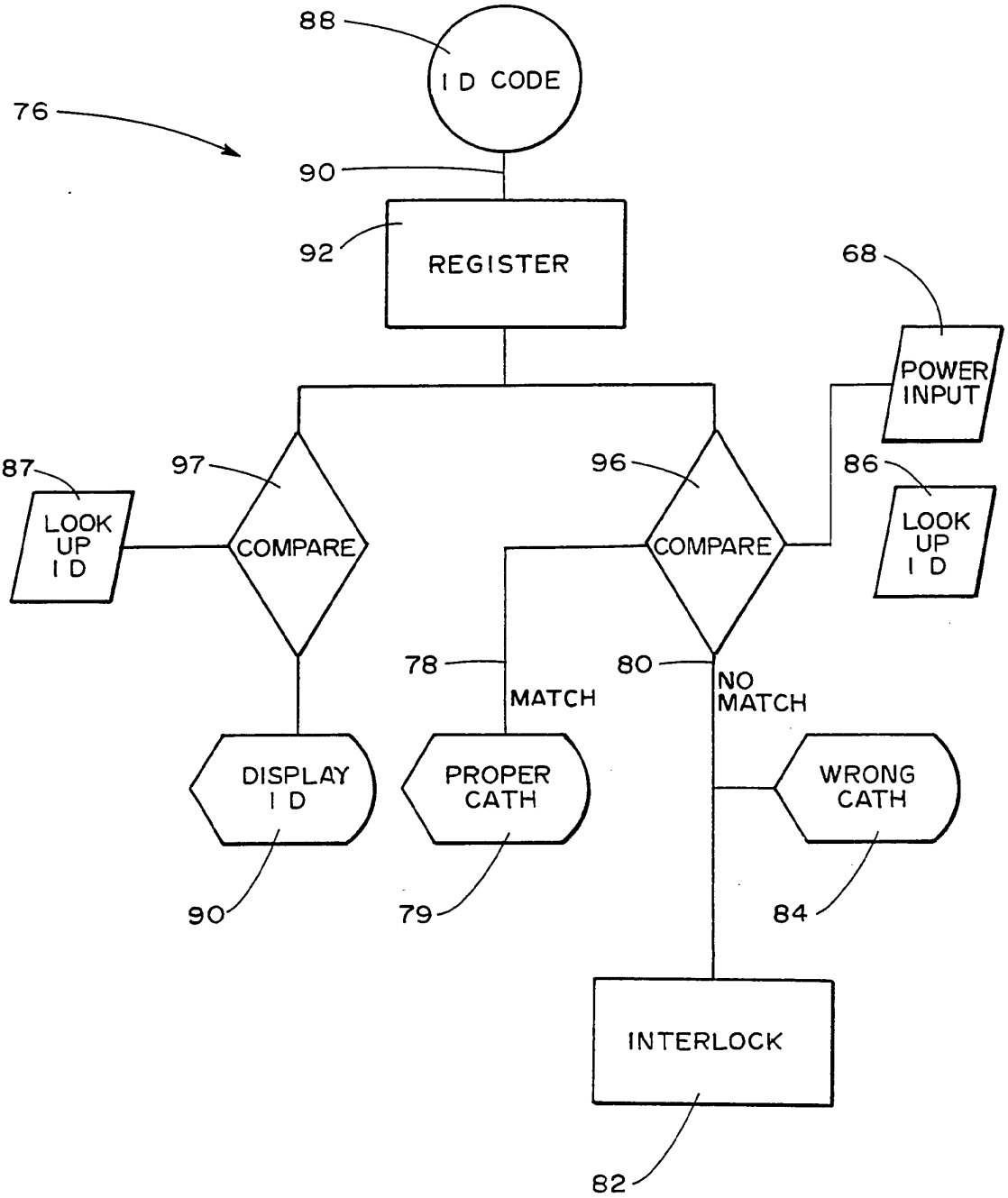


FIG. 3

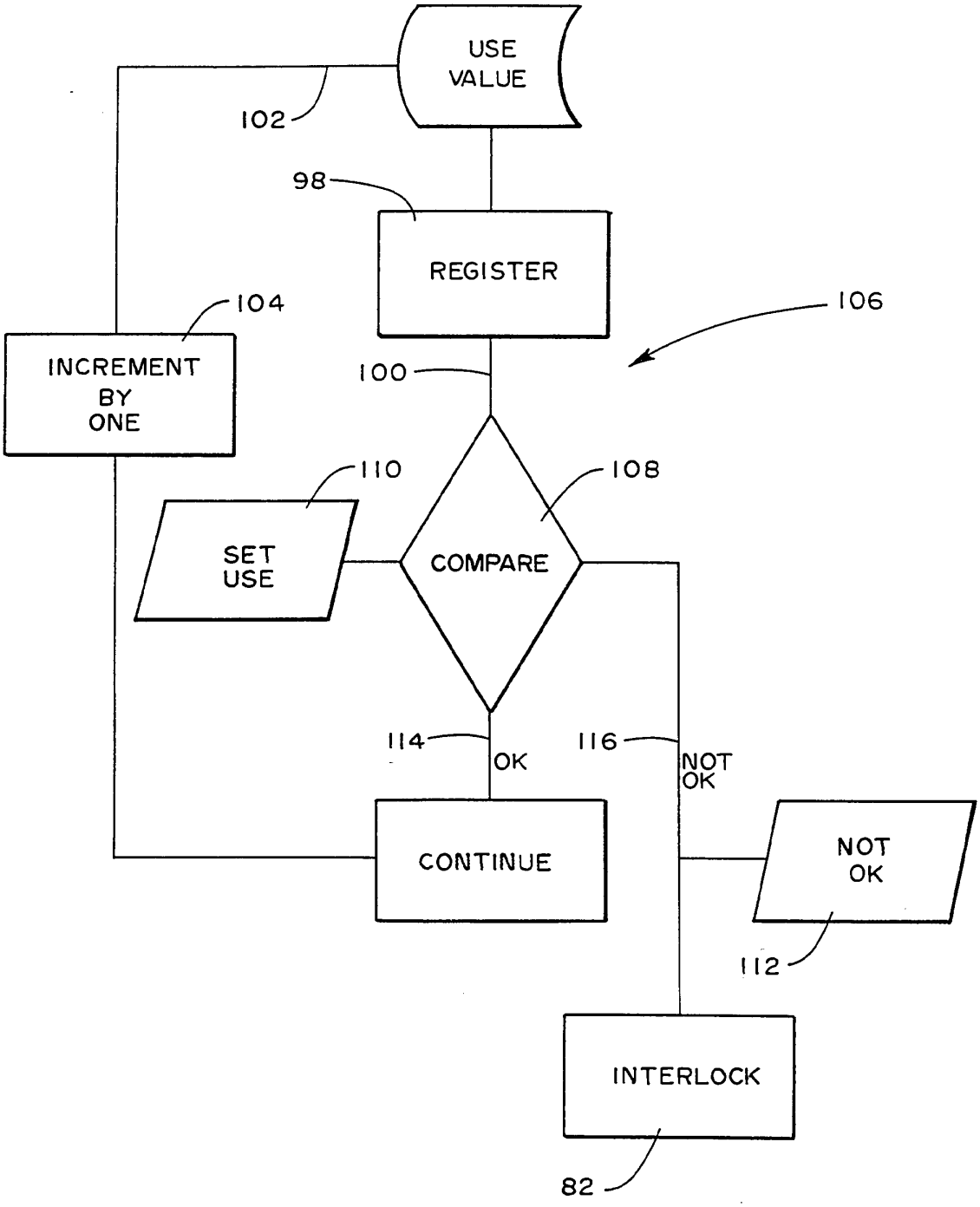
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FIG. 4



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FIG. 5



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US93/10902

A. CLASSIFICATION OF SUBJECT MATTER

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US CL :606/32

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)

U.S. : 606/1, 10-12, 32-35, 41-42, 45-50; 604/20, 21

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)

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, A, 4,580,557 (Hertzmann) 8 April 1986, Figure 3, column 6	1, 10, 14, 22, 23, 25 ---------- 2-5, 11-13, 15-17
Y	US, A, 3,929,137 (Gonser) 30 December, 1975, whole document	2-5, 11-13, 15-17
Y	US, A, 4,936,842 (D'Amelio et. al.) 26 June 1990, see Abstract, whole document	2-5, 11-13, 15-17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"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
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DEVICES FOR THERAPEUTIC NASAL NEUROMODULATION AND ASSOCIATED METHODS AND SYSTEMS

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Classification: **- international:** ***A61B18/00; A61B18/02; A61B18/04; A61B18/18; A61N1/05; A61N1/18; A61N1/32; A61N1/36***

- cooperative: **A61B17/00234 (US); A61B18/1492 (EP, US); A61B18/24 (EP, US); A61F7/123 (US); A61N1/0546 (EP, US); A61N1/18 (EP, US); A61N1/32 (EP, US); A61N1/36017 (EP, US); A61N1/36082 (EP, US); A61N1/40 (US); A61N7/00 (US);** A61B18/02 (EP, US); A61B18/1815 (EP, US); A61B2017/003 (US); A61B2018/00029 (EP, US); A61B2018/0016 (EP, US); A61B2018/00214 (EP, US); A61B2018/0022 (EP, US); A61B2018/00267 (EP, US); A61B2018/00327 (EP, US); A61B2018/00434 (EP, US); A61B2018/00577 (EP, US); A61B2018/00702 (EP, US); A61B2018/00797 (EP, US); A61B2018/1467 (EP, US); A61B2218/002 (EP, US); A61F2007/0006 (US); A61F2007/0054 (US); A61N1/36025 (EP, US); A61N2007/0021 (US); A61N5/022 (EP, US)

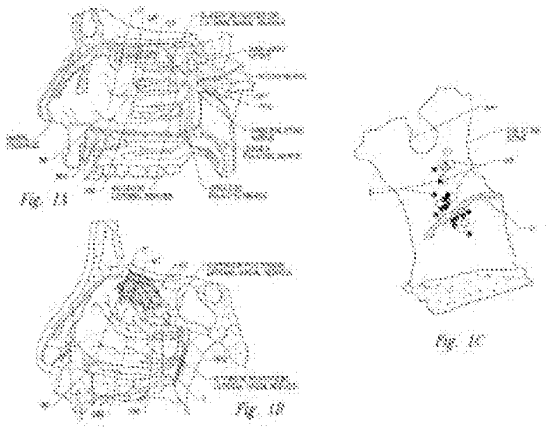
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Abstract of WO2016183337 (A2)



Devices for therapeutic nasal neuromodulation and associated systems and methods are disclosed herein. A system for therapeutic neuromodulation in a nasal region configured in accordance with embodiments of the present technology can include, for example, a shaft and a therapeutic element at a distal portion of the shaft. The shaft can locate the distal portion intraluminally at a target site inferior to a patient's sphenopalatine foramen. The therapeutic element can include an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves at microforamina of a palatine bone of the human patient for the treatment of rhinitis or other indications. In other embodiments, the therapeutic element can be configured to therapeutically modulate nerves that innervate the frontal, ethmoidal, sphenoidal, and maxillary sinuses for the treatment of chronic sinusitis.

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(74) Agents: **DUNHAM, Nicole, S.** et al.; Perkins Coie LLP, P.O. Box 1247, Seattle, WA 98111-1247 (US).

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(54) Title: DEVICES FOR THERAPEUTIC NASAL NEUROMODULATION AND ASSOCIATED METHODS AND SYSTEMS

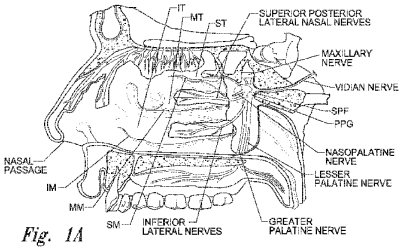


Fig. 1A

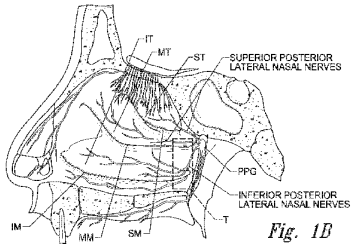


Fig. 1B

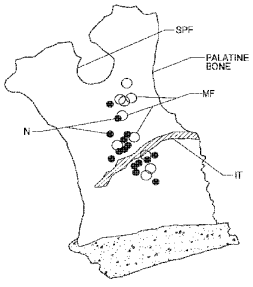


Fig. 1C

(57) Abstract: Devices for therapeutic nasal neuromodulation and associated systems and methods are disclosed herein. A system for therapeutic neuromodulation in a nasal region configured in accordance with embodiments of the present technology can include, for example, a shaft and a therapeutic element at a distal portion of the shaft. The shaft can locate the distal portion intraluminally at a target site inferior to a patient's sphenopalatine foramen. The therapeutic element can include an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves at microforamina of a palatine bone of the human patient for the treatment of rhinitis or other indications. In other embodiments, the therapeutic element can be configured to therapeutically modulate nerves that innervate the frontal, ethmoidal, sphenoidal, and maxillary sinuses for the treatment of chronic sinusitis.

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DEVICES FOR THERAPEUTIC NASAL NEUROMODULATION AND ASSOCIATED METHODS AND SYSTEMS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Patent Application No. 62/160,289, filed May 12, 2015, which is incorporated by reference herein in its entirety.

TECHNICAL FIELD

[0002] The present technology relates generally to devices, systems, and methods for therapeutically modulating nerves in or associated with a nasal region of a patient. In particular, various embodiments of the present technology are related to therapeutic neuromodulation systems and methods for the treating rhinitis and other indications.

BACKGROUND

[0003] Rhinosinusitis is characterized as an inflammation of the mucous membrane of the nose and refers to a group of conditions, including allergic rhinitis, non-allergic rhinitis, chronic rhinitis, chronic sinusitis, and medical resistant rhinitis. Symptoms of rhinosinusitis include nasal blockage, obstruction, congestion, nasal discharge (e.g., rhinorrhea and/or posterior nasal drip), facial pain, facial pressure, and/or reduction or loss of smell. Allergic rhinitis can include further symptoms, such as sneezing, watery rhinorrhea, nasal itching, and itchy or watery eyes. Severe rhinitis can lead to exacerbation of coexisting asthma, sleep disturbances, and impairment of daily activities. Depending on the duration and type of systems, rhinosinusitis can fall within four subtypes: acute rhinosinusitis, recurrent rhinosinusitis, chronic rhinosinusitis with nasal polyposis (i.e., soft, non-cancerous growths on the lining of the nasal passages or sinuses), and chronic rhinosinusitis without nasal polyposis. Acute rhinosinusitis refers to symptoms lasting for less than twelve weeks, whereas chronic rhinosinusitis (with and without nasal polyposis) refers to symptoms lasting longer than twelve weeks. Recurrent rhinosinusitis refers to four or more episodes of acute rhinosinusitis within a twelve-month period, with resolution of symptoms between each episode.

[0004] There are numerous environmental and biological causes of rhinosinusitis. Non-allergic rhinosinusitis, for example, can be caused by environmental irritants (e.g.,

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exhaust fumes, cleaning solutions, latex, perfume, dust, etc.), medications (e.g., NSAIDs, oral contraceptives, blood pressure medications including ACE inhibitors, antidepressants, etc.), foods (e.g., alcoholic beverages, spicy foods, etc.), hormonal changes (e.g., pregnancy and menstruation), and/or nasal septum deviation. Triggers of allergic rhinitis can include exposure to seasonal allergens (e.g., exposure to environmental allergens at similar times each year), perennial allergens that occur any time of year (e.g., dust mites, animal dander, molds, etc.), and/or occupational allergens (e.g., certain chemicals, grains, latex, etc.).

[0005] The treatment of rhinosinusitis can include a general avoidance of rhinitis triggers, nasal irrigation with a saline solution, and/or drug therapies. Pharmaceutical agents prescribed for rhinosinusitis include, for example, oral H1 antihistamines, topical nasal H1 antihistamines, topical intranasal corticosteroids, systemic glucocorticoids, injectable corticosteroids, anti-leukotrienes, nasal or oral decongestants, topical anticholinergic, chromoglycate, and/or anti-immunoglobulin E therapies. However, these pharmaceutical agents have limited efficacy (e.g., 17% higher than placebo or less) and undesirable side effects, such as sedation, irritation, impairment to taste, sore throat, dry nose, epistaxis (i.e., nose bleeds), and/or headaches. Immunotherapy, including sublingual immunotherapy ("SLIT"), has also been used to treat allergic rhinitis by desensitizing the patient to particular allergens by repeated administration of an allergen extract. However, immunotherapy requires an elongated administration period (e.g., 3-5 years for SLIT) and may result in numerous side effects, including pain and swelling at the site of the injection, urticarial (i.e., hives), angioedema, asthma, and anaphylaxis.

[0006] Surgical interventions have also been employed in an attempt to treat patients with drug therapy resistant, severe rhinitis symptoms. In the 1960's through 1980's, surgeries were performed to sever parasympathetic nerve fibers in the vidian canal to decrease parasympathetic tone in the nasal mucosa. More recent attempts at vidian neurectomies were found to be 50-88% effective for the treatment of rhinorrhea, with other ancillary benefits including improvements in symptoms of sneezing and nasal obstruction. These symptomatic improvements have also been correlated to histologic mucosal changes with reductions in stromal edema, eosinophilic cellular infiltration, mast cell levels, and histamine concentrations in denervated mucosa. However, despite the clinical and histologic efficacy of vidian neurectomy, resecting the vidian nerve failed to gain widespread acceptance largely due to the morbidities associated with its lack of anatomic and autonomic selectivity. For example, the site of neurectomy includes preganglionic secretomotor fibers to the lacrimal

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gland, and therefore the neurectomy often resulted in the loss of reflex tearing, i.e., lacrimation, which in severe cases can cause vision loss. Due to such irreversible complications, this technique was soon abandoned. Further, due passage of postganglionic pterygopalatine fibers through the retro-orbital plexus, the position of the vidian neurectomy relative to the target end organ (i.e., the nasal mucosa) may result in re-innervation via the autonomic plexus and otic ganglion projections traveling with the accessory meningeal artery.

[0007] The complications associated with vidian neurectomies are generally attributed to the nonspecific site of autonomic denervation. Consequently, surgeons have recently shifted the site of the neurectomy to postganglionic parasympathetic rami that may have the same physiologic effect as a vidian neurectomy, while avoiding collateral injury to the lacrimal and sympathetic fibers. For example, surgeons in Japan have performed transnasal inferior turbinate submucosal resections in conjunction with resections of the posterior nasal nerves ("PNN"), which are postganglionic neural pathways located further downstream than the vidian nerve. (*See*, Kobayashi T, Hyodo M, Nakamura K, Komobuchi H, Honda N, Resection of peripheral branches of the posterior nasal nerve compared to conventional posterior neurectomy in severe allergic rhinitis. *Auris Nasus Larynx.* 2012 Feb 15;39:593-596.) The PNN neurectomies are performed at the sphenopalatine foramen, where the PNN is thought to enter the nasal region. These neurectomies are highly complex and laborious because of a lack of good surgical markers for identifying the desired posterior nasal nerves and, even if the desired nerves are located, resection of the nerves is very difficult because the nerves must be separated from the surrounding vasculature (e.g., the sphenopalatine artery).

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Many aspects of the present technology can be better understood with reference to the following drawings. The components in the drawings are not necessarily to scale. Instead, emphasis is placed on illustrating clearly the principles of the present technology. For ease of reference, throughout this disclosure identical reference numbers may be used to identify identical or at least generally similar or analogous components or features.

[0009] Figure 1A is a cut-away side view illustrating the anatomy of a lateral nasal wall.

[0010] Figure 1B is an enlarged side view of the nerves of the lateral nasal wall of Figure 1A.

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[0011] Figure 1C is a front view of a left palatine bone illustrating geometry of microforamina in the left palatine bone.

[0012] Figure 2 is a partially schematic view of a therapeutic neuromodulation system for therapeutically modulating nerves in a nasal region in accordance with an embodiment of the present technology.

[0013] Figures 3A-3E are partial cut-away side views illustrating various approaches for delivering a distal portion of a therapeutic neuromodulation device to a target site within a nasal region in accordance with embodiments of the present technology.

[0014] Figure 4 is an isometric view of a distal portion of a therapeutic neuromodulation device configured in accordance with an embodiment of the present technology.

[0015] Figures 5A-5G are isometric views of electrode configurations of therapeutic neuromodulation devices for therapeutic neuromodulation in accordance with embodiments of the present technology.

[0016] Figures 6A and 6B are partially schematic diagrams illustrating electrode configurations at a distal portion of a therapeutic neuromodulation device for nerve detection configured in accordance with embodiments of the present technology.

[0017] Figure 7 is a graph illustrating threshold levels of electrical conductivity of nasal tissue with respect to temperature.

[0018] Figures 8 and 9 are isometric views of a distal portion of a therapeutic neuromodulation device configured in accordance with an embodiment of the present technology.

[0019] Figure 10A is an isometric view of a distal portion of a therapeutic neuromodulation device configured in accordance with another embodiment of the present technology, and Figure 10B is an isometric view illustrating the therapeutic neuromodulation device of Figure 10A at a treatment site.

[0020] Figures 11A-11D are isometric views illustrating a distal portion of a therapeutic neuromodulation device configured in accordance with yet another embodiment of the present technology.

[0021] Figure 12 is a side view of a distal portion of a therapeutic neuromodulation device configured in accordance with a further embodiment of the present technology.

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[0022] Figure 13 is a side view of a distal portion of a therapeutic neuromodulation device configured in accordance with a still further embodiment of the present technology.

[0023] Figure 14 is an isometric side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0024] Figure 15 is an isometric side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0025] Figure 16 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0026] Figure 17 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0027] Figure 18 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0028] Figure 19 is a side view of a distal portion of a therapeutic neuromodulation device configured in accordance with an additional embodiment of the present technology.

[0029] Figure 20 is a partial cut-away side view illustrating target sites proximate to ostia of nasal sinuses for a therapeutic neuromodulation device configured in accordance with embodiments of the present technology.

DETAILED DESCRIPTION

[0030] The present technology is generally directed to devices for therapeutic nasal neuromodulation and associated systems and methods. The disclosed devices are configured to provide an accurate and localized non-invasive application of energy to disrupt the parasympathetic motor sensory function in the nasal region. Specific details of several embodiments of the present technology are described herein with reference to Figures 1A-20. Although many of the embodiments are described with respect to devices, systems, and methods for therapeutically modulating nerves in the nasal region for the treatment of rhinitis, other applications and other embodiments in addition to those described herein are

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within the scope of the present technology. For example, at least some embodiments of the present technology may be useful for the treatment of other indications, such as the treatment of chronic sinusitis and epitaxis. It should be noted that other embodiments in addition to those disclosed herein are within the scope of the present technology. Further, embodiments of the present technology can have different configurations, components, and/or procedures than those shown or described herein. Moreover, a person of ordinary skill in the art will understand that embodiments of the present technology can have configurations, components, and/or procedures in addition to those shown or described herein and that these and other embodiments can be without several of the configurations, components, and/or procedures shown or described herein without deviating from the present technology.

[0031] With regard to the terms "distal" and "proximal" within this description, unless otherwise specified, the terms can reference relative positions of portions of a therapeutic neuromodulation device and/or an associated delivery device with reference to an operator and/or a location within the nasal cavity. For example, in referring to a delivery catheter suitable to deliver and position various prosthetic valve devices described herein, "proximal" can refer to a position closer to the operator of the device or access point at the entrance point of a patient's nostril, and "distal" can refer to a position that is more distant from the operator of the device or further from the access point at the entrance of the patient's nostril. Additionally, posterior, anterior, inferior and superior are used in accordance with standard medical terminology.

[0032] As used herein, the terms "therapeutic modulation" of nerves and "therapeutic neuromodulation" refer to the partial or complete incapacitation or other effective disruption of neural activity, including partial or complete ablation of nerves. Therapeutic neuromodulation, for example, can include partially or completely inhibiting, reducing, and/or blocking neural communication along neural fibers.

Anatomy of the Nasal Cavity

[0033] Figure 1A is a cut-away side view illustrating the anatomy of a lateral nasal wall, and Figure 1B is an enlarged side view of the nerves of the lateral nasal wall of Figure 1A. The sphenopalatine foramen ("SPF"; Figure 1A) is an opening or conduit defined by the palatine bone and the sphenoid bone through which the sphenopalatine vessels and the posterior superior nasal nerves travel into the nasal cavity. More specifically, the orbital and sphenoidal processes of the perpendicular plate of the palatine bone define the sphenopalatine

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notch, which is converted into the SPF by the articulation with the surface of the body of the sphenoid bone.

[0034] The location of the SPF is highly variable within the posterior region of the lateral nasal cavity, which makes it difficult to visually locate the SPF. Typically, the SPF is located in the middle meatus ("MM"; Figure 1A); however, anatomical variations also result in the SPF being located in the superior meatus ("SM"; Figure 1A) or at the transition of the superior and middle meatuses. In certain individuals, for example, the inferior border of the SPF has been measured at about 19 mm above the horizontal plate of the palatine bone (i.e., the nasal sill), which is about 13 mm above the horizontal lamina of the inferior turbinate ("IT"; Figure 1A), and the average distance from the nasal sill to the SPF is about 64.4 mm, resulting in an angle of approach from the nasal sill to the SPA of about 11.4°. However, studies to measure the precise location of the SPF are of limited practical application due to the wide variation of its location.

[0035] The anatomical variations of the SPF are expected to correspond to alterations of the autonomic and vascular pathways traversing into the nasal cavity. In general, it is thought that the posterior nasal nerves (also referred to as lateral posterior superior nasal nerves) branch from the pterygopalatine ganglion ("PPG"; also referred to as the sphenopalatine ganglion; Figure 1A) through the SPF to enter the lateral nasal wall of the nasal cavity, and the sphenopalatine artery passes from the pterygopalatine fossa through the SPF on the lateral nasal wall. The sphenopalatine artery branches into two main portions: the posterior lateral nasal branch and the posterior septal branch. The main branch of the posterior lateral nasal artery travels inferiorly into the inferior turbinate IT (e.g., between about 1.0 mm and 1.5 mm from the posterior tip of the inferior turbinate IT), while another branch enters the middle turbinate MT and branches anteriorly and posteriorly.

[0036] Beyond the SPF, studies have shown that over 30% of human patients have one or more accessory foramen that also carries arteries and nerves into the nasal cavity. The accessory foramena are typically smaller than the SPF and positioned inferior to the SPF. For example, there can be one, two, three or more branches of the posterior nasal artery and posterior nasal nerves that extend through corresponding accessory foramen. The variability in location, size, and quantity associated with the accessory foramen and the associated branching arteries and nerves that travel through the accessory foramen gives rise to a great deal of uncertainty regarding the positions of the vasculature and nerves of the sphenopalatine region. Furthermore, the natural anatomy extending from the SPF often

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includes deep inferior and/or superior grooves that carry neural and arterial pathways, which make it difficult to locate arterial and neural branches. For example the grooves can extend more than 5 mm long, more than 2 mm wide, and more than 1 mm deep, thereby creating a path significant enough to carry both arteries and nerves. The variations caused by the grooves and the accessory foramen in the sphenopalatine region make locating and accessing the arteries and nerves (positioned posterior to the arteries) extremely difficult for surgeons.

[0037] Recent microanatomic dissection of the pterygopalatine fossa (PPF) have further evidenced the highly variable anatomy of the region surrounding the SPF, showing that a multiplicity of efferent rami that project from the pterygopalatine ganglion ("PPG"; Figure 1) to innervate the orbit and nasal mucosa via numerous groups of small nerve fascicles, rather than an individual postganglionic autonomic nerves (e.g., the posterior nasal nerve). Studies have shown that at least 87% of humans have microforamina and micro rami in the palatine bone. Figure 1C, for example, is a front view of a left palatine bone illustrating geometry of microforamina and micro rami in a left palatine bone. In Figure 1C, the solid regions represent nerves traversing directly through the palatine bone, and the open circles represent nerves that were associated with distinct microforamina. Indeed, Figure 1C illustrates that a medial portion of the palatine bone can include at least 25 accessory posterolateral nerves.

[0038] The respiratory portion of the nasal cavity mucosa is composed of a type of ciliated pseudostratified columnar epithelium with a basement membrane. Nasal secretions (e.g., mucus) are secreted by goblet cells, submucosal glands, and transudate from plasma. Nasal seromucous glands and blood vessels are highly regulated by parasympathetic innervation deriving from the vidian and other nerves. Parasympathetic (cholinergic) stimulation through acetylcholine and vasoactive intestinal peptide generally results in mucus production. Accordingly, the parasympathetic innervation of the mucosa is primarily responsible submucosal gland activation/hyper activation, venous engorgement (e.g., congestion), and increased blood flow to the blood vessels lining the nose. Accordingly, severing or modulating the parasympathetic pathways that innervate the mucosa are expected to reduce or eliminate the hyper activation of the submucosal glands and engorgement of vessels that cause symptoms associated with rhinosinusitis and other indications.

[0039] As discussed above, postganglionic parasympathetic fibers that innervate the nasal mucosa (i.e., posterior superior nasal nerves) were thought to travel exclusively through the SPF as a sphenopalatine neurovascular bundle. The posterior nasal nerves are branches of the maxillary nerve that innervate the nasal cavity via a number of smaller medial and

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lateral branches extending through the mucosa of the superior and middle turbinates ST, MT (i.e., nasal chonchea) and to the nasal septum. The nasopalatine nerve is generally the largest of the medial posterior superior nasal nerves. It passes antero-inferiorly in a groove on the vomer to the floor of the nasal cavity. From here, it passes through the incisive fossa of the hard palate and communicates with the greater palatine nerve to supply the mucosa of the hard palate. The posterior superior nasal nerves pass through the pterygopalatine ganglion PPG without synapsing and onto the maxillary nerve via its ganglionic branches.

[0040] Based on the understanding that the posterior nasal nerves exclusively traverse the SPF to innervate the nasal mucosa, surgeries have been performed to selectively sever the posterior nasal nerve as it exits the SPF. However, as discussed above, the sinonasal parasympathetic pathway actually comprises individual rami project from the pterygopalatine ganglion (PPG) to innervate the nasal mucosa via multiple small nerve fascicles (i.e., accessory posterolateral nerves), not a single branch extending through the SPF. These rami are transmitted through multiple fissures, accessory foramina, and microforamina throughout the palatine bone and may demonstrate anastomotic loops with both the SPF and other accessory nerves. Thus, if only the parasympathetic nerves traversing the SPF were severed, almost all patients (e.g., 90% of patients or more) would retain intact accessory secretomotor fibers to the posterolateral mucosa, which would result in the persistence of symptoms the neurectomy was meant to alieve.

[0041] Accordingly, embodiments of the present technology are configured to therapeutically modulate nerves at precise and focused treatment sites corresponding to the sites of rami extending through fissures, accessory foramina, and microforamina throughout the palatine bone (e.g., target region T shown in Figure 1B). In certain embodiments, the targeted nerves are postganglionic parasympathetic nerves that go on to innervate the nasal mucosa. This selective neural treatment is also expected to decrease the rate of postoperative nasal crusting and dryness because it allows a clinician to titrate the degree of anterior denervation through judicious sparing of the rami orbitonasalis. Furthermore, embodiments of the present technology are also expected to maintain at least some sympathetic tone by preserving a portion of the sympathetic contributions from the deep petrosal nerve and internal maxillary periarteriolar plexi, leading to improved outcomes with respect to nasal obstruction. In addition, embodiments of the present technology are configured to target a multitude of parasympathetic neural entry locations (e.g., accessory foramen, fissures, and

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microforamina) to the nasal region to provide for a complete resection of all anastomotic loops, thereby reducing the rate of long-term re-innervation.

Selected Embodiments of Systems for Therapeutic Nasal Neuromodulation and Neural Mapping

[0042] Figure 2 is a partially schematic view of a therapeutic neuromodulation system 200 ("system 200") for therapeutically modulating nerves in a nasal region in accordance with an embodiment of the present technology. The system 200 includes a therapeutic neuromodulation catheter or device 202, a console 204, and a cable 206 extending therebetween. The therapeutic neuromodulation device 202 includes a shaft 208 having a proximal portion 208a, a distal portion 208b, a handle 210 at a proximal portion 208a of the shaft 208, and a therapeutic assembly or element 212 at the distal portion 208b of the shaft 208. The shaft 208 is configured to locate the distal portion 208b intraluminally at a treatment or target site within a nasal region proximate to postganglionic parasympathetic nerves that innervate the nasal mucosa. The target site may be a region, volume, or area in which the target nerves are located and may differ in size and shape depending upon the anatomy of the patient. For example, the target site may be a 3 cm area inferior to the SPF. In other embodiments, the target site may be larger, smaller, and/or located elsewhere in the nasal cavity to target the desired neural fibers. The therapeutic assembly 212 can include at least one energy delivery element 214 configured to therapeutically modulate the postganglionic parasympathetic nerves. In certain embodiments, for example, the therapeutic assembly 212 can therapeutically modulate the postganglionic parasympathetic nerves branching from the pterygopalatine ganglion and innervating the nasal region and nasal mucosa, such as parasympathetic nerves (e.g., the posterior nasal nerves) traversing the SPF, accessory foramen, and microforamina of a palatine bone.

[0043] As shown in Figure 2, the therapeutic assembly 212 includes at least one energy delivery element 214 configured to provide therapeutic neuromodulation to the target site. In certain embodiments, for example, the energy delivery element 214 can include one or more electrodes configured to apply electromagnetic neuromodulation energy (e.g., RF energy) to target sites. In other embodiments, the energy delivery element 214 can be configured to provide therapeutic neuromodulation using various other modalities, such as cryotherapeutic cooling, ultrasound energy (e.g., high intensity focused ultrasound ("HIFU") energy), microwave energy (e.g., via a microwave antenna), direct heating, high and/or low power laser energy, mechanical vibration, and/or optical power. In further embodiments, the

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therapeutic assembly 212 can be configured to deliver chemicals or drugs to the target site to chemically ablate or embolize the target nerves. For example, the therapeutic assembly 212 can include a needle applicator extending through an access portion of the shaft 208 and/or a separate introducer, and the needle applicator can be configured to inject a chemical into the target site to therapeutically modulate the target nerves, such as botox, alcohol, guanethidine, ethanol, phenol, a neurotoxin, or another suitable agent selected to alter, damage, or disrupt nerves.

[0044] In certain embodiments, the therapeutic assembly 212 can include one or more sensors (not shown), such as one or more temperature sensors (e.g., thermocouples, thermistors, etc.), impedance sensors, and/or other sensors. The sensor(s) and/or the energy delivery element 214 can be connected to one or more wires (not shown; e.g., copper wires) extending through the shaft 208 to transmit signals to and from the sensor(s) and/or convey energy to the energy delivery element 214.

[0045] The therapeutic neuromodulation device 202 can be operatively coupled to the console 204 via a wired connection (e.g., via the cable 206) and/or a wireless connection. The console 204 can be configured to control, monitor, supply, and/or otherwise support operation of the therapeutic neuromodulation device 202. The console 204 can further be configured to generate a selected form and/or magnitude of energy for delivery to tissue or nerves at the target site via the therapeutic assembly 212, and therefore the console 204 may have different configurations depending on the treatment modality of the therapeutic neuromodulation device 202. For example, when therapeutic neuromodulation device 202 is configured for electrode-based, heat-element-based, and/or transducer-based treatment, the console 204 can include an energy generator 216 configured to generate RF energy (e.g., monopolar, bipolar, or multi-polar RF energy), pulsed electrical energy, microwave energy, optical energy, ultrasound energy (e.g., intraluminally- delivered ultrasound and/or HIFU), direct heat energy, radiation (e.g., infrared, visible, and/or gamma radiation), and/or another suitable type of energy. When the therapeutic neuromodulation device 202 is configured for cryotherapeutic treatment, the console 204 can include a refrigerant reservoir (not shown), and can be configured to supply the therapeutic neuromodulation device 202 with refrigerant. Similarly, when the therapeutic neuromodulation device 202 is configured for chemical-based treatment (e.g., drug infusion), the console 204 can include a chemical reservoir (not shown) and can be configured to supply the therapeutic neuromodulation device 202 with one or more chemicals.

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[0046] As further shown in Figure 2, the system 200 can further include a controller 218 communicatively coupled to the therapeutic neuromodulation device 202. In the illustrated embodiment, the controller 218 is housed in the console 204. In other embodiments, the controller 218 can be carried by the handle 210 of the therapeutic neuromodulation device 202, the cable 206, an independent component, and/or another portion of the system 200. The controller 218 can be configured to initiate, terminate, and/or adjust operation of one or more components (e.g., the energy delivery element 214) of the therapeutic neuromodulation device 202 directly and/or via the console 204. The controller 218 can be configured to execute an automated control algorithm and/or to receive control instructions from an operator (e.g., a clinician). For example, the controller 218 and/or other components of the console 204 (e.g., memory) can include a computer-readable medium carrying instructions, which when executed by the controller 218, causes the therapeutic assembly 202 to perform certain functions (e.g., apply energy in a specific manner, detect impedance, detect temperature, detect nerve locations or anatomical structures, etc.). A memory includes one or more of various hardware devices for volatile and non-volatile storage, and can include both read-only and writable memory. For example, a memory can comprise random access memory (RAM), CPU registers, read-only memory (ROM), and writable non-volatile memory, such as flash memory, hard drives, floppy disks, CDs, DVDs, magnetic storage devices, tape drives, device buffers, and so forth. A memory is not a propagating signal divorced from underlying hardware; a memory is thus non-transitory.

[0047] Further, the console 204 can be configured to provide feedback to an operator before, during, and/or after a treatment procedure via evaluation/feedback algorithms 220. For example, the evaluation/feedback algorithms 220 can be configured to provide information associated with the temperature of the tissue at the treatment site, the location of nerves at the treatment site, and/or the effect of the therapeutic neuromodulation on the nerves at the treatment site. In certain embodiments, the evaluation/feedback algorithm 220 can include features to confirm efficacy of the treatment and/or enhance the desired performance of the system 200. For example, the evaluation/feedback algorithm 220, in conjunction with the controller 218, can be configured to monitor temperature at the treatment site during therapy and automatically shut off the energy delivery when the temperature reaches a predetermined maximum (e.g., when applying RF energy) or predetermined minimum (e.g., when applying cryotherapy). In other embodiments, the evaluation/feedback algorithm 220, in conjunction with the controller 218, can be configured

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to automatically terminate treatment after a predetermined maximum time, a predetermined maximum impedance rise of the targeted tissue (i.e., in comparison to a baseline impedance measurement), a predetermined maximum impedance of the targeted tissue), and/or other threshold values for biomarkers associated with autonomic function. This and other information associated with the operation of the system 200 can be communicated to the operator via a display 222 (e.g., a monitor or touchscreen) on the console 204 and/or a separate display (not shown) communicatively coupled to the console 204.

[0048] In various embodiments, the therapeutic assembly 212 and/or other portions of the system 200 can be configured to detect various parameters of the heterogeneous tissue at the target site to determine the anatomy at the target site (e.g., tissue types, tissue locations, vasculature, bone structures, foramen, sinuses, etc.), locate nerves and/or other structures, and allow for neural mapping. For example, the therapeutic assembly 212 can be configured to detect impedance, dielectric properties, temperature, and/or other properties that indicate the presence of neural fibers in the target region. As shown in Figure 2, the console 204 can include a nerve monitoring assembly 221 (shown schematically) that receives the detected electrical and/or thermal measurements of tissue at the target site taken by the therapeutic assembly 212, and process this information to identify the presence of nerves, the location of nerves, and/or neural activity at the target site. This information can then be communicated to the operator via a high resolution spatial grid (e.g., on the display 222) and/or other type of display. The nerve monitoring assembly 221 can be operably coupled to the energy delivery element 214 and/or other features of the therapeutic assembly 212 via signal wires (e.g., copper wires) that extend through the cable 206 and through the length of the shaft 208. In other embodiments, the therapeutic assembly 212 can be communicatively coupled to the nerve monitoring assembly 221 using other suitable communication means.

[0049] The nerve monitoring assembly 221 can determine neural locations and activity before therapeutic neuromodulation to determine precise treatment regions corresponding to the positions of the desired nerves, during treatment to determine the effect of the therapeutic neuromodulation, and/or after treatment to evaluate whether the therapeutic neuromodulation treated the target nerves to a desired degree. This information can be used to make various determinations related to the nerves proximate to the target site, such as whether the target site is suitable for neuromodulation. In addition, the nerve monitoring assembly 221 can also compare the detected neural locations and/or activity before and after therapeutic neuromodulation, and compare the change in neural activity to a predetermined threshold to

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assess whether the application of therapeutic neuromodulation was effective across the treatment site. For example, the nerve monitoring assembly 221 can determine electroneurogram (ENG) signals based on recordings of electrical activity of neurons taken by the therapeutic assembly 212 before and after therapeutic neuromodulation. Statistically meaningful (e.g., measurable or noticeable) decreases in the ENG signal(s) taken after neuromodulation can serve as an indicator that the nerves were sufficiently ablated.

[0050] The system 200 can further include a channel 224 extending along at least a portion of the shaft 208 and a port 226 at the distal portion 208b of the shaft in communication with the port 226. In certain embodiments, the channel 224 is a fluid pathway to deliver a fluid to the distal portion 208b of the shaft 208 via the port 226. For example, the channel 224 can deliver saline solution or other fluids to rinse the intraluminal nasal pathway during delivery of the therapeutic assembly 212, flush the target site before applying therapeutic neuromodulation to the target site, and/or deliver fluid to the target site during energy delivery to reduce heating or cooling of the tissue adjacent to the energy delivery element 214. In other embodiments, the channel 224 allows for drug delivery to the treatment site. For example, a needle (not shown) can project through the port 226 to inject or otherwise deliver a nerve block, a local anesthetic, and/or other pharmacological agent to tissue at the target site.

[0051] The therapeutic neuromodulation device 202 provides access to target sites deep within the nasal region, such as at the immediate entrance of parasympathetic fibers into the nasal cavity to therapeutically modulate autonomic activity within the nasal cavity. In certain embodiments, for example, the therapeutic neuromodulation device 202 can position the therapeutic assembly 212 inferior to the SPF at the site of access foramen and/or microforamina (e.g., as shown in Figures 1B and 1C). By manipulating the proximal portion 208a of the shaft 208 from outside the entrance of the nose, a clinician may advance the shaft 208 through the tortuous intraluminal path through the nasal cavity and remotely manipulate the distal portion 208b of the shaft 208 via the handle 210 to position the therapeutic assembly 212 at the target site. In certain embodiments, the shaft 208 can be a steerable device (e.g., a steerable catheter) with a small bend radius (e.g., a 5 mm bend radius, a 4 mm bend radius, a 3 mm bend radius or less) that allows the clinician to navigate through the tortuous nasal anatomy. The steerable shaft can further be configured to articulate in at least two different directions. For example, the steerable shaft 208 can include dual pull wire rings that allow a clinician to form the distal portion 208b of the shaft 208 into an "S"-shape to

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correspond to the anatomy of the nasal region. In other embodiments, the articulating shaft 208 can be made from a substantially rigid material (e.g., a metal material) and include rigid links at the distal portion 208b of the shaft 208 that resist deflection, yet allow for a small bend radius (e.g., a 5 mm bend radius, a 4 mm bend radius, a 3 mm bend radius or less). In further embodiments, the steerable shaft 208 may be a laser-cut tube made from a metal and/or other suitable material. The laser-cut tube can include one or more pull wires operated by the clinician to allow the clinician to deflect the distal portion 208b of the shaft 208 to navigate the tortuous nasal anatomy to the target site.

[0052] In various embodiments, the distal portion 208b of the shaft 208 is guided into position at the target site via a guidewire (not shown) using an over-the-wire (OTW) or a rapid exchange (RX) technique. For example, the distal end of the therapeutic assembly 212 can include a channel for engaging the guidewire. Intraluminal delivery of the therapeutic assembly 212 can include inserting the guide wire into an orifice in communication with the nasal cavity (e.g., the nasal passage or mouth), and moving the shaft 208 and/or the therapeutic assembly 212 along the guide wire until the therapeutic assembly 212 reaches a target site (e.g., inferior to the SPF).

[0053] In further embodiments, the therapeutic neuromodulation device 202 can be configured for delivery via a guide catheter or introducer sheath (not shown) with or without using a guide wire. The introducer sheath can first be inserted intraluminally to the target site in the nasal region, and the distal portion 208b of the shaft 208 can then be inserted through the introducer sheath. At the target site, the therapeutic assembly 212 can be deployed through a distal end opening of the introducer sheath or a side port of the introducer sheath. In certain embodiments, the introducer sheath can include a straight portion and a pre-shaped portion with a fixed curve (e.g., a 5 mm curve, a 4 mm curve, a 3 mm curve, etc.) that can be deployed intraluminally to access the target site. In this embodiment, the introducer sheath may have a side port proximal to or along the pre-shaped curved portion through which the therapeutic assembly 212 can be deployed. In other embodiments, the introducer sheath may be made from a rigid material, such as a metal material coated with an insulative or dielectric material. In this embodiment, the introducer sheath may be substantially straight and used to deliver the therapeutic assembly 212 to the target site via a substantially straight pathway, such as through the middle meatus MM (Figure 1A).

[0054] Image guidance may be used to aid the clinician's positioning and manipulation of the distal portion 208b of the shaft 208 and the therapeutic assembly 212. For example, as

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described in further detail below with respect to Figures 3A-3E, an endoscope (not shown) can be positioned to visualize the target site, the positioning of the therapeutic assembly 212 at the target site, and/or the therapeutic assembly 212 during therapeutic neuromodulation. In certain embodiments, the distal portion 208b of the shaft 208 is delivered via a working channel extending through an endoscope, and therefore the endoscope can provide direct in-line visualization of the target site and the therapeutic assembly 212. In other embodiments, an endoscope is incorporated with the therapeutic assembly 212 and/or the distal portion 208b of the shaft 208 to provide in-line visualization of the assembly 212 and/or the surrounding nasal anatomy. In still further embodiments, image guidance can be provided with various other guidance modalities, such as image filtering in the infrared (IR) spectrum to visualize the vasculature and/or other anatomical structures, computed tomography (CT), fluoroscopy, ultrasound, optical coherence tomography (OCT), and/or combinations thereof. Further, in some embodiments, image guidance components may be integrated with the therapeutic neuromodulation device 202 to provide image guidance during positioning of the therapeutic assembly 212.

[0055] Once positioned at the target site, the therapeutic modulation may be applied via the energy delivery element 214 and/or other features of the therapeutic assembly 212 to precise, localized regions of tissue to induce one or more desired therapeutic neuromodulating effects to disrupt parasympathetic motor sensory function. The therapeutic assembly 212 can selectively target postganglionic parasympathetic fibers that innervate the nasal mucosa at a target or treatment site proximate to or at their entrance into the nasal region. For example, the therapeutic assembly 212 can be positioned to apply therapeutic neuromodulation at least proximate to the SPF (Figure 1A) to therapeutically modulate nerves entering the nasal region via the SPF. The therapeutic assembly 212 can also be positioned to inferior to the SPF to apply therapeutic neuromodulation energy across accessory foramen and microforamina (e.g., in the palatine bone) through which smaller medial and lateral branches of the posterior superior lateral nasal nerve enter the nasal region. The purposeful application of the energy at the target site may achieve therapeutic neuromodulation along all or at least a portion of posterior nasal neural fibers entering the nasal region. The therapeutic neuromodulating effects are generally a function of, at least in part, power, time, and contact between the energy delivery elements and the adjacent tissue. For example, in certain embodiments therapeutic neuromodulation of autonomic neural fibers are produced by applying RF energy at a power of about 2-20 W (e.g., 5 W, 7 W, 10 W, etc.)

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for a time period of about 1-20 sections (e.g., 5-10 seconds, 8-10 seconds, 10-12 seconds, etc.). The therapeutic neuromodulating effects may include partial or complete denervation via thermal ablation and/or non-ablative thermal alteration or damage (e.g., via sustained heating and/or resistive heating). Desired thermal heating effects may include raising the temperature of target neural fibers above a desired threshold to achieve non-ablative thermal alteration, or above a higher temperature to achieve ablative thermal alteration. For example, the target temperature may be above body temperature (e.g., approximately 37° C) but less than about 90° C (e.g., 70-75°C) for non-ablative thermal alteration, or the target temperature may be about 100°C or higher (e.g., 110°C, 120°C, etc.) for the ablative thermal alteration. Desired non-thermal neuromodulation effects may include altering the electrical signals transmitted in a nerve.

[0056] Hypothermic effects may also provide neuromodulation. As described in further detail below, for example, a cryotherapeutic applicator may be used to cool tissue at a target site to provide therapeutically-effective direct cell injury (e.g., necrosis), vascular injury (e.g., starving the cell from nutrients by damaging supplying blood vessels), and sublethal hypothermia with subsequent apoptosis. Exposure to cryotherapeutic cooling can cause acute cell death (e.g., immediately after exposure) and/or delayed cell death (e.g., during tissue thawing and subsequent hyperperfusion). Embodiments of the present technology can include cooling a structure positioned at or near tissue such that the tissue is effectively cooled to a depth where the targeted postganglionic parasympathetic nerves reside. For example, the cooling structure is cooled to the extent that it causes therapeutically effective, cryogenic posterior nasal nerve modulation.

[0057] In certain embodiments, the system 200 can determine the locations of the nerves, accessory foramen, and/or microforamina before therapy such that the therapeutic neuromodulation can be applied to precise regions including parasympathetic neural fibers. For example, the system 200 may identify a target site that has a length and/or width of about 3 mm inferior to the SPF, and the therapeutic assembly 212 can apply therapeutic neuromodulation to the identified target site via one or more applications of therapeutic neuromodulation. In other embodiments, the target site may be smaller or larger (e.g., a 3 cm-long target region) based on the detected locations of neural fibers and foramena. This neural and anatomical mapping allows the system 200 to accurately detect and therapeutically modulate the postganglionic parasympathetic neural fibers that innervate the mucosa at the numerous neural entrance points into the nasal cavity. Further, because there are not any

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clear anatomical markers denoting the location of the SPF, accessory foramen, and microforamina, the neural mapping allows the operator to identify and therapeutically modulate nerves that would otherwise be unidentifiable without intricate dissection of the mucosa. In addition, anatomical mapping can also allow the operator to identify certain structures that the operator may wish to avoid during therapeutic neural modulation (e.g., certain arteries).

[0058] Sufficiently modulating at least a portion of the parasympathetic nerves is expected to slow or potentially block conduction of autonomic neural signals to the nasal mucosa to produce a prolonged or permanent reduction in nasal parasympathetic activity. This is expected to reduce or eliminate activation or hyperactivation of the submucosal glands and venous engorgement and, thereby, reduce or eliminate the symptoms of rhinosinusitis. Further, because the system 200 applies therapeutic neuromodulation to the multitude of branches of the posterior nasal nerves rather than a single large branch of the posterior nasal nerve branch entering the nasal cavity at the SPF, the system 200 provides a more complete disruption of the parasympathetic neural pathway that affects the nasal mucosa and results in rhinosinusitis. Accordingly, the system 200 is expected to have enhanced therapeutic effects for the treatment of rhinosinusitis and reduced re-innervation of the treated mucosa.

[0059] In other embodiments, the system 200 can be configured to therapeutically modulate nerves and/or other structures to treat different indications. As discussed in further detail below, for example, the system 200 can be used to locate and/or therapeutically modulate nerves that innervate the para-nasal sinuses to treat chronic sinusitis. In further embodiments, the system 200 and the devices disclosed herein can be configured therapeutically modulate the vasculature within the nasal anatomy to treat other indications, such as epistaxis (i.e., excessive bleeding from the nose). For example, the system 200 and the therapeutic neuromodulation devices described herein can be used to apply therapeutically effective energy to arteries (e.g., the sphenopalatine artery and its branches) as they enter the nasal cavity (e.g., via the SPF, accessory foramen, etc.) to partially or completely coagulate or ligate the arteries. In other embodiments, the system 200 can be configured to partially or completely coagulate or ligate veins and/or other vessels. For such embodiments in which the therapeutic assembly 212 ligates or coagulates the vasculature, the system 200 would be modified to deliver energy at significantly higher power (e.g., about 100 W) and/or longer times (e.g., 1 minute or longer) than would be required for therapeutic

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neuromodulation. In various embodiments, the system 100 could apply the anatomical mapping techniques disclosed herein to locate or detect the targeted vasculature and surrounding anatomy before, during, and/or after treatment.

[0060] Figures 3A-3E are partial cut-away side views illustrating various approaches for delivering a distal portion of the therapeutic neuromodulation device 202 of Figure 2 to a target site within a nasal region in accordance with embodiments of the present technology. As shown in Figure 3A, in various embodiments the distal portion 208b of the shaft 208 extends into the nasal passage NP, through the inferior meatus IM between the inferior turbinate IT and the nasal sill NS, and around the posterior portion of the inferior turbinate IT where the therapeutic assembly 212 is deployed at a treatment site. As shown in Figure 3A, the treatment site can be located proximate to the access point or points of postganglionic parasympathetic nerves (e.g., branches of the posterior nasal nerve and/or other parasympathetic neural fibers that innervate the nasal mucosa) into the nasal cavity. In other embodiments, the target site can be elsewhere within the nasal cavity depending on the location of the target nerves. An endoscope 330 and/or other visualization device is delivered proximate to the target site by extending through the nasal passage NP and through the middle meatus MM between the inferior and middle turbinates IT and MT. From the visualization location within the middle meatus MM, the endoscope 330 can be used to visualize the treatment site, surrounding regions of the nasal anatomy, and the therapeutic assembly 212.

[0061] As further shown in Figure 3A, the shaft 208 of the therapeutic neuromodulation device 202 can include a positioning member 332 positioned proximal to the therapeutic assembly 212 and the target site. In the illustrated embodiment, the positioning member 332 is a balloon that is expanded in an opening (e.g., in one of the meatuses) against opposing structures (e.g., between the turbinates) to consistently hold the distal portion 208b of the shaft 208 in a desired position relative to the target site and provide stability for deployment of the therapeutic assembly 212. In other embodiments, the positioning member 332 may include other expandable structures (e.g., a mesh baskets) or anchor features that can be deployed to maintain a desired position of the shaft 208 within the nasal cavity. In further embodiments, the positioning member 332 can be positioned distal to the therapeutic assembly 212 and expanded in a region distal to the therapeutic assembly 212 and the treatment site. In still further embodiments, the positioning member 332 is positioned on an introducer sheath (not shown) through which the shaft 208 and/or other devices (e.g., a fluid

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line for delivery of saline or local anesthetics, an endoscope, a sensor, etc.) can pass. The positioning member 332 can be positioned proximal to the target site (e.g., similar to the position shown in Figure 3A) or distal to the treatment site. When positioned distally, the introducer sheath can include a side exit port through which the therapeutic assembly 212 and other features can be deployed at the target site. When the positioning member 332 is positioned on the introducer sheath, the positioning member 332 can provide stability for delivery and deployment of the distal portion 208b of the shaft 208 and the therapeutic assembly 212. The positioning member 332 can be incorporated on the shaft 208, an associated introducer sheath, and/or other deliver features of the system 200 (Figure 2) when the therapeutic assembly 212 is delivered through different intraluminal passageways.

[0062] Figure 3B illustrates a differ embodiment in which the distal portion 208b of the shaft 208 extends into the nasal passage NP, through the middle meatus MM between the inferior turbinate IT and the middle turbinate, and in posterior direction where the therapeutic assembly 212 is deployed at a treatment site. In this embodiment, the endoscope 330 and/or other visualization device is delivered alongside the shaft 208 through the same intraluminal pathway as the therapeutic assembly 212. The pathway through the middle meatus MM may provide for generally straight access to the target site depending on the specific region of interest and anatomical variations of the patient. Accordingly, an approach through the middle meatus MM may require less steering and/or articulation of the shaft 208 and the endoscope 330. Further, because the distal portion 208b of the shaft 208 and the endoscope 330 travel along the same delivery path, the endoscope can provide in-line or side-by-side visualization of the therapeutic assembly 212.

[0063] Similar to the embodiment shown in Figure 3B, Figure 3C illustrates another intraluminal pathway in which the distal portion 208b of the shaft 208 and the endoscope 330 travel next to each other such that the endoscope 330 can provide in-line or side-by-side visualization of the distal portion 208b of the shaft 208, the therapeutic assembly 212, and/or the nasal anatomy. In the embodiment shown in Figure 3C, however, the intraluminal pathway extends through the inferior meatus IM to a posterior treatment site.

[0064] As shown in Figure 3D, in other embodiments the distal portion 208b of the shaft 208 extends to the treatment site via the middle meatus MM, and the endoscope 330 extends through the inferior meatus IM to a position proximate to the target site. In this embodiment, the endoscope 330 may have an articulating, steerable, or curved distal end that directs the endoscope 330 superiorly to visualize the nasal anatomy and the therapeutic

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assembly 332 at the target site. For example, the distal end portion of the endoscope 330 can be configured to bend at least 30° to visualize the treatment site.

[0065] As shown in Figure 3E, in further embodiments the distal portion 208b of the shaft 208 can be delivered to the treatment site via the mouth. In this embodiment, therapeutic neuromodulation can be applied at a treatment site posterior to the nasal cavity (e.g., posterior to the SPF). The endoscope 330 (not shown) can extend into the nasal passage NP, through the middle meatus MM or the inferior meatus IM to a position proximate to the treatment site. Alternatively, the endoscope 330 (not shown) can travel along the same pathway as the shaft 208.

[0066] Figure 4 is an isometric view of a distal portion of a therapeutic neuromodulation device 402 configured in accordance with an embodiment of the present technology. The therapeutic neuromodulation device 402 can be used in conjunction with the system 200 described above with respect to Figures 2-3E. As shown in Figure 4, the therapeutic neuromodulation device 402 can include a shaft 408 having a proximal portion (not shown) and a distal portion 408b, and a therapeutic assembly 412 at the distal portion 408b of the shaft 408. The therapeutic assembly 412 is transformable between a low-profile delivery state to facilitate intraluminal delivery of the therapeutic assembly 412 to a treatment site within the nasal region and an expanded state (shown in Figure 4). The therapeutic assembly 412 includes a plurality of struts 440 that are spaced apart from each other to form a frame or basket 442 when the therapeutic assembly 412 is in the expanded state. The struts 440 can carry one or more energy delivery elements, such as a plurality of electrodes 444. In the expanded state, the struts 440 can position at least two of the electrodes 444 against tissue at a target site within the nasal region (e.g., proximate to the palatine bone inferior to the SPF). The electrodes 444 can apply bipolar or multi-polar radiofrequency (RF) energy to the target site to therapeutically modulate postganglionic parasympathetic nerves that innervate the nasal mucosa proximate to the target site. In various embodiments, the electrodes 444 can be configured to apply pulsed RF energy with a desired duty cycle (e.g., 1 second on/0.5 seconds off) to regulate the temperature increase in the target tissue.

[0067] In the embodiment illustrated in Figure 4, the basket 442 includes eight branches 446 spaced radially apart from each other to form at least a generally spherical structure, and each of the branches 446 includes two struts 440 positioned adjacent to each other. In other embodiments, however, the basket 442 can include fewer than eight branches 446 (e.g., two, three, four, five, six, or seven branches) or more than eight branches 446. In further

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embodiments, each branch 446 of the basket 442 can include a single strut 440, more than two struts 440, and/or the number of struts 440 per branch can vary. In still further embodiments, the branches 446 and struts 440 can form baskets or frames having other suitable shapes for placing the electrodes 444 in contact with tissue at the target site. For example, when in the expanded state, the struts 440 can form an ovoid shape, a hemispherical shape, a cylindrical structure, a pyramid structure, and/or other suitable shapes.

[0068] As shown in Figure 4, the therapeutic assembly 412 can further include an internal or interior support member 448 that extends distally from the distal portion 408b of the shaft 408. A distal end portion 450 of the support member 448 can support the distal end portions of the struts 440 to form the desired basket shape. For example, as shown in Figure 4, the struts 440 can extend distally from the distal potion 408b of the shaft 408 and the distal end portions of the struts 440 can attach to the distal end portion 450 of the support member 448. In certain embodiments, the support member 448 can include an internal channel (not shown) through which electrical connectors (e.g., wires) coupled to the electrodes 444 and/or other electrical features of the therapeutic element 412 can run. In various embodiments, the internal support member 448 can also carry an electrode (not shown) at the distal end portion 450 and/or along the length of the support member 448.

[0069] The basket 442 can transform from the low-profile delivery state to the expanded state (Figure 4) by manipulating a handle (e.g., the handle 210 of Figure 2) and/or other feature at the proximal portion of the shaft 408 and operably coupled to the basket 442. For example, to move the basket 442 from the expanded state to the delivery state, an operator can push the support member 448 distally to bring the struts 440 inward toward the support member 448. An introducer or guide sheath (not shown) can be positioned over the low-profile therapeutic assembly 412 to facilitate intraluminal delivery or removal of the therapeutic assembly 412 from or to the target site. In other embodiments, the therapeutic assembly 412 is transformed between the delivery state and the expanded state using other suitable means.

[0070] The individual struts 440 can be made from a resilient material, such as a shape-memory material (e.g., Nitinol) that allows the struts 440 to self-expand into the desired shape of the basket 442 when in the expanded state. In other embodiments, the struts 440 can be made from other suitable materials and/or the therapeutic assembly 412 can be mechanically expanded via a balloon or by proximal movement of the support member 448. The basket 442 and the associated struts 440 can have sufficient rigidity to support the

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electrodes 444 and position or press the electrodes 444 against tissue at the target site. In addition, the expanded basket 442 can press against surrounding anatomical structures proximate to the target site (e.g., the turbinates, the palatine bone, etc.) and the individual struts 440 can at least partially conform to the shape of the adjacent anatomical structures to anchor the therapeutic element 412 at the treatment site during energy delivery. In addition, the expansion and conformability of the struts 440 can facilitate placing the electrodes 444 in contact with the surrounding tissue at the target site.

[0071] At least one electrode 444 is disposed on individual struts 440. In the illustrated embodiment, two electrodes 444 are positioned along the length of each strut 440. In other embodiments, the number of electrodes 444 on individual struts 440 be only one, more than two, zero, and/or the number of electrodes 444 on the different struts 440 can vary. The electrodes 444 can be made from platinum, iridium, gold, silver, stainless steel, platinum-iridium, cobalt chromium, iridium oxide, polyethylenedioxythiophene ("PEDOT"), titanium, titanium nitride, carbon, carbon nanotubes, platinum grey, Drawn Filled Tubing ("DFT") with a silver core made by Fort Wayne Metals of Fort Wayne, Indiana, and/or other suitable materials for delivery RF energy to target tissue.

[0072] In certain embodiments, each electrode 444 can be operated independently of the other electrodes 444. For example, each electrode can be individually activated and the polarity and amplitude of each electrode can be selected by an operator or a control algorithm (e.g., executed by the controller 218 of Figure 2). Various embodiments of such independently controlled electrodes 444 are described in further detail below with reference to Figures 5A-5G. The selective independent control of the electrodes 444 allows the therapeutic assembly 412 to deliver RF energy to highly customized regions. For example, a select portion of the electrodes 444 can be activated to target neural fibers in a specific region while the other electrodes 444 remain inactive. In certain embodiments, for example, electrodes 444 may be activated across the portion of the basket 442 that is adjacent to tissue at the target site, and the electrodes 444 that are not proximate to the target tissue can remain inactive to avoid applying energy to non-target tissue. Such configurations facilitate selective therapeutic modulation of nerves on the lateral nasal wall within one nostril without applying energy to structures in other portions of the nasal cavity.

[0073] The electrodes 444 can be electrically coupled to an RF generator (e.g., the generator 216 of Figure 2) via wires (not shown) that extend from the electrodes 444, through the shaft 408, and to the RF generator. When each of the electrodes 444 is independently

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controlled, each electrode 444 couples to a corresponding wire that extends through the shaft 408. In other embodiments, multiple electrodes 444 can be controlled together and, therefore, multiple electrodes 444 can be electrically coupled to the same wire extending through the shaft 408. The RF generator and/or components operably coupled (e.g., a control module) thereto can include custom algorithms to control the activation of the electrodes 444. For example, the RF generator can deliver RF power at about 200-300 W to the electrodes 444, and do so while activating the electrodes 444 in a predetermined pattern selected based on the position of the therapeutic element 412 relative to the treatment site and/or the identified locations of the target nerves. In other embodiments, the RF generator delivers power at lower levels (e.g., less than 15 W, 15-50 W, 50-150 W, etc.) and/or higher power levels.

[0074] As shown in Figure 4, the therapeutic assembly 412 can further include one or more temperature sensors 452 disposed on the struts 440 and/or other portions of the therapeutic assembly 412 and configured to detect the temperature adjacent to the temperature sensor 452. The temperature sensors 452 can be electrically coupled to a console (e.g., the console 204 of Figure 2) via wires (not shown) that extend through the shaft 408. In various embodiments, the temperature sensors 452 can be positioned proximate to the electrodes 444 to detect the temperature at the interface between tissue at the target site and the electrodes 444. In other embodiments, the temperature sensors 452 can penetrate the tissue at the target site (e.g., a penetrating thermocouple) to detect the temperature at a depth within the tissue. The temperature measurements can provide the operator or the system with feedback regarding the effect of the therapeutic neuromodulation on the tissue. For example, in certain embodiments the operator may wish to prevent or reduce damage to the tissue at the treatment site (e.g., the nasal mucosa), and therefore the temperature sensors 452 can be used to determine if the tissue temperature reaches a predetermined threshold for irreversible tissue damage. Once the threshold is reached, the application of therapeutic neuromodulation energy can be terminated to allow the tissue to remain intact. In certain embodiments, the energy delivery can automatically terminate based on an evaluation/feedback algorithm (e.g., the evaluation/feedback algorithm 220 of Figure 2) stored on a console (e.g., the console 204 of Figure 2) operably coupled to the temperature sensors 452.

[0075] Figures 5A-5G are isometric views of examples of electrode configurations of therapeutic neuromodulation devices (identified individually as first through fourth therapeutic neuromodulation devices 502a-502d, respectively; referred to collectively as

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therapeutic neuromodulation devices 502) for therapeutic neuromodulation in accordance with embodiments of the present technology. The therapeutic neuromodulation devices 502 of Figures 5A-5G can include features generally similar to the features of the therapeutic neuromodulation device 402 of Figure 4. For example, the therapeutic neuromodulation devices 502 include a plurality of struts 440 that form a basket 442 when in an expanded state, and a plurality of electrodes 444 disposed on one or more of the struts 440. In the illustrated embodiments, the first through third therapeutic neuromodulation device 502a-c shown in Figures 5A-5E include a single strut 440 corresponding to each branch 446 of the basket 442, whereas the fourth therapeutic neuromodulation device 502d shown in Figures 5F and 5G includes two adjacent struts 440 in each branch 446 of the basket 442. In other embodiments, however, the branches 446 of the therapeutic neuromodulation devices 502 may have different quantities of struts 440, and apply RF energy in the same manner as described below with reference to Figures 5A-5G. As shown in Figures 5A-5G, the electrodes 444 can be independently controlled and activated via instructions from a controller (e.g., the controller 218 of Figure 2) or a generator (e.g., the generator 216 of Figure 2) to apply RF energy across selected regions or segments of the therapeutic assembly 412.

[0076] In the embodiment shown in Figure 5A, two electrodes 444 of the therapeutic assembly 412 are activated in the first therapeutic neuromodulation device 502a. More specifically, a first electrode 444a on a first strut 440a is activated at a positive polarity, and a second electrode 444b on a second strut 440b spaced radially apart from the first strut 440a is activated at a negative polarity. The remainder of the electrodes 444 remain inactive. Accordingly, as indicated by the arrows, current can flow from the first electrode 444a to the second electrode 444b through the target tissue across a circumferential or peripheral segment of the therapeutic assembly 412. This configuration may be used to therapeutically modulate nerves positioned proximate to the peripheral segment. In other embodiments, different or additional electrodes 444 can be activated to have a selected polarity to apply therapeutic neuromodulation across selected regions of the therapeutic assembly 412 in a predetermined manner.

[0077] In the embodiment shown in Figure 5B, the first therapeutic neuromodulation device 502a is configured to have three selectively active electrodes 444. A first electrode 444a on a first strut 440a is activated at a positive polarity, and second and third electrodes 444b and 444c on corresponding second and third struts 440b and 440c are activated at a

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negative polarity. The remainder of the electrodes 444 remain inactive. As indicated by the arrows, current can flow through the tissue from the first electrode 444a to the second and third electrodes 444b and 444c across a segment of the therapeutic assembly 412, and therefore therapeutically modulate nerves positioned proximate to the peripheral segment. In the illustrated embodiment, the second and third activated electrodes 444b and 444c are positioned on struts 440b, 440c that are radially spaced apart from but adjacent to the first strut 440a carrying the first active electrode 444a. In other embodiments, however, electrodes 444 positioned on struts 440 spaced further from the first strut 440a to apply energy across a larger and/or wider segment of the therapeutic assembly 412.

[0078] In the embodiment shown in Figure 5C, all of the electrodes 444 in a first hemispherical region 501a of the therapeutic assembly 412 are activated, while the electrodes 444 of the second hemispherical region 501b are not activated. A first electrode on a first strut 440a is selectively activated at a positive polarity, and a plurality of electrodes 444 (identified individually as second through fifth electrodes 444b-444e, respectively) within the first hemispherical region 501a are selectively activated at a negative polarity such that RF energy is applied across the first hemispherical region 501a. This electrode activation configuration may be used to apply RF energy across one side of the basket 442 to therapeutically modulate nerves on the lateral nasal wall in one nostril. When the therapeutic assembly 412 is positioned in the other nostril, a different set of electrodes 444 can be activated across a hemispherical region of the therapeutic assembly 412 based on the orientation of the basket 442 with respect to the lateral nasal wall. Further, because the basket 442 has a generally symmetrical shape (e.g., circular, oval, etc.) and because the electrodes 444 can be selectively activated, the orientation of the basket 442 with respect to the target site on the lateral nasal wall does not matter. Instead, the operator can deploy the therapeutic assembly 412 at the target site irrespective of orientation, and selectively activate the electrodes 444 in a desired arrangement to apply RF energy across the target site.

[0079] In the embodiment shown in Figure 5D, the second therapeutic neuromodulation device 502b is configured to selectively control the polarity of a plurality of the electrodes 444 across at least a portion of the therapeutic assembly 412 to apply RF energy in a sesquipolar fashion (i.e., the sequential or transient bipolar pairing of electrodes). In the illustrated embodiment, a first electrode 444a is biased at a positive polarity and second through seventh electrodes 444b-444g are controlled to have negative polarities. The second through seventh electrodes 444b-444g are spaced substantially equal distances apart from the

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first electrode 444a such that the electrodes 444 are dimensionally predisposed to multiplex in sequence. In operation, the first through seventh electrodes 444a-444g are concurrently activated. However, rather than all of the negative electrodes 444 pairing or multiplexing with the positive first electrode 444a simultaneously, the first electrode 444a will pair with the individual negative electrodes 444 in a sequential manner based on the path of least resistance. This path of least resistance is dictated by the natural anatomy of the treatment site in contact with the electrodes 444. For example, based on the anatomy at the target site, the first electrode 444a may initially pair with the second electrode 444b. After this initial pairing preference has dissipated, a second pairing (e.g., with the third electrode 444c) will occur based on the path of least resistance. The first electrode 444a will continue to sequentially pair with the remaining activated negative electrodes in a similar manner until a threshold is reached and the electrodes 444 are in a state of equilibrium in which there is homogenized current flow between all of the electrode pairs. With each sequential pairing, the therapeutic assembly 412 increases the size of the ablation zone (i.e., the region in which therapeutic neuromodulation energy is applied). As indicated by the numbers 1-6 in Figure 5D, this sequential pairing of the electrodes 444 may occur in a circular direction (e.g., in a counter clockwise or clockwise direction) based on the impedance changes between the electrodes 444. In other embodiments, the sequential pairing of electrodes 444 may occur in a different pattern based on the anatomical surroundings and/or the positioning of the electrodes 444. For example, in the illustrated embodiment, the activated electrodes 444 are positioned in a quadrant of the therapeutic element 412 with equal radial distances between the individual electrode pairs. In other embodiments, the activated electrodes 444 can be positioned across larger or smaller regions of the therapeutic element 412 to apply energy across larger or smaller treatment regions.

[0080] The sesquipolar application of RF energy allows the therapeutic assembly 412 to intelligently apply RF energy across a target site to therapeutically modulate nerves proximate to the treatment site. For example, when in an equidistant radial relationship to each other, the naturally occurring impedance changes between the electrode pairs cause the therapeutic assembly 412 to radially increase the zone of energy application with each pairing. In other embodiments, the electrodes 444 can be configured to sequentially pair with each other in a manner such that the zone of energy application increases in a transverse and/or longitudinal manner based on the naturally occurring impedance changes between the electrodes 444. Further, due to the sequential impedance-based pairing of the electrodes 444,

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the sesquipolar arrangement of the therapeutic assembly 412 can inherently limit the energy applied to tissue at the target site because once the impedance exceeds a threshold in one electrode pairing, the next electrode pairing will occur with a lower impedance. In other embodiments, a controller (e.g., the controller 218 of Figure 2) can include instructions (e.g., software) that provides for the sequential pairing of electrodes in a radial, transverse, longitudinal, and/or spiral manner.

[0081] In further embodiments, portions of the struts 440 themselves can define the electrodes 444. In this embodiment, the struts 440 are made from an electrically conductive material and coated with an insulative material (e.g., poly-xylene polymers, including Paralyene C). Portions of the struts 440 can remain uncoated to define electrodes 444. The locations of the uncoated portions of the struts 440 (i.e., the electrodes 444) can be selected to provide a desired neuromodulation pattern. For example, the uncoated portions can be spaced equally apart from a central electrode 444 to allow for sesquipolar RF application. In this embodiment, the conductive struts 440 serve as the electrical connectors and, therefore, the therapeutic assembly 412 does not require as many wires as if the electrodes 444 were separate elements positioned on the struts 440.

[0082] In the embodiment shown in Figure 5E, the third therapeutic neuromodulation device 502c includes a return electrode 503 at the distal end portion 450 of the support member 448 and selective polarity control of the individual electrodes 444 on the struts 440 to provide radial multiplexing of the electrodes 444. The return electrode 503 has a negative polarity, and the other electrodes 444 have a positive polarity. In the illustrated embodiment, all of the electrodes 444 are activated, but in other embodiments the electrodes 444 can be selectively activated based on a desired energy application zone. As indicated by the arrows, this configuration applies RF energy across a distal hemispherical region of the basket 442. In other embodiments, the return electrode 503 can be positioned elsewhere on the therapeutic assembly 412, and the electrodes 444, 503 can be used to apply RF energy across different regions of the basket 442. In further embodiments, the return electrode 503 can be activated in conjunction with two or more of the electrodes 444 on the struts to apply RF energy in a sesquipolar manner.

[0083] In the embodiment shown in Figure 5F, the fourth therapeutic neuromodulation device 502d includes branches 446 having two adjacent struts 440, and the electrodes 444 on the adjacent struts are spaced apart from each other in a longitudinal direction and selectively activated to apply energy in a radial direction across discrete zones. For example, a first

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electrode 444a on a first strut 440a of a first branch 446a may be selectively activated to have a first polarity and a second electrode 444b on the adjacent second strut 440b of the first branch 446a may be selectively activated to have a second polarity opposite the first polarity. As indicated by the arrows in Figure 5F, the first and second electrodes 444a and 444b can then apply bipolar RF energy in a radial direction within a specific region of the therapeutic assembly 412.

[0084] As further shown in Figure 5F, the individual struts 440 can include multiple electrodes 444 disposed thereon, and the adjacent strut 440 in the same branch 446 can have a corresponding quantity of electrodes 444 to allow for bipolar coupling of each of the electrode pairs along discrete regions of the branch 446. In certain embodiments, the electrodes of one strut 440 can all have the same polarity (e.g., coupled to a first wire; not shown), and the electrodes 444 of the adjacent strut 440 in the same branch 446 can all have the opposite polarity (e.g., coupled to a second wire; not shown). In other embodiments, the electrodes 444 on an individual strut 440 can be independently controlled to have a desired polarity.

[0085] In various embodiments, the electrode pairing configurations shown in Figure 5F can be used to detect impedance across selected regions of the therapeutic assembly 412 defined by the bipolar electrode pairs. The impedance measurements can then be used to identify the presence of neural fibers in the selected regions. If nerves are detected in one or more specific regions associated with an electrode pair, the same electrode pair can be used to apply RF energy to that region and therapeutically modulate the nerves in that region.

[0086] In the embodiment shown in Figure 5G, the fourth therapeutic neuromodulation device 502d is configured to selectively control the polarity of a plurality of the electrodes 444 across at least a portion of the therapeutic assembly 412 to apply RF energy in a multi-polar manner in a circular or spiral pattern. As shown in Figure 5G, electrodes 444 of one branch 446 can be activated to have negative polarities and electrodes 444 of another branch 446 can be activated to have positive polarities. The arrangement of the electrodes 444 and the variable distances between the electrodes 444 can differ such that the energy application zone has a different shape or pattern. In other embodiments, the positive and negative electrodes 444 are spaced apart from each other at variable distances. Impedance changes resulting from the surrounding anatomical structures causes the electrodes to pair with each other in a sequential manner and, thereby, continuously increase

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the zone or region in which energy is applied in a radial direction and in a generally spiral manner.

[0087] Energy generally travels deeper into the adjacent target tissue the further the positive and negative electrode pairs are spaced apart from each other. Thus, the depth of influence of the therapeutic neuromodulation energy is expected to increase as the coupled electrode pairs are spaced further apart from each other on the basket 442. In the embodiment illustrated in Figure 5G, for example, electrode pairs at the distal and proximal regions of the basket 442 apply energy to shallower depths in the target tissue than the electrode pairs positioned on the medial region of the basket 442. Accordingly, the electrodes pairs positioned closer together can therapeutically modulate nerves at shallower depths than the electrode pairs spaced further apart from each other. As shown in the illustrated embodiment, some of the electrodes 444 and/or entire branches 446 of the basket 442 can remain inactive to achieve the desired depth of energy application and/or neuromodulation pattern.

Selected Embodiments of Neural Detection and Mapping

[0088] Various embodiments of the present technology can include features that measure bio-electric, dielectric, and/or other properties of heterogeneous tissue at target sites within the nasal region to determine the presence, location, and/or activity of neural fibers and, optionally, map the locations of the detected nerves. The features discussed below can be incorporated into any of the systems and/or devices disclosed herein to provide an accurate depiction of nerves at the target site.

[0089] Neural detection can occur (a) before the application of a therapeutic neuromodulation energy to determine the presence or location of nerves at the target site and/or record baseline levels of neural activity; (b) during therapeutic neuromodulation to determine the effect of the energy application on the neural fibers at the treatment site; and/or (c) after therapeutic neuromodulation to confirm the efficacy of the treatment on the targeted nerves. Due to the anatomical variations of the number and locations of the parasympathetic neural fibers that innervate the nasal cavity and the numerous access points (e.g., the SPF, accessory foramen, and microforamina) through which they enter the nasal cavity, such neural detection and mapping can provide an accurate representation of the neural anatomy to adequately treat the parasympathetic nerves, not just the one or two main branches of the posterior nasal nerves traversing the SPF.

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[0090] In certain embodiments, the systems disclosed herein can use bioelectric measurements, such as impedance, resistance, voltage, current density, and/or other parameters (e.g., temperature) to determine the anatomy, in particular the neural anatomy, at the target site. The location of the neural anatomy can then be used to determine where the treatment site(s) should be with respect to various anatomical structures for therapeutically effective neuromodulation of the targeted parasympathetic nasal nerves. For example, the information can be used to determine the treatment site(s) with respect to the location of the turbinates or meatuses.

[0091] The bioelectric properties can be detected via electrodes (e.g., the electrodes 444 of the therapeutic neuromodulation devices 402-502d of Figures 4-5G). The electrode pairings on a device (e.g., the therapeutic assemblies 412 described with respect to Figures 4-5G) can be selected to obtain the bioelectric data at specific zones or regions and at specific depths of the targeted regions. Figures 6A and 6B, for example, are partially schematic diagrams illustrating configurations of electrodes 644 for nerve detection configured in accordance with embodiments of the present technology. As shown in Figure 6A, the further the electrodes 644 are apart from each other, the deeper into the tissue the current flows. Accordingly, electrodes 644 can be selectively activated based on the depth at which the desired measurements should be taken. As shown in Figure 6B, the spacing between the electrodes 644 along a plane (e.g., the surface of the tissue, can affect the region in which the measurements are taken. Thus, electrodes 644 can be selectively activated to obtain information (e.g., impedance) at a desired depth and across a desired region. In other embodiments, the bioelectric properties can be detected using optical coherent tomography (OCT), ultrasound, and/or other suitable detection modalities.

[0092] The measurement of bioelectric properties can provide information associated not only with neural fiber locations, but also the identification of gross anatomy (e.g., turbinates, meatuses, bone, etc.), which can be used to facilitate system delivery and identification of the target nerves with respect to the gross anatomy. For example, gross target identification can be determined by evaluating of the incident electromagnetic field on soft and hard tissues within the nasal region, which is in turn dependent upon the local geometry and the dielectric properties of those features. For example, because of the layered structure of the anatomy of the nasal cavity (e.g., nasal mucosa, submucosa, periosteum, and bony plates), there are large distinctions in the relative conductance of the soft and hard

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tissues that can be used to differentiate the "deeper" mucosal tissue on the turbinates from the "shallow" tissue off the turbinates.

[0093] In certain embodiments, measurements for neuro-mapping can be obtained by applying a constant current to electrodes and measuring the voltage differences between adjacent pairs of electrodes to produce a spectral profile or map the tissues at the target site. Impedance data can be obtained while applying high, medium, and/or low frequencies to the target tissue. At high frequencies, the current passes directly through cell membranes, and the resultant measurements are indicative of the tissue and liquids both inside and outside the cells. At low frequencies, cell membranes impede current flow to provide different defining characteristics of the tissue. Accordingly, bioimpedance can be used to measure targeted shapes or electrical properties of tissue and/or other structures of the nasal cavity. In addition, complex neural mapping can be performed using frequency difference reconstruction, which requires measurement data (e.g., impedance) at two different frequencies.

[0094] When detecting neural locations and activity via bioelectric properties, the spatial orientation, direction, and activity of the detected nerve bundles can be used to further identify and characterize the nerves. For example, the measured bioelectric properties can distinguish between terminating axons (i.e., entering a detection region, but not exiting), branching axons (i.e., entering the detection region and increasing in number upon exiting the detecting region), travelling axons (i.e., entering and exiting the detection region within no change in geometry or numerical value), and/or other properties of nerves. In addition, axon orientations relative to the electrode array can be identified to indicate whether the neural fibers extend parallel (X direction), perpendicular (Y direction), depth penetrating (Z direction), and/or any relative position or angulation to these parameters. This information can then be used to selectively treat specific neural fibers. For example, selected electrode configurations can be applied to treat a specific region and/or the therapeutic assembly can be moved or manipulated to treat the nerves from a different orientation or location.

[0095] In certain embodiments, temperature measurements can be taken to determine the effect of therapeutic neuromodulation on nasal tissue. Figure 7, for example, is a graph illustrating threshold levels of electrical conductivity of nasal tissue with respect to temperature. A first curve 701 depicts the electrical conductivity (σ) of tissue in response to temperature and indicates that a temperature of about 70°C corresponds to a first threshold of the irreversible change in impedance of the tissue. A second curve 703 shows that the

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electrical conductivity of the tissue permanently increases significantly (i.e., impedance decreases) after the tissue has been exposed to temperatures of 70°C, as it may during therapeutic neuromodulation. If the therapeutic neuromodulation was stopped when the tissue temperature was detected to be about 70°C, it is expected that there would be a permanent measurable change in the conductivity of the tissue without reaching a phase in which the tissue is structurally changed or damaged (e.g., due to vaporization, desiccation, etc.). However, if the tissue is exposed to temperatures above a second thermal threshold of about 90°C, the tissue undergoes a high degree of tissue desiccation, and thus a significant decrease in electrical conductivity (i.e., and a higher level of in the electrical impedance). A third curve 705 illustrates this lower electrical conductivity of the tissue after exposure to temperatures above 90°C. Accordingly, in various embodiments, systems disclosed herein can be configured to stop neuromodulation when the temperature reaches about 70°C (e.g., 70-80°C) to avoid structural changes or damage to the mucosa, but still providing what is expected to be therapeutically effective neuromodulation.

[0096] Neural detection and mapping can provide a pre-procedural assessment of the neural anatomy, a mid-procedure assessment and feedback on temporal changes in tissue during neuromodulation, and/or a post procedural assessment of the neural activity as a confirmation of effectiveness. In various embodiments, the bioelectric measurements taken pre-, mid-, and post-procedurally can be taken multiple times during each stage of the procedure to assess and confirm findings. Pre-procedural assessment can be used to evaluate the bioelectric properties of the native/host tissue to determine a baseline for subsequent actions and as a reference guide against source biological signatures to identify anatomical targets of interest (e.g., nerves, microforamina, etc.). This information can be determined by placing a multi-electrode array in a known spatial configuration to detect and then map electro-anatomical characteristics (e.g., variations in the impedance of different tissue types). The resultant anatomical mapping can comprise a composition of multiple (high density) activation sequence in multiple planes, relying on the variations in impedance to identify different tissue types and structures. During the procedure, the impedance measurements can be used to confirm that the electrodes maintain good contact with tissue at the target site. During and after the procedure, the data can be used to determine whether the mid- or post-procedural recorded spectra has a shape consistent with the expected tissue types. Post-procedurally, the information can be used to determine whether the targeted nerves were therapeutically treated.

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[0097] In other embodiments, the action potentials of neural fibers can be detected via electrodes and or other contacts to dynamically map the locations and/or activity of nerves in the target region. For example, the recorded action potentials can be used to numerically measure, map, and/or produce images of fast neuronal depolarization to generate an accurate picture of neural activity. In general, the depolarization of the neuronal membrane can cause drops in voltage of about 110 μV, has about 2 ms, and have an impedance/resistance from 1000 Ω cm to 25 Ω cm. In further embodiments, the metabolic recovery processes associated with action potential activity (i.e., to restore ionic gradients to normal) can also be detected and used for dynamically mapping nerves at the target site. The detection of the bioelectric properties associated with these features has the advantage that the changes are much larger (e.g., approximately a thousand times larger) and, therefore, easier to measure.

[0098] In various embodiments, a nontherapeutic stimulation (e.g., RF energy) can be applied to the tissue at the detection region via two or more electrodes of an electrode array to enhance the recording of action potentials. The stimulating energy application can temporarily activate the neural fibers and the resultant action potential can be recorded. For example, two or more electrodes of a therapeutic assembly can deliver a stimulating pulse of energy, and two or more other electrodes can be configured to detect the resultant action potential. The stimulating energy pulses are expected to enhance the action potential signal, making it easier to record.

Selected Embodiments of Therapeutic Neuromodulation Devices

[0099] Figures 8 and 9 are isometric views of a distal portion of a therapeutic neuromodulation device 802 ("device 802") configured in accordance with an embodiment of the present technology. The device 802 can include various features generally similar to the features of the therapeutic neuromodulation devices 402 and 502a-d described above with reference to Figures 4-5G. For example, the device 802 includes a therapeutic assembly 812 at a distal portion 408b of a shaft 408. The therapeutic assembly 812 includes a plurality of struts 440 that form branches 446 and define an expandable frame or basket 442, and one or more electrodes 444 disposed on one or more of the struts 440. As shown in Figures 8 and 9, the device 902 can further include an expandable member 856 (e.g., a balloon) carried by the support member 448 and expandable within the basket 442. The expandable member 856 can include a plurality of electrodes 858 disposed on the outer surface of the expandable member 856. The electrodes 858 can be used for detection of bioelectric features (e.g.,

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impedance) to allow for mapping of the neural anatomy at the target site before, during, and/or after therapeutic neuromodulation via the other electrodes 444. In other embodiments, the electrodes 858 can be configured to apply energy for therapeutic neuromodulation.

[00100] As shown in Figures 8 and 9, the electrodes 858 can be positioned on the expandable member 856 in a substantially symmetrical manner and a uniform distribution. This provides an expansive array with which impedance and/or other properties can be detected across the tissue and, therefore, may provide a more detailed mapping of the tissue and nerves at the treatment site. In other embodiments, the electrodes 858 can be clustered toward the medial portion of the expandable member 856 and/or around different portions of the expandable member 856. In certain embodiments, the electrodes 858 can be selectively activated at a specific polarity, and therefore the electrode array can be configured in a variety of static configurations and a dynamically change sequences (e.g., sesquipolar application of current) that may be advantageous for mapping functions.

[00101] In operation, the expandable member 856 can be inflated or otherwise expanded (Figure 9) to place at least a portion of the electrodes 858 into contact with tissue at the target site. The electrodes 858 can measure various bioelectric properties of the tissue (e.g., impedance, action potentials, etc.) to detect, locate, and/or map the nerves at the treatment site. In certain embodiments, the electrodes 444 on the struts 440 and/or a portion of the electrodes 858 on the expandable member 856 can apply a stimulating pulse of RF energy, and the electrodes 858 can detect the resultant neural response. After mapping, the expandable member 856 can be deflated or collapsed (Figure 8), and the electrodes 444 on the struts 440 can apply therapeutically effective neuromodulation energy to the target site. For example, the ablation pattern of the electrodes 444 can be based on the neural locations identified via the information detected from the sensing electrodes 858 on the expandable member 856. In other embodiments, the expandable member 856 may remain expanded during neuromodulation, and the electrodes 858 can detect neural activity during the neuromodulation procedure or the electrodes 858 can themselves be configured to apply neuromodulation energy to the treatment site. After applying the neuromodulation energy, the electrodes 858 on the expandable member 856 can again be placed into contact with tissue at the target site, and used to record bioelectric properties (e.g., impedance). The detected properties (e.g., impedances) taken before, during, and/or after neuromodulation can be compared to each other to determine whether the neuromodulation was therapeutically effective. If not, the electrodes 444 can again apply therapeutic neuromodulation energy to

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the same treatment site, or the configuration of the active electrodes 444 can be changed to apply therapeutic neuromodulation energy in a different pattern or sequence, and/or the therapeutic assembly 812 can be moved to a different treatment site.

[00102] Figure 10A is an isometric view of a distal portion of a therapeutic neuromodulation device 1002 ("device 1002") configured in accordance with another embodiment of the present technology, and Figure 10B is an isometric view illustrating the therapeutic neuromodulation device 1002 of Figure 10A at a treatment site. The device 1002 can include various features generally similar to the features of the therapeutic neuromodulation devices 402, 502a-d, and 802 described above with reference to Figures 4-5G, 8 and 9. For example, the device 1002 includes a shaft 1008 and a therapeutic assembly 1012 at a distal portion 1008b of the shaft 1008. The therapeutic assembly 1012 includes a plurality of struts 1040 that form branches 1046 and define an expandable frame or basket 1042, and one or more electrodes 1044 disposed on one or more of the struts 1040. As shown in Figure 10A, the device 1002 can further include a secondary or return electrode 1060 disposed along the distal portion of the shaft 1008. In the illustrated embodiment, the return electrode 1060 is a ring electrode having a ring-like shape, but in other embodiments the return electrode 1060 may have other shapes or configurations.

[00103] The return electrode 1060 may be biased at a negative polarity, and at least a portion of the electrodes 1044 on the struts 1040 and/or on other portions of the therapeutic assembly 1012 may be biased at a positive polarity. As indicated by the arrows in Figure 10A, bipolar RF energy can flow across a region spanning from the therapeutic assembly 1012 to the return electrode 1060 on this distal portion 1008b of the shaft 1008. In various embodiments, the RF energy can be applied in a sesquipolar manner (i.e., imbalanced bipolar energy).

[00104] As shown in Figure 10B, the therapeutic assembly 1012 can be positioned inferior to the SPF and superior to the inferior turbinate IT and at least a portion of the microforamina MF and nerves N traversing the palatine bone. The return electrode 1060 can be positioned inferior to the inferior turbinate IT and at least a portion of the microforamina MF and nerves N traversing the palatine bone. RF energy can then be applied across a wide region spanning from the therapeutic assembly 1012 to the return electrode 1060. As shown in Figure 10B, for example, the device 1002 can apply energy across the top and bottom portions of the inferior turbinate, where a high density of microforamina reside.

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[00105] Figures 11A-11D are isometric views illustrating distal portions of therapeutic neuromodulation devices 1102 (referred to individually as a first device 1102a and a second device 1102b) configured in accordance with further embodiments of the present technology. The first device 1102a can include various features generally similar to the features of the therapeutic neuromodulation devices 402, 502a-d, 802 and 1002 described above with reference to Figures 4-5G and 8-10B. For example, the first device 1102a includes a shaft 1108 and a therapeutic assembly 1112 at a distal portion 1108b of the shaft 1108. The therapeutic assembly 1112 includes a flexible membrane 1162 that carries a plurality of electrodes 1144 and/or other energy delivery elements arranged in an array across the flexible membrane 1162.

[00106] As shown in Figures 11A-11C, the flexible membrane 1162 can be configured to transform from a low-profile delivery state (Figure 11A), to an expanded state (Figure 11B) via self-expansion or mechanical expansion means, and back to the low-profile delivery or retrieval state (Figure 11C) for removal of the device from the nasal cavity. In the expanded state shown in Figure 11B, the flexible membrane can conform to the irregular anatomy of the nasal space (e.g., turbinates, sinus, and/or other para-nasal) to enhance the contact area between the flexible membrane 1162 (and the electrodes 1144 disposed thereon) with the non-planar anatomy. The flexible membrane 1162 can be made from a flexible and dynamic material to support the electrodes 1144. For example, in certain embodiments the flexible membrane 1162 can comprise polymer filaments and/or other materials that add support and structure to the flexible membrane 1162. In various embodiments, the flexible membrane 1162 can have pre-set geometry to retain a predetermined shape. For example, the flexible membrane 1162 and/or the electrode array on the flexible membrane 1162 can retain spherical curvature (e.g., as shown in Figure 11A).

[00107] In various embodiments, the shaft 1108 can be movable relative to the flexible membrane 1162 to allow for deployment and recapture of the flexible membrane 1162. For example, the flexible membrane 1162 may be curled or otherwise folded into a circular shape when in the delivery state (Figure 11A). To move to the expanded state (Figure 11B), components of the shaft 1108 can be rotated and/or moved axially relative to the flexible membrane 1162 to unwind or otherwise expand the flexible membrane 1162 such that the flexible membrane 1162 at least partially opens and conforms to the structures of the surrounding anatomy to place the electrodes 1144 into contact with tissue at the target site.

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To recapture the device to the retracted state (Figure 11C), the shaft 1108 can again be moved axially or rotational manner to close wind or otherwise fold the flexible membrane 1162.

[00108] As shown in Figures 11A-11C, the electrodes 1144 may be interconnected through a plurality of connectors 1164, such as nano-ribbons, nano-wires, direct inking, multidirectional printing/deposition, and/or other suitable electrical connectors. In various embodiments, the interconnections 1164 between the electrodes 1144 can include periodic undulating conduits or lines having a "U", "S", or elliptical shapes. These undulating connectors 1164 may form a multidimensional spring within the flexible membrane 1162 and/or impose a predetermined shape on the flexible membrane 1162 that facilitates apposition of the flexible membrane 1162 to the tissue at the target site to improve energy conductivity/transference.

[00109] The electrodes 1144 may be surface mounted on the flexible membrane 1162 or embedded within a multi-layered composite structure of the flexible membrane 1162. In various embodiments, the electrodes 1144 may be relatively small in size, having diameters ranging from 50-2,000 microns. The electrodes 1144 may be configured to deliver energy in a mono-polar, bipolar, or multipolar manner. For example, multipolar electrodes can be used in a bipolar arrangement and in a quad-polar arrangement to facilitate a linear and an angulated (diagonal) energy connectivity between the electrodes 1144.

[00110] The electrodes 1144 can be connected to a connection pad (not shown) housed within the shaft 1108 and/or features connected to proximal portions of the shaft 1108, such as a handle or console. The electrodes 1144 can be connected to the connection pad through a conductive connector cable (e.g., a metallic cable, a polymeric cable, and/or combinations thereof).

[00111] In certain embodiments, the flexible membrane 1162 may also house a feedback system (not shown) to control the delivery of the RF energy and maintain predefined treatment parameters. For example, the electronic circuits of the flexible membrane 1162 may include thermal sensors that provide temperature feedback to control energy dissipation and depth penetration of the RF energy. The features of electronic circuits of the flexible membrane 1162 may also measure resistance and temperature at the treatment site to determine the effects of the therapeutic energy application. This information may be used to regulate energy application and avoid collateral damage to host tissue. For example, energy delivery via the electrodes 1144 may be automatically terminated if the detected temperature

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and/or resistance reaches a predetermined threshold maximum (e.g., a threshold temperature associated with tissue damage). Energy delivery via the electrodes 1144 may be automatically or manually adjusted if the detected temperature and/or resistance is below a predetermined threshold range indicative of parameters associated with therapeutically effective modulation of the parasympathetic nasal nerves. In other embodiments, the feedback system can be incorporated to components communicatively coupled with the electrodes 1144 and any additional sensors on the flexible membrane 1162. For example, the feedback system can be stored on the console 204 of Figure 2 and executed by the controller 218 (Figure 2).

[00112] In the embodiment shown in Figure 11D, the second device 1102b can include various features generally similar to the features of the first device 1102a described above with reference to Figures 11A-11C. For example, the device 1102b of Figure 11D includes the flexible membrane 1162 that carries a plurality of electrodes 1144 and associated electrical connectors 1164 disposed on or embedded in the flexible membrane 1162. The device 1102b further includes an expandable frame 1166 carrying the flexible membrane 1162. The frame 1166 may have a U-shape and can be made from a shape memory material (e.g., Nitinol). In other embodiments, the frame may have different shapes and/or be made from different materials suitable for supporting the flexible membrane 1162.

[00113] In operation, the frame 1166 facilitates the deployment of the flexible membrane 1162 against the anatomy of the nasal cavity, and provides support for the flexible membrane 1162 and the associated array of electrodes 1144. The U-shaped frame 1166 can enhance the ability of the flexible membrane 1162 to contact the non-planar anatomy at the target site. In various embodiments, for example, the frame 1166 may act as a cantilever spring to establish a positive directional apposition of the membrane 1162 to the target surface tissue to improve energy conductivity/transference from the electrodes 1144 to the target tissue.

[00114] Figure 12 is a side view of a distal portion of a therapeutic neuromodulation device 1202 ("device 1202") configured in accordance with a further embodiment of the present technology. The device 1202 includes include various features generally similar to the features of the therapeutic neuromodulation devices 402, 502a-d, 802, 1002 and 1102 described above with reference to Figures 4-5G and 8-11. For example, the device 1202 includes a shaft 1208 and a therapeutic assembly 1212 including a plurality of energy delivery elements, such as electrodes 1244, at a distal portion 1208b of the shaft 1208. In the illustrated embodiment, the therapeutic assembly 1212 includes four electrodes 1244 are

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arranged along a spiral/helical section 1268 at the distal portion 1208b of the shaft 1208. In other embodiments, however, the therapeutic assembly 1212 may include one, two, three, or more than four electrodes 1244, and/or may include different energy delivery elements. The therapeutic assembly 1212 can also include a temperature sensor 1252 (e.g., a thermocouple) and/or other type of sensor to detect various properties at the treatment site before, during, and/or after applying therapeutic neuromodulation energy, and provide feedback that may be used to control the operation of the therapeutic assembly 1212. Such sensors can be incorporated in any of the other embodiments of therapeutic assemblies disclosed herein.

[00115] During delivery of the therapeutic assembly 1212, the spiral/helical section 1168 of the shaft 1208 is positioned in a low-profile delivery state in which the section 1268 is substantially straitened or flattened within an introducer sheath and/or via mechanical components associated with the shaft 1208. At the target site, the operator can transform the spiral/helical section 1268 to an expanded state (shown in Figure 12) to place one or more of the electrodes 1244 in contact with the target tissue. One or more of the electrodes 1244 can then be selectively activated to apply RF energy (e.g., monopolar and/or bipolar RF energy) to tissue at a target site in the nasal region to therapeutically modulate nerves proximate to the treatment site. In other embodiments, the distal section of the shaft 1208 can have other suitable shapes, sizes, and/or configurations that facilitate placing the electrodes 1244 in contact with tissue at the target site. For example, in further embodiments, the distal portion 1208b of the shaft 1208 can have a semi-circular, curved, bent, or straight shape and/or the therapeutic assembly 1212 can include multiple support members configured to carry one or more of the electrodes 1244.

[00116] Figure 13 is a side view of a distal portion of a therapeutic neuromodulation device 1302 ("device 1302") configured in accordance with a still further embodiment of the present technology. The device 1302 includes include various features generally similar to the features of the therapeutic neuromodulation devices 402, 502a-d, 802, 1002, 1102 and 1202 described above with reference to Figures 4-5G and 8-12. For example, the device 1302 includes a shaft 1308 and a therapeutic assembly 1312 including a plurality of energy delivery elements, such as an array of electrodes 1344, at a distal portion 1308b of the shaft 1308. In the embodiment illustrated in Figure 13, the therapeutic assembly 1312 includes a balloon 1370 that carries the electrodes 1344. A support member 1372 can extend through the length of the balloon 1370 to support the balloon 1370 and, optionally, include a channel through which a guidewire (not shown) can extend to facilitate delivery of the therapeutic

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assembly 1312 to the target site. In other embodiments, the support member 1372 may be omitted.

[00117] The electrodes 1344 can be made from conductive ink that is printed, sprayed, and/or otherwise disposed on the surface of the balloon 1370. Such conductive ink electrodes facilitates the use of complex electrode configurations. In addition, thermocouples (not shown) can also be incorporated onto the surface of the balloon 1370 using conductive ink and/or other suitable methods. In other embodiments, the electrodes 1344 can be made from foil and adhered to the surface of the balloon 1370. In further embodiments, the electrodes 1344 can be made from other suitable materials that may be disposed on the surface of the balloon 1370 and/or embedded within the material of the balloon 1370.

[00118] The balloon 1370 can be made from various different materials and have various different shapes. As shown in Figure 13, for example, the balloon 1370 can have an ovoid shape when in the expanded state, which is expected to improve the conformance to anatomical variations at the target site within the nasal cavity. In other embodiments, the balloon 1370 can have a circular shape, a spherical shape, an irregular shape, and/or other suitable shape for expansion within the nasal anatomy. The balloon 1370 can be made from a compliant material (e.g., a urethane material) that allows the balloon 1370 to conform to anatomical variances when expanded within the nasal region. In other embodiments, the balloon may be made from a non-compliant material (e.g., polyethylene terephthalate, nylon, etc.) that allows the balloon 1370 to have a defined shape when expanded and facilitates the attachment of electrodes 1344 to the balloon surface. In further embodiments, the balloon 1370 may be dip-coated and form a bulbous tip at the distal end of the shaft 1308.

[00119] The balloon 1370 may be inflated with a fluid via an opening or port 1374 in the support member 1372 and/or an opening in the shaft 1308 in fluid communication with the interior of the balloon 1370. For example, the support member 1372 and/or the shaft 1308 can include a channel extending along the length of the shaft 1308 and connected to a fluid supply at the proximal portion of the shaft 1308 such that fluid can be delivered to the balloon 1370. The balloon 1370 can inflate against the nasal anatomy at the target site to places the electrodes 1344 in contact with tissue at the target site.

[00120] At the target site, the electrodes 1344 deliver RF energy to tissue to therapeutically modulate nerves at the treatment site. In certain embodiments, the array of electrodes 1344 can be arranged on the balloon 1370 and/or selectively activated to apply

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transverse bipolar RF energy across a radial regions of the balloon 1370 (i.e., extending around circumferential portions of the balloon 1370). In other embodiments, the array of electrodes 1344 can be arranged on the balloon 1370 and/or selectively activated to apply longitudinal bipolar RF energy across longitudinal regions of the balloon 1370 (i.e., extending between proximal and distal portions of the balloon 1370).

[00121] In various embodiments, the therapeutic assembly 1312 may include features that facilitate with positioning of the balloon 1370 within the nasal anatomy and proper placement of the electrodes 1344 at the treatment site. As shown in Figure 13, for example, an endoscope 1371 may be positioned on the surface of the balloon 1370 to provide direct, in-line visualization of the balloon 1370 and the target site during placement at the target site. The therapeutic assembly 1312 can also include graduated markings 1373 along the support member 1372 and/or the surface of the balloon 1370 to depict spatial orientation and/or depth positioning of the therapeutic assembly 1312.

[00122] In certain embodiments, the balloon 1370 can be configured to allow for a slow perfusion of fluid through the balloon wall to cool the electrodes 1344 while energy is applied to the target tissue. For example, such a "weeping" balloon 1370 can include laser-driller holes and/or other small openings or pores along at least a portion of the balloon 1370 to allow for the slow perfusion of a fluid (e.g., saline solution) through the balloon wall. When the balloon perfuses saline solution, the saline solution is expected to improve the electrical conductivity between the electrodes 1344 and the target tissue and may enhance the effect of the RF energy on the nerves at the target site. In other embodiments, a cooled fluid can be circulated through the balloon 1470 during activation of the electrodes 1444 to cool the electrodes 1444 and the surrounding tissue during energy delivery.

[00123] Figure 14 is a side view of a distal portion of a therapeutic neuromodulation device 1402 ("device 1402") configured in accordance with an additional embodiment of the present technology. The device 1402 includes include various features generally similar to the features of the therapeutic neuromodulation device 1302 described above with reference to Figure 13. For example, the device 1402 includes a shaft 1408 and a therapeutic assembly 1412 at a distal portion 1408b of the shaft 1408. The therapeutic assembly 1412 includes a balloon 1470, a support member 1472 supporting the balloon 1470, and a plurality of energy delivery elements, such as an array of electrodes 1444 disposed on the balloon 1470. In the embodiment illustrated in Figure 14, the electrodes 1444 are part of a flex circuit 1476 adhered to the surface of the balloon 1470. The flex circuit 1476 facilitates the creation of

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complex electrode arrays that can create highly customizable neuromodulation patterns. In certain embodiments, for example, the flex circuit 1476 can include a conductive return electrode along the surface of the balloon 1470 and a plurality of electrodes on a proximal or distal portion of the balloon 1470 (e.g., a conical end portion of the balloon 1470). In addition, the flex circuit 1476 can incorporate thermocouples and/or thermistors into the circuitry on the surface of the balloon 1470 to detect temperature at the treatment site before, during, and/or after energy application.

[00124] Figure 15 is an isometric side view of a distal portion of a therapeutic neuromodulation device 1502 ("device 1502") configured in accordance with an additional embodiment of the present technology. The device 1502 includes include various features generally similar to the features of the therapeutic neuromodulation devices 1302 and 1402 described above with reference to Figures 13 and 14. For example, the device 1502 includes a shaft 1508 and a therapeutic assembly 1512 at a distal portion 1508b of the shaft 1508. The therapeutic assembly 1512 includes a plurality of balloons 1578 positioned around an inner support member 1580, and a plurality of energy delivery elements, such as electrodes 1544 disposed on one or more of the balloons 1578. In certain embodiments, the balloons 1578 are independently inflatable. This allows for asymmetrical or variable inflation of the balloons 1578 and, thereby, enhances the ability of the therapeutic assembly 1512 to conform to the irregular geometry of the nasal region at the target site and facilitates apposition of the electrodes 1544 against tissue at the target site.

[00125] In the illustrated embodiment, four independently inflated balloons 1578 are positioned around the perimeter of the inner support member 1580. In other embodiments, however, the device 1502 can include less than four balloons 1578 or more than four balloons 1578 arranged around the inner support member 1580. In further embodiments, the balloons 1578 can have different sizes and/or shapes, and can be positioned along various portions of the inner support member 1580. In still further embodiments, the balloons 1578 re configured as struts that are attached at end portions to the inner support member 1580 and extend outwardly away from the inner support member 1580 when inflated (e.g., in a similar manner as the struts 440 of the therapeutic neuromodulation device 402 of Figure 4).

[00126] During energy delivery, the electrodes 1544 can be configured to apply bipolar RF energy across the electrodes 1544 on different balloons 1578 and/or between electrodes 1544 on the same balloon 1578. In other embodiments, the electrodes 1544 apply energy in a sesquipolar manner. For example, the inner support member 1580 can include a return

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electrode (not shown), and the electrodes 1544 on two or more of the balloons 1578 may be activated for sesquipolar RF energy delivery.

[00127] Figure 16 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device 1602 ("device 1602") configured in accordance with an additional embodiment of the present technology. The device 1602 includes various features generally similar to the features of the therapeutic neuromodulation devices described above. For example, the device 1602 includes a shaft 1608 and a therapeutic assembly 1612 at a distal portion 1608b of the shaft 1608. In the embodiment illustrated in Figure 16, the therapeutic assembly 1612 is configured to apply cryotherapeutic cooling to therapeutically modulate nerves at the target site. As shown in Figure 16, the cryotherapeutic assembly 1612 can include an expansion chamber 1682 (e.g., a balloon, inflatable body, etc.) in fluid communication with one or more supply tubes or lumens 1684 via corresponding orifices 1686 in the supply lumens 1684. The supply lumens 1682 can extend along at least a portion of the shaft 1608 and be configured to transport a refrigerant in an at least a partially liquid state to the distal portion 1608b of the shaft 1608. An exhaust tube or lumen 1689 (e.g., defined by a portion of the shaft 1608) can be placed in fluid communication with the interior of the expansion chamber 1682 via an outlet 1688 such that the exhaust lumen 1689 can return the refrigerant to the proximal portion of the shaft 1608. For example, in one embodiment, a vacuum (not shown) at the proximal portion of the shaft 1608 may be used to exhaust the refrigerant from the expansion chamber 1682 via the exhaust lumen 1689. In other embodiments, the refrigerant may be transported to the proximal portion of the shaft 1608 using other suitable mechanisms known to those having skill in the art.

[00128] During cryotherapy, the orifices 1686 of the supply lumens 1684 can restrict refrigerant flow to provide a high pressure differential between the supply lumen 1684 and the expansion chamber 1682, thereby facilitating the expansion of the refrigerant to the gas phase within the expansion chamber 1682. The pressure drop as the liquid refrigerant passes through the orifices 1682 causes the refrigerant to expand to a gas and reduces the temperature to a therapeutically effective temperature that can modulate neural fibers proximate a treatment site within the nasal cavity. In the illustrated embodiment, the expansion chamber 1682 includes heat transfer portions 1691 that contact and cool tissue at the target site at a rate sufficient to cause cryotherapeutic neuromodulation of postganglionic parasympathetic neural fibers that innervate the nasal mucosa. For example, the therapeutic assembly 1602 can operate at temperatures of -40°C, -60°C, -80°C, or lower. In other

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embodiments, the therapeutic assembly 1602 can operated at higher cryotherapeutic temperatures (e.g., 5°C and -15°C, -20°C, etc.).

[00129] The refrigerant used for cryogenic cooling in the device 1602 can be a compressed or condensed gas that is stored in at least a substantially liquid phase, such as nitrous oxide (N_2O), carbon dioxide (CO_2), hydrofluorocarbon (e.g., FREON made available by E. I. du Pont de Nemours and Company of Wilmington, DE), and/or other suitable fluids that can be stored at a sufficiently high pressure to be in at least a substantially liquid phase at about ambient temperature. For example, R-410A, a zeotropic, but near-azeotropic mixture of difluoromethane (CH_2F_2; also known as HFC-32 or R-32) and pentafluoroethane (CHF_2CF_3; also known as HFC-125 or R-125), can be in at least a substantially liquid phase at about ambient temperature when contained at a pressure of about 1.45 MPa (210 psi). Under proper conditions, these refrigerants can reach cryotherapeutic temperatures at or near their respective normal boiling points (e.g., approximately -88°C for nitrous oxide) to effectuate therapeutic neuromodulation.

[00130] In other embodiments, the therapeutic assembly 1612 can include a cryotherapeutic applicator rather than the expansion chamber 1682 of Figure 16. Such a cryotherapeutic applicator can be used for very targeted treatment of the nerves.

[00131] As further shown in Figure 16, the device 1602 can also include a support member 1690 extending through the expansion chamber 1682 and configured to carry the distal portion of the expansion chamber 1682. The support member 1690 can also include a channel extending along its length and an opening 1692 at the distal end portion of the support member 1690 to facilitate delivery of the therapeutic assembly 1612 to the treatment site via a guidewire GW.

[00132] Figure 17 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device 1702 ("device 1702") configured in accordance with an additional embodiment of the present technology. The device 1702 includes various features generally similar to the features of the therapeutic neuromodulation devices described above. For example, the device 1702 includes a shaft 1708 and a therapeutic assembly 1712 at a distal portion 1708b of the shaft 1708. In the embodiment illustrated in Figure 17, the therapeutic assembly 1712 is configured to apply direct conductive heating to thermally therapeutically modulate nerves at the target site. As shown in Figure 17, the therapeutic assembly 1712 can include a balloon 1770 in fluid communication with a supply tube or lumen 1794 (e.g.,

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defined by a portion of the shaft 1708) via an outlet at a distal portion of the supply lumen 1794. The supply lumen 1794 can extend along at least a portion of the shaft 1708 and be insulated to transport a heated fluid (e.g., heated saline) to the balloon 1770 at the distal portion 1708b of the shaft 1708. An exhaust or return tube or lumen 1796 (e.g., defined by a portion of the shaft 1708) can be placed in fluid communication with the interior of the balloon 1770 via an outlet such that the return lumen 1796 can exhaust the fluid to the proximal portion of the shaft 1708 (e.g., using a vacuum at the proximal portion of the shaft 1708).

[00133] During thermal therapeutic neural modulation, the supply lumen 1794 can supply a heated fluid to the balloon 1770, and the exhaust lumen 1796 can be used to exhaust the fluid from the balloon 1770 such that the heated fluid circulates through the balloon 1770 (e.g., as indicated by the arrows). The heated fluid can be heated to a therapeutically effective temperature that causes time-dependent thermal damage (e.g., determined using the Arrhenius equation) to the target tissue at a treatment site within the nasal cavity and modulates neural fibers within or proximate to the heated target tissue. In the illustrated embodiment, for example, the wall of the balloon 1770 and/or portions thereof can contact and heat tissue at the target site at a rate and time sufficient to cause thermal damage to the target tissue to provide therapeutic neuromodulation of postganglionic parasympathetic neural fibers that innervate the nasal mucosa.

[00134] As shown in Figure 17, the device 1702 can also include a support member 1790 extending through the balloon 1770 and configured to carry the distal portion of the balloon 1770. The support member 1790 can also include a channel extending along its length and an opening 1792 at the distal end portion of the support member 1790 that can be used to facilitate delivery of the therapeutic assembly 1712 to the treatment site via a guidewire GW.

[00135] Figure 18 is a cross-sectional side view of a distal portion of a therapeutic neuromodulation device 1802 ("device 1802") configured in accordance with an additional embodiment of the present technology. The device 1802 includes various features generally similar to the features of the therapeutic neuromodulation devices described above. For example, the device 1802 includes a shaft 1808 and a therapeutic assembly 1812 at a distal portion 1808b of the shaft 1808. The therapeutic assembly 1812 can include an inflatable balloon 1870 and a support member 1890 extending through the balloon 1870. The support member 1890 may also include a channel with an opening 1892 that allows for guidewire delivery of the therapeutic assembly 1812 to the treatment site.

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[00136] Similar to the therapeutic assembly 1712 of Figure 17, the therapeutic assembly 1812 can apply therapeutically effective heating to tissue at a target site to cause time-dependent thermal tissue damage (e.g., determined using the Arrhenius equation) and modulate neural fibers within or proximate to the heated target tissue. In the embodiment illustrated in Figure 18, however, heating is supplied via a heating element 1898 positioned within the balloon 1880 and carried by the support member 1890 and/or another feature of the therapeutic assembly 1812. The heating element 1898 may be a plate or other structure heated using resistive heating (via a generator) and/or other suitable heating mechanism. In operation, the heat from the heating element 1898 can transfer from the heating element 1898 to the fluid within the balloon 1870, and then through the wall of the balloon 1870 to the adjacent tissue at the treatment site. The fluid heated by the heating element 1898 can be heated to a therapeutically effective temperature that causes thermal damage to the target tissue at a treatment site within the nasal cavity and modulates neural fibers within or proximate to the heated target tissue. In certain embodiments, the balloon 1870 can include conductive features (e.g., metallic panels) on its surface to concentrate the heating effect at targeted regions of the balloon 1870.

[00137] In other embodiments, the balloon 1870 can be heated via capacitive coupling to reach therapeutically effective temperatures that causes thermal damage to the target tissue at a treatment site within the nasal cavity and modulate neural fibers within or proximate to the heated target tissue. For example, the balloon 1870 can be inflated with an isotonic solution, and the balloon 1870 can be ionically agitated at a high frequency to allow capacitive energy to discharge across the membrane of the balloon 1870 to the target tissue.

[00138] Figure 19 is a side view of a distal portion of a therapeutic neuromodulation device 1902 ("device 1902") configured in accordance with an additional embodiment of the present technology. The device 1902 includes various features generally similar to the features of the therapeutic neuromodulation devices described above. For example, the device 1902 includes a shaft 1908 and a therapeutic assembly 1912 at a distal portion 1908b of the shaft 1908. In the embodiment illustrated in Figure 19, the therapeutic assembly 1912 is configured to apply plasma or laser ablation to therapeutically modulate nerves at the target site. As shown in Figure 19, the therapeutic assembly 1912 can include an ablation element 1999 (e.g., an electrode) on a distal end portion of the shaft 1908. The ablation element 1999 can apply high energy laser pulses to ionize molecules within the first few portion of the pulse. This process leads to a small bubble or field of plasma (e.g., 100-200 μm) that can be

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used to desiccate or otherwise destroy tissue and nerves at the target site. The ablation element 1999 can operate at temperatures lower than 100°C and can limit the thermal effects on surrounding tissue.

[00139] In other embodiments, the ablation element 1999 can perform laser ablation of nerves at the target site. For example, a nerve tracer (e.g., indocyanine green (ICG)) can be injected at the target site to dye nerves at the target site. The ablation element 1999 can be a laser that is tuned to absorb the spectrum of the nerve tracer and, thereby, ablate the dyed nerves in the target site.

Selected Embodiments of Therapeutic Neuromodulation for the Treatment of Chronic Sinusitis

[00140] Figure 20 is a partial cut-away side view illustrating target sites proximate to ostia of nasal sinuses for a therapeutic neuromodulation device configured in accordance with embodiments of the present technology. Any of the therapeutic modulation devices and system described above can be used to therapeutically modulate nerves that innervate the para-nasal sinuses to treat chronic sinusitis and/or similar indications. Referring to Figure 20, the para-nasal sinuses include the frontal sinuses FS, the sphenoidal sinuses SS, the maxillary sinuses ("MS"; not shown), and the ethmoidal sinuses or ethmoidal cells (not shown), which include the posterior ethmoidal cells ("PEC"), the middle ethmoidal cells ("MEC"), and the anterior ethmoidal cells ("AEC"). Each sinus opens to the nasal cavity at one or more discrete ostia. Figure 20 illustrates the general locations of the ostium of the frontal sinus, the sphenoidal sinus, the maxillary sinus, and the ostia of posterior, middle, and anterior ethmoidal cells.

[00141] Parasympathetic nerves innervate the mucosa of the sinuses and stimulate the production of mucus in the sinuses. Hyperactivity of the parasympathetic nerves innervating the sinuses can cause hyper production of mucus and the soft tissue engorgement. The inflammation of the soft tissue proximate to the sinuses can cause can obstruct the conduit between a sinus and the nasal cavity and block the ostium to the sinus. In addition, the hyperactive mucosa and/or the blockage of the ostium can cause the pooling of mucosal secretions within the sinus occurs due to the lack of drainage from the sinus. This can lead to infection and, eventually, a chronic sinusitis state.

[00142] Therapeutic modulation the parasympathetic nerves that control autonomic function of the sinuses is expected to reduce or eliminate the hyperactive mucosal secretions

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and soft tissue engorgement and, thereby, treat chronic sinusitis or related indications. Any of the therapeutic neuromodulation devices described above can be used to apply therapeutically effective neuromodulation energy at or proximate to the ostia of the affected sphenoidal, maxillary, frontal, and/or ethmoidal sinuses to modulate the autonomic function of the sinuses. For example, therapeutic neuromodulation devices can be used to apply RF energy, microwave energy, ultrasound energy, cryotherapeutic cooling, therapeutic heating, plasma ablation, and/or laser ablation to treatment sites at and around the ostia of the sinuses. Similar to the devices described above, the therapeutic neuromodulation devices can be delivered intraluminally via the nasal passage and through the superior, middle, and/or inferior meatuses to access the ostium or ostia of the desired sinus. In various embodiments, neural mapping techniques similar to those described above with respect to Figures 6A-9 can be used to locate or detect the parasympathetic nerves that innervate the ostia before, during, and/or after treatment. The application of therapeutic neuromodulation at the target sites proximate to the sinus ostia can disrupt the parasympathetic signals to the sinus tissues, leading to the opening of the ostia and the ability to drain fluid.

Additional Examples

1. A system for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site inferior to a sphenopalatine foramen of the human patient; and

a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly comprises an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the human patient.

2. The system of example 1 wherein the energy delivery element is configured to deliver at least one of ultrasound energy, microwave energy, laser energy, or radiofrequency (RF) energy to therapeutically modulation the postganglionic parasympathetic nerves.

3. The system of example 1 or 2 wherein the therapeutic assembly is configured to dispense a drug to chemically modulate the postganglionic parasympathetic nerves.

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4. The system of any one of examples 1-3 wherein the shaft comprises a drug delivery channel with an outlet at the distal portion of the shaft, and wherein the drug delivery channel is configured to deliver at least one of a local anesthetic or a nerve block to the target site.

5. The system of any one of examples 1-4 wherein the shaft comprises a fluid channel with an outlet at the distal portion of the shaft, and wherein the fluid channel is configured to deliver saline to the target site to rinse the treatment area with saline.

6. The system of any one of examples 1-5, further comprising an introducer having a rigid metal portion, and wherein the rigid metal portion is sized and shaped to extend through a nasal meatus to the target site to deliver the therapeutic assembly to the target site.

7. The system of any one of examples 1-6 wherein the shaft is a steerable catheter shaft and the distal portion of the shaft has a bend radius of 3 mm or less.

8. The system of any one of examples 1-6 wherein the distal portion of the shaft comprises an articulating region with rigid links sized and shaped to have a bend radius of 3 mm or less.

9. The system of any one of examples 1-8, further comprising an anchor member along the shaft, wherein the anchor member includes a balloon configured to expand in a lumen of the nasal region to hold the distal portion of the shaft in place for deployment of the therapeutic assembly at the target site.

10. The system of any one of examples 1-9 wherein the energy delivery element of the therapeutic assembly comprises a plurality of electrodes configured to apply RF energy to therapeutically modulate postganglionic parasympathetic nerves.

11. The system of any one of examples 1-10 wherein the therapeutic assembly comprises a plurality of sensing electrodes configured to detect neural activity at least one of before therapeutic modulation, during therapeutic modulation, or after therapeutic neuromodulation.

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12. The system of any one of examples 1-11 wherein the therapeutic assembly comprises:

a basket transformable between a low-profile delivery state and an expanded state, wherein the basket includes plurality of struts spaced radially apart from each other when the basket is in the expanded state; and

a plurality of electrodes disposed on the struts, wherein the plurality of struts are configured to position at least two of the electrodes at the target site when the basket is in the expanded state, and

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

13. The system of any one of examples 1-11 wherein the therapeutic assembly comprises:

a flexible membrane transformable between a low-profile delivery state and an expanded state; and

a plurality of electrodes disposed on the flexible membrane,

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

14. The system of example 13 wherein the therapeutic assembly further comprises a frame supporting the flexible membrane.

15. The system of any one of examples 1-11 wherein:

the distal portion of the shaft is transformable between a low-profile delivery state and an expanded state,

the distal portion of the shaft has a spiral/helical shape when the distal portion of the shaft is in the expanded state; and

the energy delivery element comprises a plurality of electrodes disposed on the distal portion of the shaft and configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site,

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wherein the distal portion of the shaft is configured to place at least one of the electrodes in contact tissue at the target site when the distal portion of the shaft is in the expanded state.

16. The system of any one of examples 1-11 wherein the therapeutic assembly comprises:

a balloon transformable between a low-profile delivery state to an expanded state; and

a plurality of electrodes disposed on the balloon, wherein the plurality of electrodes are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

17. The system of example 16 wherein the balloon comprises a plurality of holes configured to allow perfusion of a fluid through the balloon when the balloon is in the expanded state.

18. The system of example 16, further comprising:

a support extending through the balloon; and

a plurality of graduated markings on at least one of the support or the balloon to identify spatial positioning of the balloon.

19. The system of any one of examples 1-11 wherein the therapeutic assembly comprises:

a balloon transformable between a low-profile delivery state to an expanded state, wherein the balloon comprises a proximal cone portion;

a return electrode on the balloon; and

a flex circuit on the proximal cone portion, wherein the return electrode and the flex circuit are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

20. The system of any one of examples 1-11 wherein the therapeutic assembly comprises:

a plurality of balloons extending distally from the distal portion of the shaft, wherein the balloons are independently expandable; and

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at least one electrode on each of the balloons, wherein the electrodes are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

21. The system of example 20, further comprising:

an internal support member extending through a region between the balloons and configured to carry the balloons, wherein the internal support member includes a return electrode.

22. The system of any one of examples 1-9 wherein the therapeutic assembly comprises a cryotherapeutic balloon configured to apply cryogenic cooling to tissue at the target site to therapeutically modulate autonomic activity.

23. The system of any one of examples 1-9 wherein the therapeutic assembly comprises a balloon sized and shaped to contact tissue at the target state when expanded, and wherein the balloon is configured to circulate a fluid heated to at least 60° C to thermally modulate autonomic activity.

24. The system of any one of examples 1-9 wherein the therapeutic assembly comprises:

a balloon configured to be expanded with a fluid, wherein the balloon is sized and shaped to contact tissue at the target state when expanded; and

a heating member within the balloon, wherein the heating member is configured to heat the fluid in the balloon to thermally modulate autonomic activity.

25. The system of any one of examples 1-9 wherein the therapeutic assembly comprises a plasma ablation probe.

26. A system for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site, wherein the target site is at least one of proximate to the sphenopalatine foramen of a human patient or inferior to the sphenopalatine foramen; and

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a therapeutic assembly at the distal portion of the shaft and transformable between a low-profile delivery state and an expanded state, wherein the therapeutic assembly comprises a plurality of struts and a plurality of electrodes disposed on the struts, and wherein the plurality of struts form a basket that positions at least two of the electrodes at the target site inferior to a sphenopalatine foramen of the human patient when the therapeutic assembly is in the expanded state, and

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

27. The system of example 26 wherein:

the plurality of struts comprise at least three struts spaced radially apart from each other in the expanded state to define the basket; and

each of the three struts includes at least one of the electrodes.

28. The system of example 26 or 27 wherein:

the basket comprises at least three branches radially spaced apart from each other in the expanded state to form the basket;

each branch comprises at least two struts positioned adjacent to each other; and

each strut includes at least one of the electrodes.

29. The system of any one of examples 26-28, further comprising a thermocouple positioned at least proximate to one of the electrodes, wherein the thermocouple is configured to detect temperature at an interface between the electrode and tissue adjacent to the electrode when the therapeutic assembly is in the expanded state.

30. The system of any one of examples 26-29 wherein each of the electrodes is configured to be independently activated and independently assigned a selective polarity to apply therapeutic neuromodulation across selected regions of the basket.

31. The system of any one of examples 26-30 wherein the basket has a spherical or ovoid shape, and wherein the electrodes are configured to be selectively activated to apply RF energy across at least one of a segment, quadrant, or hemisphere of the basket.

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32. The system of any one of examples 26-31 wherein:

the plurality of electrodes comprises first through third electrodes disposed on corresponding first through third struts; and

the system further comprises a controller operably coupled to the plurality of electrodes, the controller having a computer-readable medium carrying instructions, which when executed by the controller, activates first through third electrodes of the plurality of electrodes such that—

the first electrode has a positive polarity;

the second and third electrodes have a negative polarity; and

the electrodes apply RF energy in a sesquipolar manner across a selected peripheral region of the basket.

33. The system of any one of examples 26-31 wherein:

the basket comprises an internal support member extending through a region between the plurality of struts and having a distal end portion supporting distal end portions of the plurality of struts;

the plurality of struts comprises at least a first strut and a second strut;

the plurality of electrodes comprises a first electrode disposed on the first strut, a second electrode disposed on the second strut, and a third electrode disposed on the distal end portion of the internal support member; and

the system further comprises a controller operably coupled to the plurality of electrodes, the controller having a computer-readable medium carrying instructions, which when executed by the controller, activates first through third electrodes of the plurality of electrodes such that—

the first and second electrodes have a positive polarity;

the third electrode has a negative polarity; and

the electrodes apply RF energy across a distal region of the basket.

34. The system of any one of examples 26-31 wherein:

the basket comprises at least two branches radially spaced apart from each other when the therapeutic assembly is in the expanded state; and

each branch comprises at least a first strut and a second strut positioned adjacent to each other, the first strut having a first electrode disposed thereon and the second strut having a second electrode disposed thereon, wherein the first and

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second electrodes are configured to have opposite polarity and apply RF energy between the first and second electrodes.

35. The system of any one of examples 26-31 wherein:

the basket comprises at least two branches radially spaced apart from each other when the therapeutic assembly is in the expanded state; and

each branch comprises at least a first strut and a second strut positioned adjacent to each other, the first strut having a first electrode disposed thereon and the second strut having a second strut disposed thereon, wherein—

the first and second electrodes of the first branch are configured to have a positive polarity,

the first and second electrodes of the second branch are configured to have a negative polarity, and apply

the therapeutic assembly is configured to delivery RF energy between the first and second branches across a peripheral portion of the basket.

36. The system of any one of examples 26-31, further comprising:

a return electrode disposed on the distal portion of the shaft positioned proximal to the therapeutic assembly,

wherein the electrodes on the struts are configured to have a positive polarity and the return electrode is configured to have a negative polarity.

37. The system of any one of examples 26-36 wherein at least a portion of the electrodes are configured to detect impedance at the target site to determine locations of nerves at the target site.

38. The system of any one of examples 26-37 wherein:

the plurality of electrodes on the struts are a first plurality of electrodes;

the therapeutic assembly further comprises—

an expandable balloon disposed within the struts; and

a second plurality of electrodes on the expandable balloon,

wherein, when in the expanded state, the expandable balloon places at least a portion of the second plurality of electrodes in contact with tissue at the target site to detect neural activity at the target site.

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39. The system of any one of examples 26-38, further comprising an RF generator operably connected to the therapeutic assembly, wherein the RF generator includes a controller having a computer-readable medium carrying instructions, which when executed by the controller, causes the therapeutic assembly to detect at least one of impedance or temperature at least proximate to the target site.

40. The system of any one of examples 26-39, further comprising an RF generator operably connected to the therapeutic assembly, wherein the RF generator includes a controller having a computer-readable medium carrying instructions, which when executed by the controller, causes the therapeutic assembly to apply RF energy to the target site in a predetermined pattern.

41. A system for neural mapping and therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site proximate to a sphenopalatine foramen of the human patient;

a plurality of electrodes at the distal portion of the shaft, wherein the electrodes are configured to detect locations of the parasympathetic nerves at the target site; and

a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly is comprises an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves innervating a nasal mucosa at the target site.

42. The system of example 41 wherein the electrodes define the energy delivery element and are configured to apply radiofrequency (RF) energy to the target site.

43. The system of example 41 or 42 wherein the electrodes are configured to detect dielectric properties of heterogeneous tissue at the target site to identify locations of parasympathetic nerves.

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44. The system of any one of examples 41-43 wherein the electrodes are configured to detect impedance properties of heterogeneous tissue at the target site to identify locations of parasympathetic nerves.

45. A method of therapeutically modulating nerves in a nasal region of a human patient, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within the nasal region, wherein the target site is proximate to parasympathetic nerves spanning across at least one of an accessory foramen or microforamina proximate to the sphenopalatine foramen; and

applying energy, with the therapeutic assembly, to the target site to therapeutically modulate autonomic activity within at least one of a nasal cavity, a nasopharynx, or paranasal cavities.

46. The method of example 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly at a palatine bone of the human patient inferior to the sphenopalatine foramen.

47. The method of example 45 or 46 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through an inferior meatus, and to the target site.

48. The method of example 45 or 46 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through a middle meatus, and to the target site.

49. The method of any one of examples 45-48, further comprising intraluminally advancing an endoscope through an entrance of a nose of the human patient and through a middle meatus to visualize the therapeutic assembly at the target site.

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50. The method of any one of examples 45-48, further comprising intraluminally advancing an endoscope through an entrance of a nose of the human patient and through an inferior meatus to visualize the therapeutic assembly at the target site.

51. The method of example 45 or 46 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through an inferior meatus, and to the target site; and

the method further comprises intraluminally advancing an endoscope through the entrance of the nose of the human patient and through the inferior meatus to visualize the therapeutic assembly at the target site.

52. The method of example 45 or 46 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through an middle meatus, and to the target site; and

the method further comprises intraluminally advancing an endoscope through the entrance of the nose of the human patient and through the middle meatus to visualize the therapeutic assembly at the target site.

53. The method of example 45 or 46, further comprising:

intraluminally advancing an endoscope through an entrance of a nose of the human patient, through one of an inferior meatus or a middle meatus, to a region at least proximate to the target site; and

wherein intraluminally advancing the therapeutic assembly to the target site comprises—

advancing the distal portion of the shaft through a channel of the endoscope beyond the target site, and

advancing the therapeutic assembly out of an opening at a distal portion of the endoscope.

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54. The method of example 45 or 46 wherein intraluminally advancing the therapeutic assembly to the target site comprises advancing the distal portion of the shaft through a mouth and oropharynx of the human patient, and to the target site.

55. The method of any one of examples 45-54, further comprising imaging the target site via infrared (IR) spectroscopy to visualize vasculature at least proximate to the target site.

56. The method of any one of examples 45-55, further comprising expanding an anchor member positioned along the distal portion of the shaft in a lumen of the nasal region, wherein the anchor member holds the distal portion of the shaft in place for deployment of the therapeutic assembly at the target site.

57. The method of any one of examples 45-56 wherein the target site is a first target site, wherein applying energy to the target site comprises applying energy to the first target site, and wherein the method further comprises:

repositioning the therapeutic assembly to a second target site within the nasal region; and

applying energy, with the therapeutic assembly, to the second target site to therapeutically modulate parasympathetic nerves proximate to the second target site.

58. The method of any one of examples 45-57 wherein applying energy comprises applying pulsed radiofrequency (RF) energy to the target site via a plurality of electrodes of the thereapeutic element.

59. The method of any one of examples 45-58 further comprising detecting impedance at the target site to identify positions of parasympathetic nerves spanning across at least one of an accessory foramen or microforamina proximate to the sphenopalatine foramen.

60. The method of example 59 wherein applying energy to the target site comprises applying energy to a discrete region of the therapeutic assembly corresponding to the positions of the parasympathetic nerves identified via impedance measurements.

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61. The method of any one of examples 45-60 wherein the therapeutic assembly comprises a plurality of electrodes, and wherein applying energy to the target site comprises independently activating the individual electrodes and selecting the polarity of the individual electrodes to apply therapeutic neuromodulation across a selective region of the therapeutic assembly.

62. The method of example 61 wherein applying energy to the target site further comprises applying energy in a first hemispherical portion of the therapeutic assembly, wherein the therapeutic assembly does not apply energy to a second hemispherical portion of the therapeutic assembly.

63. The method of any one of examples 45-62 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes disposed on the struts, and wherein applying energy to the target site comprises:

activating a first electrode of the plurality of electrodes to have a positive polarity; and

activating at least a second electrode and a third electrode of the plurality of electrodes to have a negative polarity, wherein first, second, and third electrodes are concurrently activated and the second and third electrodes sequentially pair with the first electrode based on path of least resistance to sequentially apply therapeutic neuromodulation across a region of the basket.

64. The method of any one of examples 45-62 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes disposed on the struts, and wherein applying energy to the target site comprises:

activating a first electrode of the plurality of electrodes to have a positive polarity; and

activating at least second through sixth electrodes of the plurality of electrodes to have a negative polarity, wherein first through sixth electrodes are concurrently activated and the second through sixth electrodes sequentially pair with the first electrode based on path of least resistance to sequentially apply therapeutic neuromodulation across a hemispherical region of the basket.

65. The method of any one of examples 45-62 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes

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disposed on the struts and an internal support member comprising a return electrode at a distal end portion of the internal support member, and wherein applying energy to the target site comprises:

activating the electrodes on the struts to have positive polarities; and

activating the return electrode to have a negative polarity, wherein the electrodes apply RF energy across a distal region of the basket.

66. The method of any one of examples 45-62 wherein the therapeutic assembly comprises an expandable basket having a plurality of branches radially spaced apart from each other when the therapeutic assembly is in an expanded state, wherein each branch comprises at least two adjacent struts with an electrode positioned on each strut, and wherein applying energy to the target site comprises:

activating the electrodes on adjacent struts of at least one of the branches such that the electrodes have opposite polarities; and

applying RF energy between the electrodes on the adjacent struts.

67. The method of any one of examples 45-62 wherein the therapeutic assembly comprises a plurality of electrodes, and wherein applying energy to the target site comprises:

activating the electrodes of the therapeutic assembly to have positive polarities; and

activating a return electrode disposed on the distal portion of the shaft proximal to the therapeutic assembly, wherein the return electrode has a negative polarity, and

wherein activating the electrodes and the return electrodes applies RF energy across a turbinate of the human patient.

68. The method of any one of examples 45-67, further comprising:

detecting, via a plurality of sensing electrodes, neural activity at the target site before applying energy to the target site to therapeutically modulate autonomic activity; and

mapping locations of nerves at the target site based on the detected neural activity,

wherein applying energy to the target site comprises selectively applying energy to a region based on the locations of detected nerves.

69. The method of example 68, further comprising applying non-therapeutic neural stimulation to the target site before detecting neural activity.

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70. The method of example 68, further comprising detecting, via the plurality of sensing electrodes, neural activity after applying energy to the target site to determine whether the application of energy has therapeutically modulated nerves at the target site.

71. The method of any one of examples 45-62 wherein:

the therapeutic assembly comprises a flexible membrane carrying a plurality of electrodes;

before applying energy, the method further comprises expanding the flexible membrane at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

72. The method of any one of examples 45-62, further comprising:

transforming the distal portion of the shaft from a low-profile delivery state to an expanded state such that a plurality of electrodes disposed on the distal portion of the shaft are placed in contact with tissue at the target site, wherein the distal portion of the shaft has a spiral/helical shape in the expanded state; and

wherein applying energy at the target site comprises applying RF energy to the target site via the electrodes.

73. The method of any one of examples 45-62 wherein:

the therapeutic assembly comprises a balloon carrying a plurality of electrodes;

before applying energy, the method further comprises expanding the balloon at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

74. The method of example 73 wherein applying energy to the target site further comprises:

selectively activating the electrodes to apply current in a radial direction across a circumferential segment of the balloon.

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75. The method of example 73 wherein applying energy to the target site further comprises:

selectively activating the electrodes to apply current in a longitudinal direction across a longitudinal region of the balloon.

76. The method of example 73 wherein expanding the balloon comprises filling the balloon with a fluid, and wherein the balloon comprises a plurality of holes that allow for perfusion of the fluid through the balloon during energy application.

77. The method of example 73 wherein expanding the balloon comprises circulating a fluid through the balloon, wherein the fluid cools the electrodes during energy application.

78. The method of any one of examples 45-62 wherein:

the therapeutic assembly comprises a plurality of balloons extending distally from the distal portion of the shaft and a plurality of electrodes disposed on the balloons;

before applying energy, the method further comprises independently expanding the balloons at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

79. The method of example 78 wherein applying energy to the target site further comprises:

activating a return electrode on an internal support member extending through the plurality of balloons; and

activating at least a portion of the electrodes on the balloons.

80. The method of any one of examples 45-79, further comprising:

measuring temperature of tissue at the target site during energy application; and

terminating energy application when a threshold maximum temperature is reached.

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81. The method of any one of examples 45-80, further comprising terminating energy application after a predetermined maximum time period.

82. The method of any one of examples 45-81, further comprising:

detecting impedance of tissue at the target site during energy application; and

terminating energy application when a threshold impedance value is reached.

83. The method of any one of examples 45-82, further comprising:

detecting impedance of tissue at the target site before energy application to define a baseline impedance;

detecting impedance of tissue at the target site during energy application; and

terminating energy application when a threshold change in impedance from the baseline impedance is reached.

84. The method of any one of examples 45-57 wherein applying energy to the target site comprises applying therapeutic cryogenic cooling to tissue at the target site to therapeutically modulate autonomic activity within the nasal cavity, the nasopharynx, and/or the paranasal cavities.

85. The method of any one of examples 45-57 wherein applying energy to the target site comprises:

circulating a heated fluid within a balloon such that an exterior surface of the balloon contacts tissue at the target site and heats the tissue to thermally modulate autonomic activity at the target site.

86. The method of any one of examples 45-57 wherein applying energy to the target site comprises:

expanding a balloon such that an exterior surface of the balloon contacts tissue at the target site; and

heating a heating member within the balloon, wherein the heat from the heating member transfers to the fluid and to the tissue adjacent to the balloon to thermally modulate autonomic activity.

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87. The method of any one of examples 45-57 wherein applying energy to the target site comprises generating a plasma field to therapeutically modulate nerves at the target site.

88. The method of any one of examples 45-87 wherein applying energy to the target site therapeutically modulates cholinergic pathways that send signals to submucosal glands.

89. The method of any one of examples 45-88 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly to parasympathetic nerve points of entrance into the nasal region via accessory foramen and/or microforamina within at least one of a superior meatus, a middle meatus, an inferior meatus, or a pterygopalatine fossa.

90. A method of therapeutically modulating nerves in a nasal region, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within a nasal region, wherein the target site is proximate to parasympathetic nerves proximate to the sphenopalatine foramen;

detecting locations of the parasympathetic nerves at the target site; and

applying energy, with the therapeutic assembly, to the target site based on the detected locations of the parasympathetic nerves, wherein applying energy therapeutically modulates autonomic activity within at least one of a nasal cavity, a nasopharynx, or paranasal cavities.

91. The method of example 90 wherein detecting locations of the parasympathetic nerves at the target site comprises measuring dielectric properties of heterogeneous tissue within at least one of the nasal cavity, the nasopharynx, and/or the paranasal cavities on a high resolution spatial grid.

92. The method of example 90 or 92 wherein detecting locations of the parasympathetic nerves at the target site comprises measuring the dipole properties of

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heterogeneous tissue within the nasal cavity, the nasopharynx, and/or the paranasal cavities on a high resolution spatial grid.

93. The method of any one of examples 90-92 wherein detecting locations of the parasympathetic nerves at the target site comprises detecting impedance of heterogeneous tissue within at least one of the nasal cavity, the nasopharynx, or the paranasal cavities on a high resolution spatial grid.

94. A device for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a delivery catheter having a distal portion, wherein the delivery catheter is configured to locate the distal portion at a target site within the nasal region;

a flexible support at the distal portion of the delivery catheter; and

a plurality of electrodes carried by the flexible support,

wherein the flexible support is configured to conform to irregularities of local anatomy at the target site to provide topographical compliance and a linkage for electrical activation of at least a portion of the electrodes, and

wherein the electrodes are configured to therapeutically modulate parasympathetic nerves of mucosal and sub-mucosal structures in direct or in-direct contact with the electrodes.

95. The device of example 94, further comprising a controllable recapturing mechanism configured to recapture the flexible support after energy delivery to allow withdrawal of the flexible support from a nasal cavity.

96. The device of example 94 or 94 wherein the target site is at a sphenopalatine foramen.

97. The device of any one of examples 94-46 wherein the electrodes are configured to be selectively activated to control energy direction and associated dissipation for accurate and localized energy delivery.

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98. A method of therapeutically modulating nerves in a nasal region of a human patient, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within the nasal region, wherein the target site is at least proximate to an ostium of at least one of a frontal sinus, an ethmoidal sinus, a sphenoidal sinus, or a maxillary sinus of the human patient; and

applying energy, with the therapeutic assembly, to the target site to therapeutically modulate parasympathetic nerves at the target site to treat chronic sinusitis.

99. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the frontal sinus; and

applying energy to the target site comprises applying energy to at least one of a supraorbital nerve, a supratrochlear nerve, branches of the supraorbital nerve, branches of the supratrochlear nerve, or other parasympathetic neural fibers that innervate mucosa of the frontal sinus.

100. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the ethmoidal sinus; and

applying energy to the target site comprises applying energy to at least one of an anterior ethmoidal branch of a nasociliary nerve, a posterior ethmoidal branch of the nasociliary nerve, a maxillary nerve, branches of the nasociliary nerve, branches of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the ethmoidal sinus.

101. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the maxillary sinus; and

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applying energy to the target site comprises applying energy to at least one of an infra-orbital branch of a maxillary nerve, an alveolar branch of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the maxillary sinus.

102. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the sphenoidal sinus; and

applying energy to the target site comprises applying energy to at least one of a posterior ethmoidal branch of an ophthalmic nerve, a maxillary nerve, branches of the ophthalmic nerve, branches of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the sphenoidal sinus.

103. A system for therapeutic neuromodulation in a nasal region of a human patient for treatment of chronic sinusitis, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site, wherein the target site is at least proximate to an ostium of at least one of a frontal sinus, an ethmoidal sinus, a sphenoidal sinus, or a maxillary sinus of the human patient; and

a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly is comprises an energy delivery element configured to therapeutically modulate parasympathetic nerves that innervate mucosa of at least one of the frontal sinus, the ethmoidal sinus, the sphenoidal sinus, or the maxillary sinus.

Conclusion

[00143] This disclosure is not intended to be exhaustive or to limit the present technology to the precise forms disclosed herein. Although specific embodiments are disclosed herein for illustrative purposes, various equivalent modifications are possible without deviating from the present technology, as those of ordinary skill in the relevant art will recognize. In some cases, well-known structures and functions have not been shown and/or described in detail to avoid unnecessarily obscuring the description of the

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embodiments of the present technology. Although steps of methods may be presented herein in a particular order, in alternative embodiments the steps may have another suitable order. Similarly, certain aspects of the present technology disclosed in the context of particular embodiments can be combined or eliminated in other embodiments. Furthermore, while advantages associated with certain embodiments may have been disclosed in the context of those embodiments, other embodiments can also exhibit such advantages, and not all embodiments need necessarily exhibit such advantages or other advantages disclosed herein to fall within the scope of the present technology. Accordingly, this disclosure and associated technology can encompass other embodiments not expressly shown and/or described herein.

[00144] Throughout this disclosure, the singular terms "a," "an," and "the" include plural referents unless the context clearly indicates otherwise. Similarly, unless the word "or" is expressly limited to mean only a single item exclusive from the other items in reference to a list of two or more items, then the use of "or" in such a list is to be interpreted as including (a) any single item in the list, (b) all of the items in the list, or (c) any combination of the items in the list. Additionally, the terms "comprising" and the like are used throughout this disclosure to mean including at least the recited feature(s) such that any greater number of the same feature(s) and/or one or more additional types of features are not precluded. Directional terms, such as "upper," "lower," "front," "back," "vertical," and "horizontal," may be used herein to express and clarify the relationship between various elements. It should be understood that such terms do not denote absolute orientation. Reference herein to "one embodiment," "an embodiment," or similar formulations means that a particular feature, structure, operation, or characteristic described in connection with the embodiment can be included in at least one embodiment of the present technology. Thus, the appearances of such phrases or formulations herein are not necessarily all referring to the same embodiment. Furthermore, various particular features, structures, operations, or characteristics may be combined in any suitable manner in one or more embodiments.

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CLAIMS

I/We claim:

1. A system for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site inferior to a sphenopalatine foramen of the human patient; and

a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly comprises an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves innervating nasal mucosa at microforamina of a palatine bone of the human patient.

2. The system of claim 1 wherein the energy delivery element is configured to deliver at least one of ultrasound energy, microwave energy, laser energy, or radiofrequency (RF) energy to therapeutically modulation the postganglionic parasympathetic nerves.

3. The system of claim 1 wherein the therapeutic assembly is configured to dispense a drug to chemically modulate the postganglionic parasympathetic nerves.

4. The system of claim 1 wherein the shaft comprises a drug delivery channel with an outlet at the distal portion of the shaft, and wherein the drug delivery channel is configured to deliver at least one of a local anesthetic or a nerve block to the target site.

5. The system of claim 1 wherein the shaft comprises a fluid channel with an outlet at the distal portion of the shaft, and wherein the fluid channel is configured to deliver saline to the target site to rinse the treatment area with saline.

6. The system of claim 1, further comprising an introducer having a rigid metal portion, and wherein the rigid metal portion is sized and shaped to extend through a nasal meatus to the target site to deliver the therapeutic assembly to the target site.

7. The system of claim 1 wherein the shaft is a steerable catheter shaft and the distal portion of the shaft has a bend radius of 3 mm or less.

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8. The system of claim 1 wherein the distal portion of the shaft comprises an articulating region with rigid links sized and shaped to have a bend radius of 3 mm or less.

9. The system of claim 1, further comprising an anchor member along the shaft, wherein the anchor member includes a balloon configured to expand in a lumen of the nasal region to hold the distal portion of the shaft in place for deployment of the therapeutic assembly at the target site.

10. The system of claim 1 wherein the energy delivery element of the therapeutic assembly comprises a plurality of electrodes configured to apply RF energy to therapeutically modulate postganglionic parasympathetic nerves.

11. The system of claim 1 wherein the therapeutic assembly comprises a plurality of sensing electrodes configured to detect neural activity at least one of before therapeutic modulation, during therapeutic modulation, or after therapeutic neuromodulation.

12. The system of claim 1 wherein the therapeutic assembly comprises:

a basket transformable between a low-profile delivery state and an expanded state, wherein the basket includes plurality of struts spaced radially apart from each other when the basket is in the expanded state; and

a plurality of electrodes disposed on the struts, wherein the plurality of struts are configured to position at least two of the electrodes at the target site when the basket is in the expanded state, and

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

13. The system of claim 1 wherein the therapeutic assembly comprises:

a flexible membrane transformable between a low-profile delivery state and an expanded state; and

a plurality of electrodes disposed on the flexible membrane,

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

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14. The system of claim 13 wherein the therapeutic assembly further comprises a frame supporting the flexible membrane.

15. The system of claim 1 wherein:

the distal portion of the shaft is transformable between a low-profile delivery state and an expanded state,

the distal portion of the shaft has a spiral/helical shape when the distal portion of the shaft is in the expanded state; and

the energy delivery element comprises a plurality of electrodes disposed on the distal portion of the shaft and configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site,

wherein the distal portion of the shaft is configured to place at least one of the electrodes in contact tissue at the target site when the distal portion of the shaft is in the expanded state.

16. The system of claim 1 wherein the therapeutic assembly comprises:

a balloon transformable between a low-profile delivery state to an expanded state; and

a plurality of electrodes disposed on the balloon, wherein the plurality of electrodes are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

17. The system of claim 16 wherein the balloon comprises a plurality of holes configured to allow perfusion of a fluid through the balloon when the balloon is in the expanded state.

18. The system of claim 16, further comprising:

a support extending through the balloon; and

a plurality of graduated markings on at least one of the support or the balloon to identify spatial positioning of the balloon.

19. The system of claim 1 wherein the therapeutic assembly comprises:

a balloon transformable between a low-profile delivery state to an expanded state, wherein the balloon comprises a proximal cone portion;

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a return electrode on the balloon; and

a flex circuit on the proximal cone portion, wherein the return electrode and the flex circuit are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

20. The system of claim 1 wherein the therapeutic assembly comprises:

a plurality of balloons extending distally from the distal portion of the shaft, wherein the balloons are independently expandable; and

at least one electrode on each of the balloons, wherein the electrodes are configured to deliver radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

21. The system of claim 20, further comprising:

an internal support member extending through a region between the balloons and configured to carry the balloons, wherein the internal support member includes a return electrode.

22. The system of claim 1 wherein the therapeutic assembly comprises a cryotherapeutic balloon configured to apply cryogenic cooling to tissue at the target site to therapeutically modulate autonomic activity.

23. The system of claim 1 wherein the therapeutic assembly comprises a balloon sized and shaped to contact tissue at the target state when expanded, and wherein the balloon is configured to circulate a fluid heated to at least 60° C to thermally modulate autonomic activity.

24. The system of claim 1 wherein the therapeutic assembly comprises:

a balloon configured to be expanded with a fluid, wherein the balloon is sized and shaped to contact tissue at the target state when expanded; and

a heating member within the balloon, wherein the heating member is configured to heat the fluid in the balloon to thermally modulate autonomic activity.

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25. The system of claim 1 wherein the therapeutic assembly comprises a plasma ablation probe.

26. A system for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site, wherein the target site is at least one of proximate to the sphenopalatine foramen of a human patient or inferior to the sphenopalatine foramen; and

a therapeutic assembly at the distal portion of the shaft and transformable between a low-profile delivery state and an expanded state, wherein the therapeutic assembly comprises a plurality of struts and a plurality of electrodes disposed on the struts, and wherein the plurality of struts form a basket that positions at least two of the electrodes at the target site inferior to a sphenopalatine foramen of the human patient when the therapeutic assembly is in the expanded state, and

wherein the electrodes are configured to apply radiofrequency (RF) energy to the target site to therapeutically modulate parasympathetic nerves proximate to the target site.

27. The system of claim 26 wherein:

the plurality of struts comprise at least three struts spaced radially apart from each other in the expanded state to define the basket; and

each of the three struts includes at least one of the electrodes.

28. The system of claim 26 wherein:

the basket comprises at least three branches radially spaced apart from each other in the expanded state to form the basket;

each branch comprises at least two struts positioned adjacent to each other; and

each strut includes at least one of the electrodes.

29. The system of claim 26, further comprising a thermocouple positioned at least proximate to one of the electrodes, wherein the thermocouple is configured to detect

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temperature at an interface between the electrode and tissue adjacent to the electrode when the therapeutic assembly is in the expanded state.

30. The system of claim 26 wherein each of the electrodes is configured to be independently activated and independently assigned a selective polarity to apply therapeutic neuromodulation across selected regions of the basket.

31. The system of claim 26 wherein the basket has a spherical or ovoid shape, and wherein the electrodes are configured to be selectively activated to apply RF energy across at least one of a segment, quadrant, or hemisphere of the basket.

32. The system of claim 26 wherein:

the plurality of electrodes comprises first through third electrodes disposed on corresponding first through third struts; and

the system further comprises a controller operably coupled to the plurality of electrodes, the controller having a computer-readable medium carrying instructions, which when executed by the controller, activates first through third electrodes of the plurality of electrodes such that—

the first electrode has a positive polarity;

the second and third electrodes have a negative polarity; and

the electrodes apply RF energy in a sesquipolar manner across a selected peripheral region of the basket.

33. The system of claim 26 wherein:

the basket comprises an internal support member extending through a region between the plurality of struts and having a distal end portion supporting distal end portions of the plurality of struts;

the plurality of struts comprises at least a first strut and a second strut;

the plurality of electrodes comprises a first electrode disposed on the first strut, a second electrode disposed on the second strut, and a third electrode disposed on the distal end portion of the internal support member; and

the system further comprises a controller operably coupled to the plurality of electrodes, the controller having a computer-readable medium carrying

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instructions, which when executed by the controller, activates first through third electrodes of the plurality of electrodes such that—

the first and second electrodes have a positive polarity;

the third electrode has a negative polarity; and

the electrodes apply RF energy across a distal region of the basket.

34. The system of claim 26 wherein:

the basket comprises at least two branches radially spaced apart from each other when the therapeutic assembly is in the expanded state; and

each branch comprises at least a first strut and a second strut positioned adjacent to each other, the first strut having a first electrode disposed thereon and the second strut having a second electrode disposed thereon, wherein the first and second electrodes are configured to have opposite polarity and apply RF energy between the first and second electrodes.

35. The system of claim 26 wherein:

the basket comprises at least two branches radially spaced apart from each other when the therapeutic assembly is in the expanded state; and

each branch comprises at least a first strut and a second strut positioned adjacent to each other, the first strut having a first electrode disposed thereon and the second strut having a second strut disposed thereon, wherein—

the first and second electrodes of the first branch are configured to have a positive polarity,

the first and second electrodes of the second branch are configured to have a negative polarity, and apply

the therapeutic assembly is configured to delivery RF energy between the first and second branches across a peripheral portion of the basket.

36. The system of claim 26, further comprising:

a return electrode disposed on the distal portion of the shaft positioned proximal to the therapeutic assembly,

wherein the electrodes on the struts are configured to have a positive polarity and the return electrode is configured to have a negative polarity.

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37. The system of claim 26 wherein at least a portion of the electrodes are configured to detect impedance at the target site to determine locations of nerves at the target site.

38. The system of claim 26 wherein:

the plurality of electrodes on the struts are a first plurality of electrodes;

the therapeutic assembly further comprises—

an expandable balloon disposed within the struts; and

a second plurality of electrodes on the expandable balloon,

wherein, when in the expanded state, the expandable balloon places at least a portion of the second plurality of electrodes in contact with tissue at the target site to detect neural activity at the target site.

39. The system of claim 26, further comprising an RF generator operably connected to the therapeutic assembly, wherein the RF generator includes a controller having a computer-readable medium carrying instructions, which when executed by the controller, causes the therapeutic assembly to detect at least one of impedance or temperature at least proximate to the target site.

40. The system of claim 26, further comprising an RF generator operably connected to the therapeutic assembly, wherein the RF generator includes a controller having a computer-readable medium carrying instructions, which when executed by the controller, causes the therapeutic assembly to apply RF energy to the target site in a predetermined pattern.

41. A system for neural mapping and therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site proximate to a sphenopalatine foramen of the human patient;

a plurality of electrodes at the distal portion of the shaft, wherein the electrodes are configured to detect locations of the parasympathetic nerves at the target site; and

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a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly is comprises an energy delivery element configured to therapeutically modulate postganglionic parasympathetic nerves innervating a nasal mucosa at the target site.

42. The system of claim 41 wherein the electrodes define the energy delivery element and are configured to apply radiofrequency (RF) energy to the target site.

43. The system of claim 41 wherein the electrodes are configured to detect dielectric properties of heterogeneous tissue at the target site to identify locations of parasympathetic nerves.

44. The system of claim 41 wherein the electrodes are configured to detect impedance properties of heterogeneous tissue at the target site to identify locations of parasympathetic nerves.

45. A method of therapeutically modulating nerves in a nasal region of a human patient, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within the nasal region, wherein the target site is proximate to parasympathetic nerves spanning across at least one of an accessory foramen or microforamina proximate to the sphenopalatine foramen; and

applying energy, with the therapeutic assembly, to the target site to therapeutically modulate autonomic activity within at least one of a nasal cavity, a nasopharynx, or paranasal cavities.

46. The method of claim 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly at a palatine bone of the human patient inferior to the sphenopalatine foramen.

47. The method of claim 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly

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through an entrance of a nose of the human patient, through an inferior meatus, and to the target site.

48. The method of claim 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through a middle meatus, and to the target site.

49. The method of claim 45, further comprising intraluminally advancing an endoscope through an entrance of a nose of the human patient and through a middle meatus to visualize the therapeutic assembly at the target site.

50. The method of claim 45, further comprising intraluminally advancing an endoscope through an entrance of a nose of the human patient and through an inferior meatus to visualize the therapeutic assembly at the target site.

51. The method of claim 45 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through an inferior meatus, and to the target site; and

the method further comprises intraluminally advancing an endoscope through the entrance of the nose of the human patient and through the inferior meatus to visualize the therapeutic assembly at the target site.

52. The method of claim 45 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly through an entrance of a nose of the human patient, through an middle meatus, and to the target site; and

the method further comprises intraluminally advancing an endoscope through the entrance of the nose of the human patient and through the middle meatus to visualize the therapeutic assembly at the target site.

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53. The method of claim 45, further comprising:

intraluminally advancing an endoscope through an entrance of a nose of the human patient, through one of an inferior meatus or a middle meatus, to a region at least proximate to the target site; and

wherein intraluminally advancing the therapeutic assembly to the target site comprises—

advancing the distal portion of the shaft through a channel of the endoscope beyond, and

advancing the therapeutic assembly out of an opening at a distal portion of the endoscope.

54. The method of claim 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises advancing the distal portion of the shaft through a mouth and oropharynx of the human patient, and to the target site.

55. The method of claim 45, further comprising imaging the target site via infrared (IR) spectroscopy to visualize vasculature at least proximate to the target site.

56. The method of claim 45, further comprising expanding an anchor member positioned along the distal portion of the shaft in a lumen of the nasal region, wherein the anchor member holds the distal portion of the shaft in place for deployment of the therapeutic assembly at the target site.

57. The method of claim 45 wherein the target site is a first target site, wherein applying energy to the target site comprises applying energy to the first target site, and wherein the method further comprises:

repositioning the therapeutic assembly to a second target site within the nasal region; and

applying energy, with the therapeutic assembly, to the second target site to therapeutically modulate parasympathetic nerves proximate to the second target site.

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58. The method of claim 45 wherein applying energy comprises applying pulsed radiofrequency (RF) energy to the target site via a plurality of electrodes of the thereapeutic element.

59. The method of claim 45 further comprising detecting impedance at the target site to identify positions of parasympathetic nerves spanning across at least one of an accessory foramen or microforamina proximate to the sphenopalatine foramen.

60. The method of claim 59 wherein applying energy to the target site comprises applying energy to a discrete region of the therapeutic assembly corresponding to the positions of the parasympathetic nerves identified via impedance measurements.

61. The method of claim 45 wherein the therapeutic assembly comprises a plurality of electrodes, and wherein applying energy to the target site comprises independently activating the individual electrodes and selecting the polarity of the individual electrodes to apply therapeutic neuromodulation across a selective region of the therapeutic assembly.

62. The method of claim 61 wherein applying energy to the target site further comprises applying energy in a first hemispherical portion of the therapeutic assembly, wherein the therapeutic assembly does not apply energy to a second hemispherical portion of the therapeutic assembly.

63. The method of claim 45 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes disposed on the struts, and wherein applying energy to the target site comprises:

activating a first electrode of the plurality of electrodes to have a positive polarity; and

activating at least a second electrode and a third electrode of the plurality of electrodes to have a negative polarity, wherein first, second, and third electrodes are concurrently activated and the second and third electrodes sequentially pair with the first electrode based on path of least resistance to sequentially apply therapeutic neuromodulation across a region of the basket.

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64. The method of claim 45 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes disposed on the struts, and wherein applying energy to the target site comprises:

activating a first electrode of the plurality of electrodes to have a positive polarity; and

activating at least second through sixth electrodes of the plurality of electrodes to have a negative polarity, wherein first through sixth electrodes are concurrently activated and the second through sixth electrodes sequentially pair with the first electrode based on path of least resistance to sequentially apply therapeutic neuromodulation across a hemispherical region of the basket.

65. The method of claim 45 wherein the therapeutic assembly comprises an expandable basket having a plurality of struts with a plurality electrodes disposed on the struts and an internal support member comprising a return electrode at a distal end portion of the internal support member, and wherein applying energy to the target site comprises:

activating the electrodes on the struts to have positive polarities; and

activating the return electrode to have a negative polarity, wherein the electrodes apply RF energy across a distal region of the basket.

66. The method of claim 45 wherein the therapeutic assembly comprises an expandable basket having a plurality of branches radially spaced apart from each other when the therapeutic assembly is in an expanded state, wherein each branch comprises at least two adjacent struts with an electrode positioned on each strut, and wherein applying energy to the target site comprises:

activating the electrodes on adjacent struts of at least one of the branches such that the electrodes have opposite polarities; and

applying RF energy between the electrodes on the adjacent struts.

67. The method of claim 45 wherein the therapeutic assembly comprises a plurality of electrodes, and wherein applying energy to the target site comprises:

activating the electrodes of the therapeutic assembly to have positive polarities; and

activating a return electrode disposed on the distal portion of the shaft proximal to the therapeutic assembly, wherein the return electrode has a negative polarity, and

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wherein activating the electrodes and the return electrodes applies RF energy across a turbinate of the human patient.

68. The method of claim 45, further comprising:

detecting, via a plurality of sensing electrodes, neural activity at the target site before applying energy to the target site to therapeutically modulate autonomic activity; and

mapping locations of nerves at the target site based on the detected neural activity,

wherein applying energy to the target site comprises selectively applying energy to a region based on the locations of detected nerves.

69. The method of claim 68, further comprising applying non-therapeutic neural stimulation to the target site before detecting neural activity.

70. The method of claim 68, further comprising detecting, via the plurality of sensing electrodes, neural activity after applying energy to the target site to determine whether the application of energy has therapeutically modulated nerves at the target site.

71. The method of claim 45 wherein:

the therapeutic assembly comprises a flexible membrane carrying a plurality of electrodes;

before applying energy, the method further comprises expanding the flexible membrane at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

72. The method of claim 45, further comprising:

transforming the distal portion of the shaft from a low-profile delivery state to an expanded state such that a plurality of electrodes disposed on the distal portion of the shaft are placed in contact with tissue at the target site, wherein the distal portion of the shaft has a spiral/helical shape in the expanded state; and

wherein applying energy at the target site comprises applying RF energy to the target site via the electrodes.

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73. The method of claim 45 wherein:

the therapeutic assembly comprises a balloon carrying a plurality of electrodes;

before applying energy, the method further comprises expanding the balloon at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

74. The method of claim 73 wherein applying energy to the target site further comprises:

selectively activating the electrodes to apply current in a radial direction across a circumferential segment of the balloon.

75. The method of claim 73 wherein applying energy to the target site further comprises:

selectively activating the electrodes to apply current in a longitudinal direction across a longitudinal region of the balloon.

76. The method of claim 73 wherein expanding the balloon comprises filling the balloon with a fluid, and wherein the balloon comprises a plurality of holes that allow for perfusion of the fluid through the balloon during energy application.

77. The method of claim 73 wherein expanding the balloon comprises circulating a fluid through the balloon, wherein the fluid cools the electrodes during energy application.

78. The method of claim 45 wherein:

the therapeutic assembly comprises a plurality of balloons extending distally from the distal portion of the shaft and a plurality of electrodes disposed on the balloons;

before applying energy, the method further comprises independently expanding the balloons at the target site to place at least a portion of the electrodes in contact with tissue at the target site; and

applying energy to the target site comprises applying RF energy to the target site via the electrodes.

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79. The method of claim 78 wherein applying energy to the target site further comprises:

activating a return electrode on an internal support member extending through the plurality of balloons; and

activating at least a portion of the electrodes on the balloons.

80. The method of claim 45, further comprising:

measuring temperature of tissue at the target site during energy application; and

terminating energy application when a threshold maximum temperature is reached.

81. The method of claim 45, further comprising terminating energy application after a predetermined maximum time period.

82. The method of claim 45, further comprising:

detecting impedance of tissue at the target site during energy application; and

terminating energy application when a threshold impedance value is reached.

83. The method of claim 45, further comprising:

detecting impedance of tissue at the target site before energy application to define a baseline impedance;

detecting impedance of tissue at the target site during energy application; and

terminating energy application when a threshold change in impedance from the baseline impedance is reached.

84. The method of claim 45 wherein applying energy to the target site comprises applying therapeutic cryogenic cooling to tissue at the target site to therapeutically modulate autonomic activity within the nasal cavity, the nasopharynx, and/or the paranasal cavities.

85. The method of claim 45 wherein applying energy to the target site comprises:

circulating a heated fluid within a balloon such that an exterior surface of the balloon contacts tissue at the target site and heats the tissue to thermally modulate autonomic activity at the target site.

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86. The method of claim 45 wherein applying energy to the target site comprises:

expanding a balloon such that an exterior surface of the balloon contacts tissue at the target site; and

heating a heating member within the balloon, wherein the heat from the heating member transfers to the fluid and to the tissue adjacent to the balloon to thermally modulate autonomic activity.

87. The method of claim 45 wherein applying energy to the target site comprises generating a plasma field to therapeutically modulate nerves at the target site.

88. The method of claim 45 wherein applying energy to the target site therapeutically modulates cholinergic pathways that send signals to submucosal glands.

89. The method of claim 45 wherein intraluminally advancing the therapeutic assembly to the target site comprises intraluminally advancing the therapeutic assembly to parasympathetic nerve points of entrance into the nasal region via accessory foramen and/or microforamina within at least one of a superior meatus, a middle meatus, an inferior meatus, or a pterygopalatine fossa.

90. A method of therapeutically modulating nerves in a nasal region, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within a nasal region, wherein the target site is proximate to parasympathetic nerves proximate to the sphenopalatine foramen;

detecting locations of the parasympathetic nerves at the target site; and

applying energy, with the therapeutic assembly, to the target site based on the detected locations of the parasympathetic nerves, wherein applying energy therapeutically modulates autonomic activity within at least one of a nasal cavity, a nasopharynx, or paranasal cavities.

91. The method of claim 90 wherein detecting locations of the parasympathetic nerves at the target site comprises measuring dielectric properties of heterogeneous

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tissue within at least one of the nasal cavity, the nasopharynx, and/or the paranasal cavities on a high resolution spatial grid.

92. The method of claim 90 wherein detecting locations of the parasympathetic nerves at the target site comprises measuring the dipole properties of heterogeneous tissue within the nasal cavity, the nasopharynx, and/or the paranasal cavities on a high resolution spatial grid.

93. The method of claim 90 wherein detecting locations of the parasympathetic nerves at the target site comprises detecting impedance of heterogeneous tissue within at least one of the nasal cavity, the nasopharynx, or the paranasal cavities on a high resolution spatial grid.

94. A device for therapeutic neuromodulation in a nasal region of a human patient, the system comprising:

a delivery catheter having a distal portion, wherein the delivery catheter is configured to locate the distal portion at a target site within the nasal region;

a flexible support at the distal portion of the delivery catheter; and

a plurality of electrodes carried by the flexible support,

wherein the flexible support is configured to conform to irregularities of local anatomy at the target site to provide topographical compliance and a linkage for electrical activation of at least a portion of the electrodes, and

wherein the electrodes are configured to therapeutically modulate parasympathetic nerves of mucosal and sub-mucosal structures in direct or in-direct contact with the electrodes.

95. The device of claim 94, further comprising a controllable recapturing mechanism configured to recapture the flexible support after energy delivery to allow withdrawal of the flexible support from a nasal cavity.

96. The device of claim 94 wherein the target site is at a sphenopalatine foramen.

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97. The device of claim 94 wherein the electrodes are configured to be selectively activated to control energy direction and associated dissipation for accurate and localized energy delivery.

98. A method of therapeutically modulating nerves in a nasal region of a human patient, the method comprising:

intraluminally advancing a therapeutic assembly at a distal portion of a shaft of a therapeutic device to a target site within the nasal region, wherein the target site is at least proximate to an ostium of at least one of a frontal sinus, an ethmoidal sinus, a sphenoidal sinus, or a maxillary sinus of the human patient; and

applying energy, with the therapeutic assembly, to the target site to therapeutically modulate parasympathetic nerves at the target site to treat chronic sinusitis.

99. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the frontal sinus; and

applying energy to the target site comprises applying energy to at least one of a supraorbital nerve, a supratrochlear nerve, branches of the supraorbital nerve, branches of the supratrochlear nerve, or other parasympathetic neural fibers that innervate mucosa of the frontal sinus.

100. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the ethmoidal sinus; and

applying energy to the target site comprises applying energy to at least one of an anterior ethmoidal branch of a nasociliary nerve, a posterior ethmoidal branch of the nasociliary nerve, a maxillary nerve, branches of the nasociliary nerve, branches of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the ethmoidal sinus.

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101. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the maxillary sinus; and

applying energy to the target site comprises applying energy to at least one of an infra-orbital branch of a maxillary nerve, an alveolar branch of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the maxillary sinus.

102. The method of claim 98 wherein:

intraluminally advancing the therapeutic assembly to the target site comprises positioning the therapeutic assembly proximate to the ostium of the sphenoidal sinus; and

applying energy to the target site comprises applying energy to at least one of a posterior ethmoidal branch of an ophthalmic nerve, a maxillary nerve, branches of the ophthalmic nerve, branches of the maxillary nerve, or other parasympathetic neural fibers that innervate mucosa of the sphenoidal sinus.

103. A system for therapeutic neuromodulation in a nasal region of a human patient for treatment of chronic sinusitis, the system comprising:

a shaft having a proximal portion and a distal portion, wherein the shaft is configured to locate the distal portion intraluminally at a target site, wherein the target site is at least proximate to an ostium of at least one of a frontal sinus, an ethmoidal sinus, a sphenoidal sinus, or a maxillary sinus of the human patient; and

a therapeutic assembly at the distal portion of the shaft, wherein the therapeutic assembly is comprises an energy delivery element configured to therapeutically modulate parasympathetic nerves that innervate mucosa of at least one of the frontal sinus, the ethmoidal sinus, the sphenoidal sinus, or the maxillary sinus.

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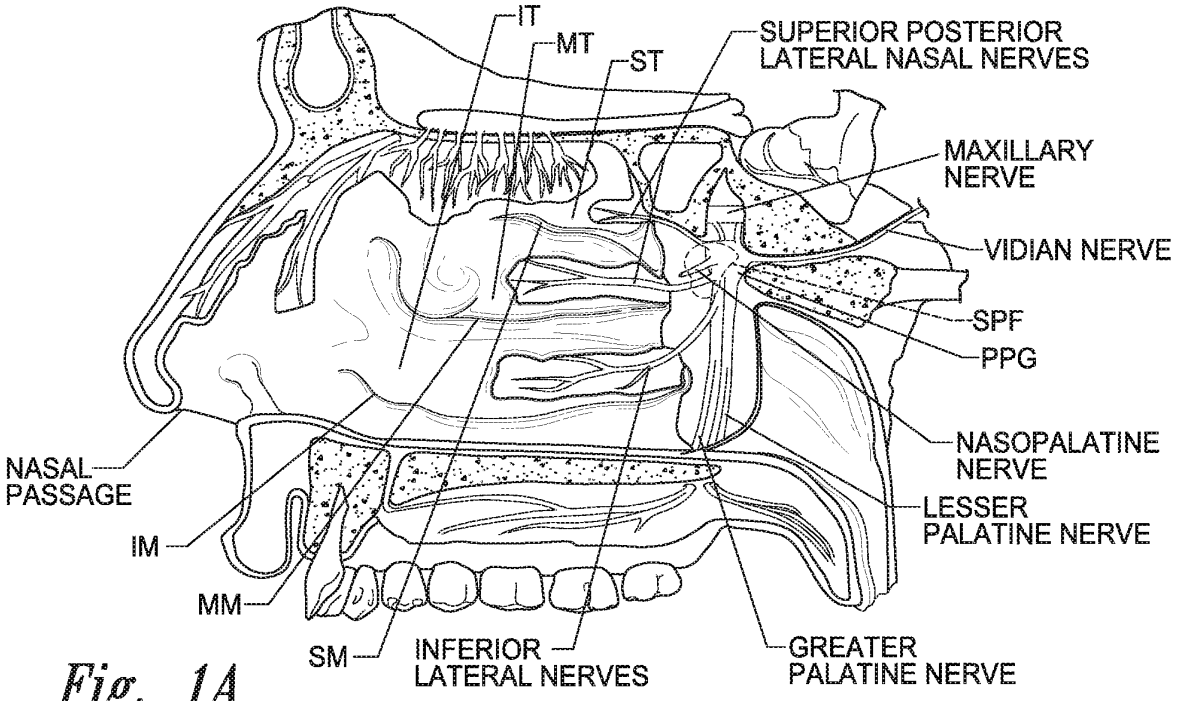

IT
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SUPERIOR POSTERIOR LATERAL NASAL NERVES
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VIDIAN NERVE
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NASOPALATINE NERVE
LESSER PALATINE NERVE
NASAL PASSAGE
IM
MM
SM
INFERIOR LATERAL NERVES
GREATER PALATINE NERVE

Fig. 1A

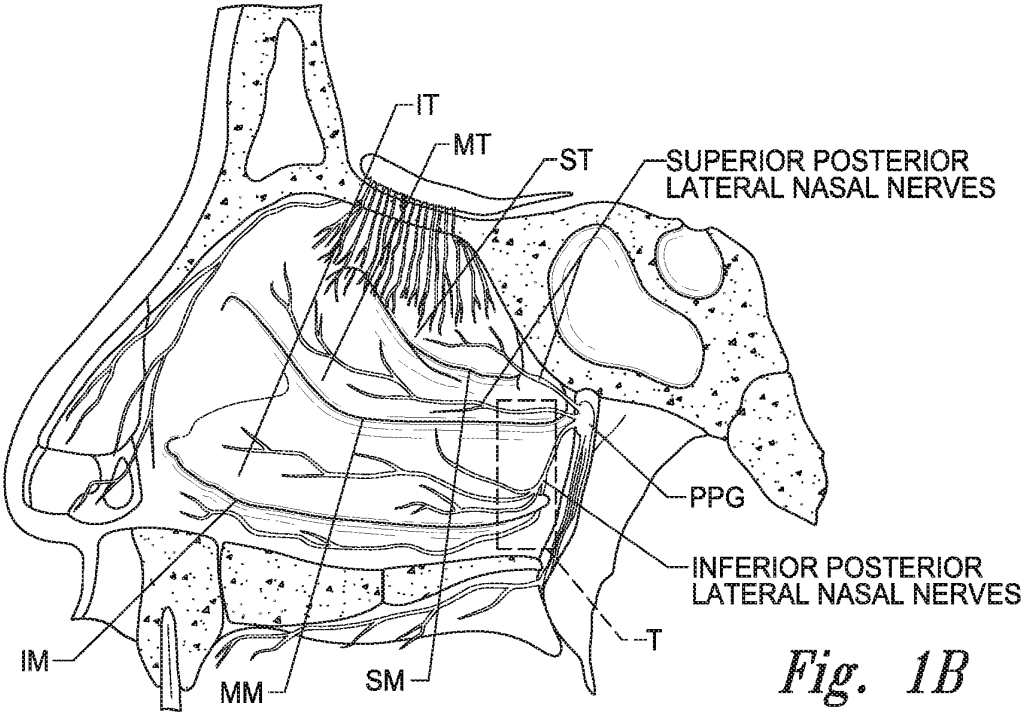

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Fig. 1B

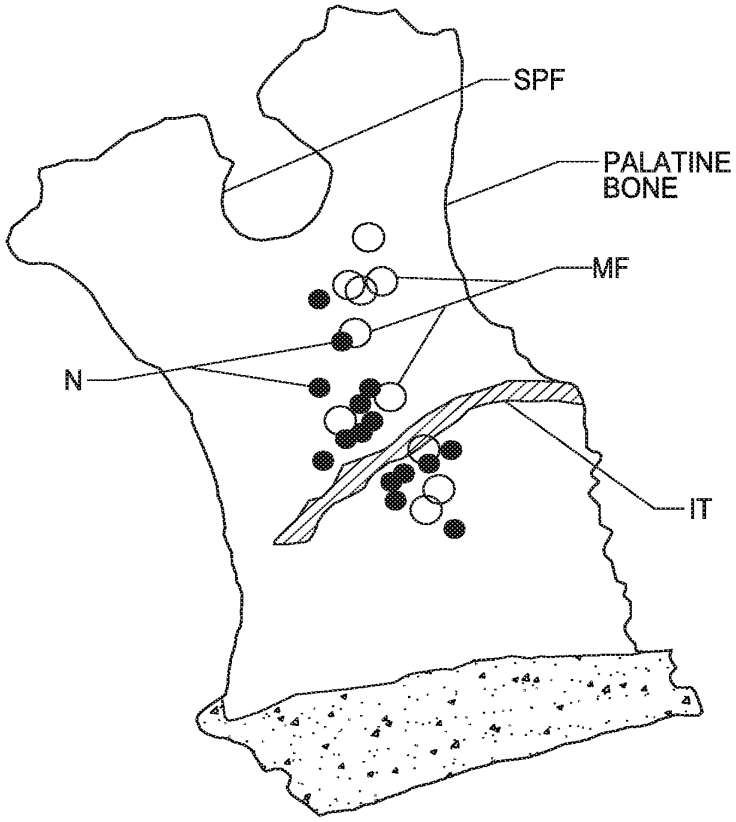


Fig. 1C

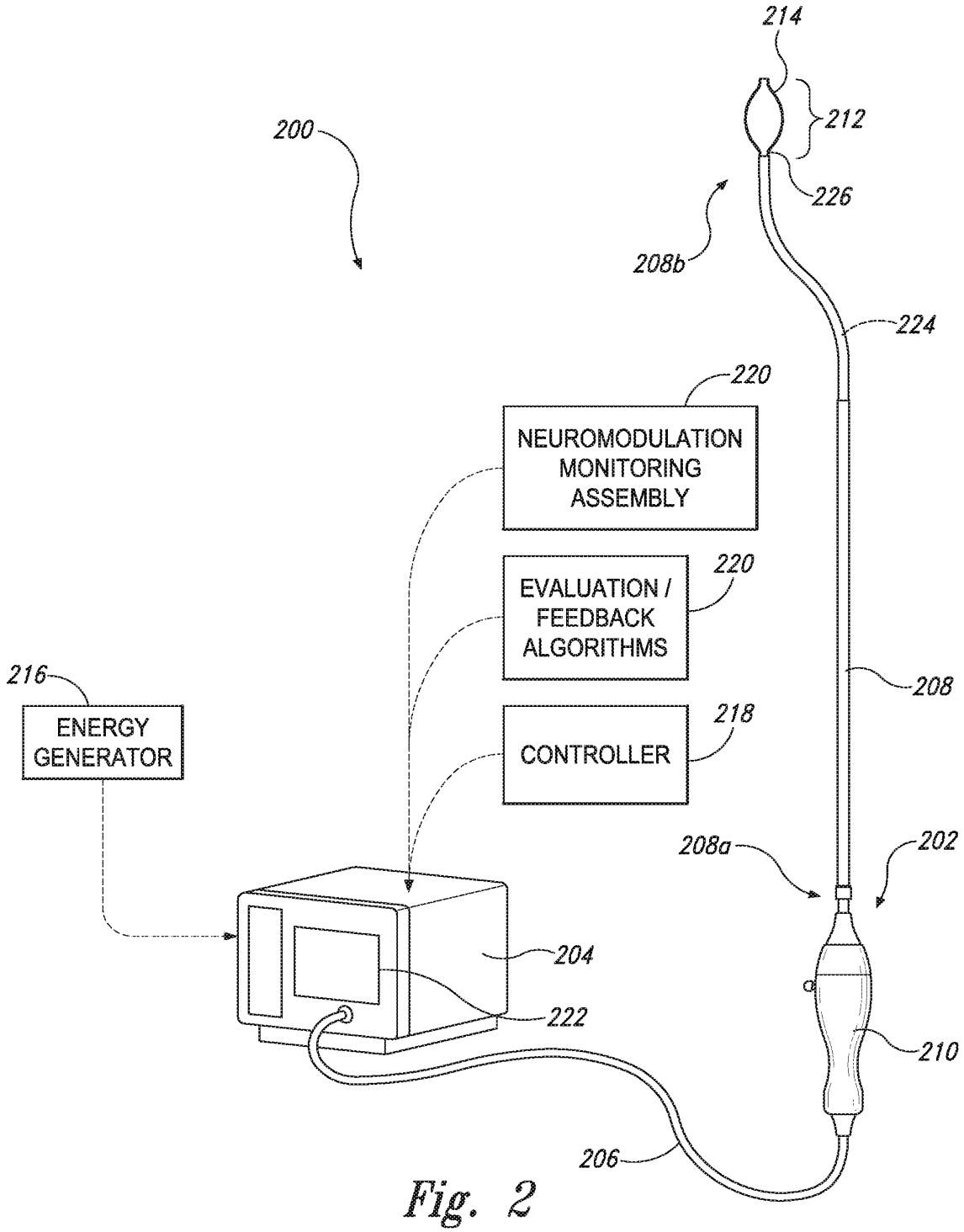

214
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208b
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NEUROMODULATION MONITORING ASSEMBLY
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EVALUATION / FEEDBACK ALGORITHMS
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ENERGY GENERATOR
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CONTROLLER
208a
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Fig. 2

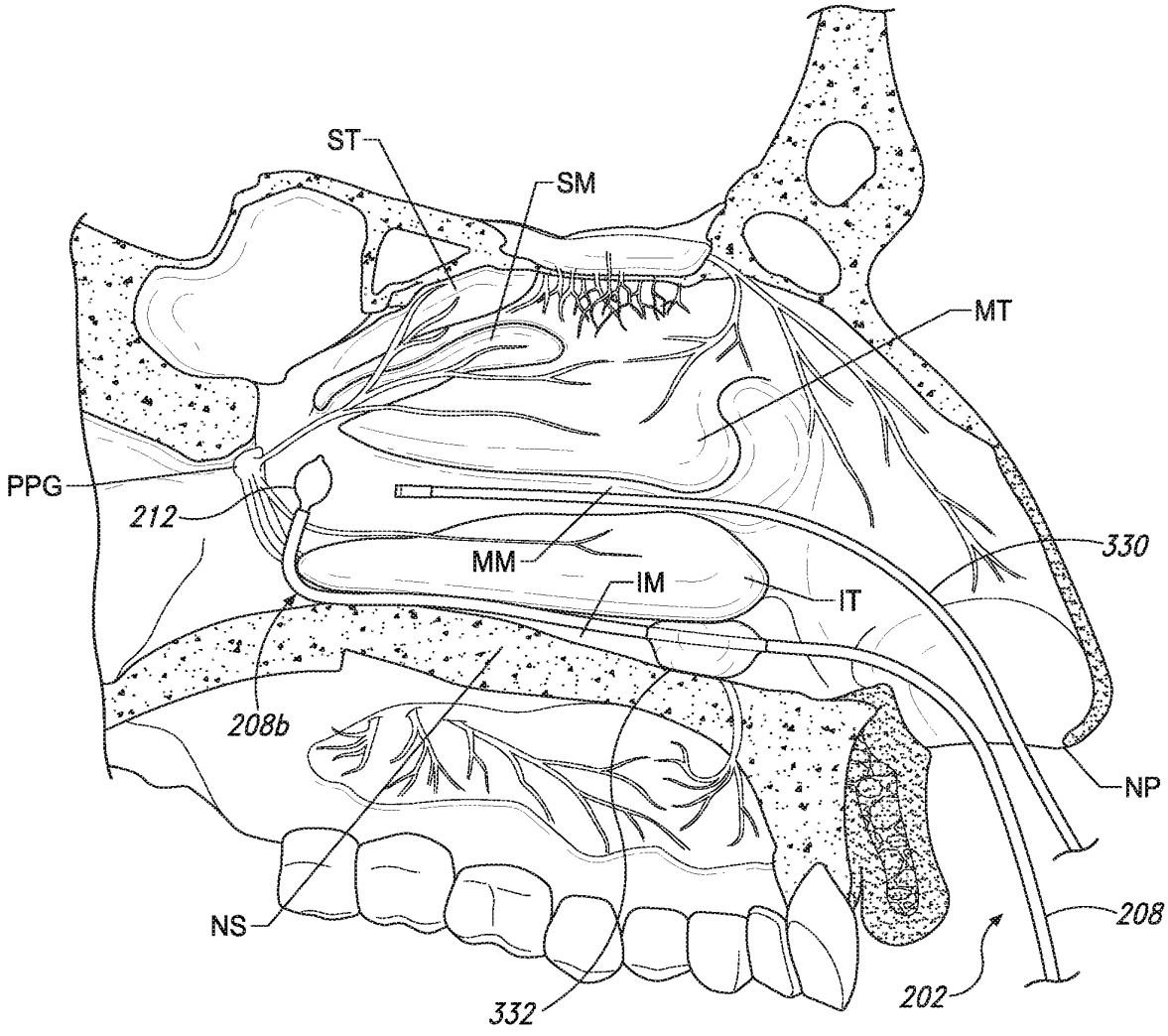


Fig. 3A

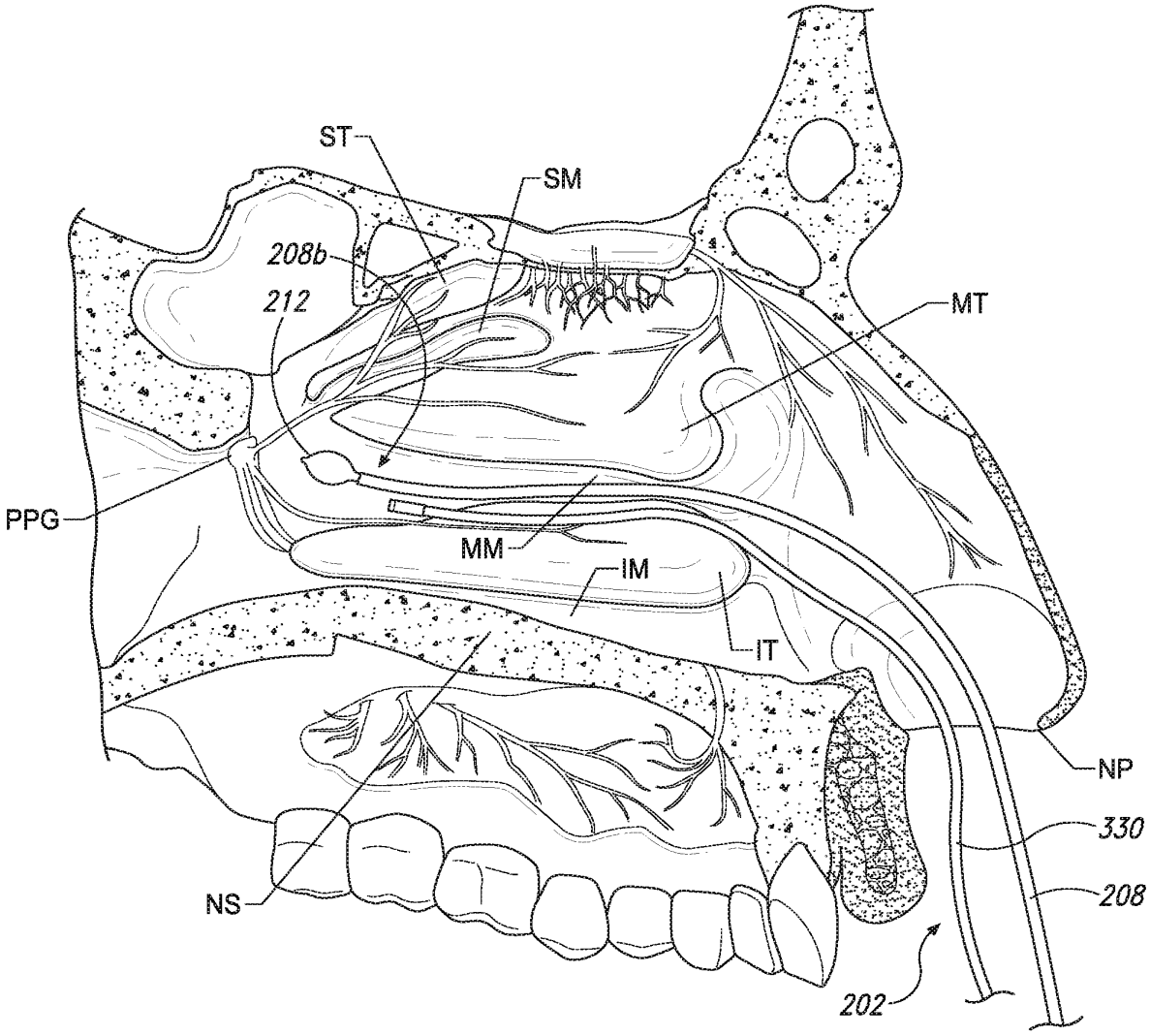


Fig. 3B

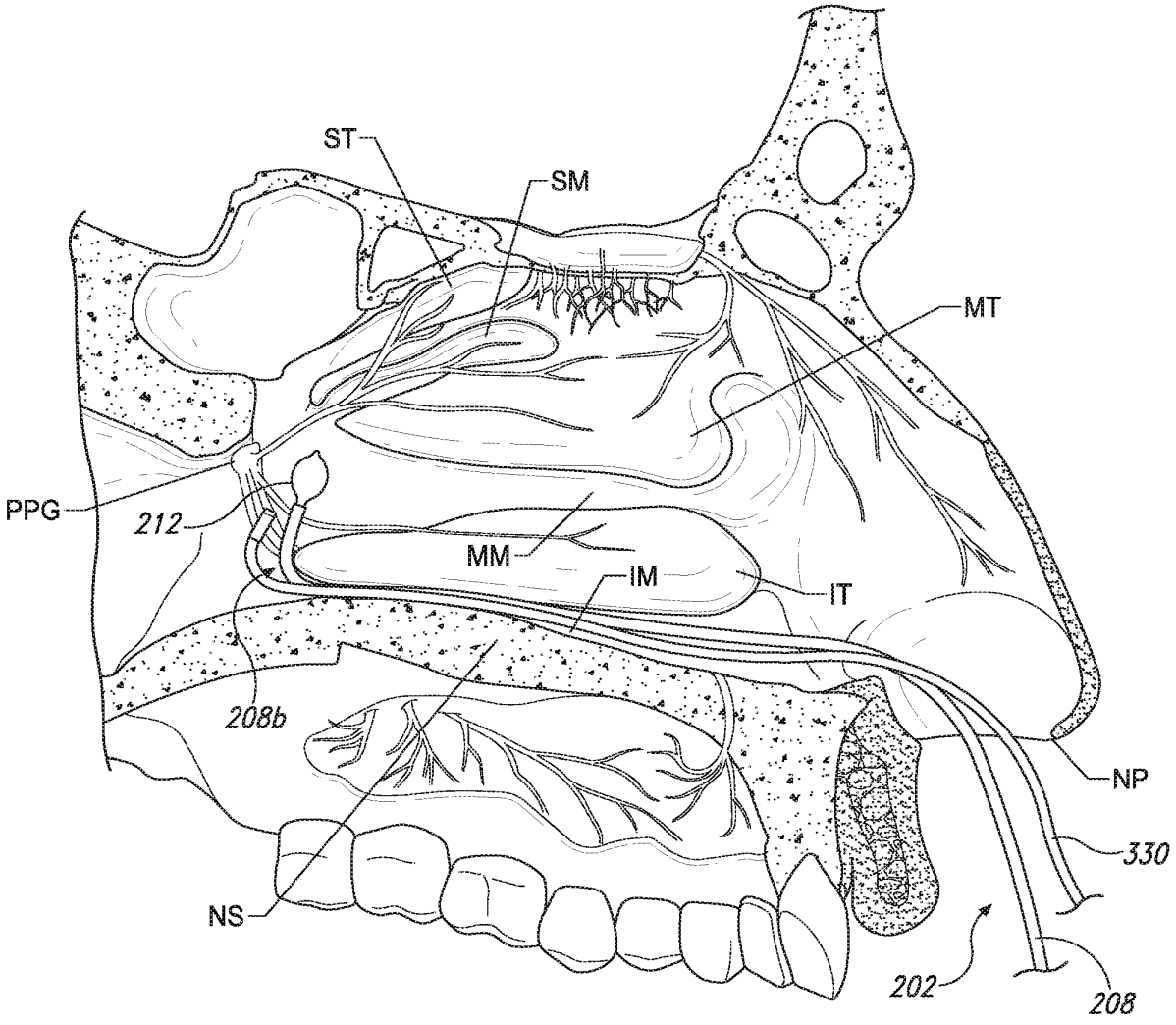


Fig. 3C

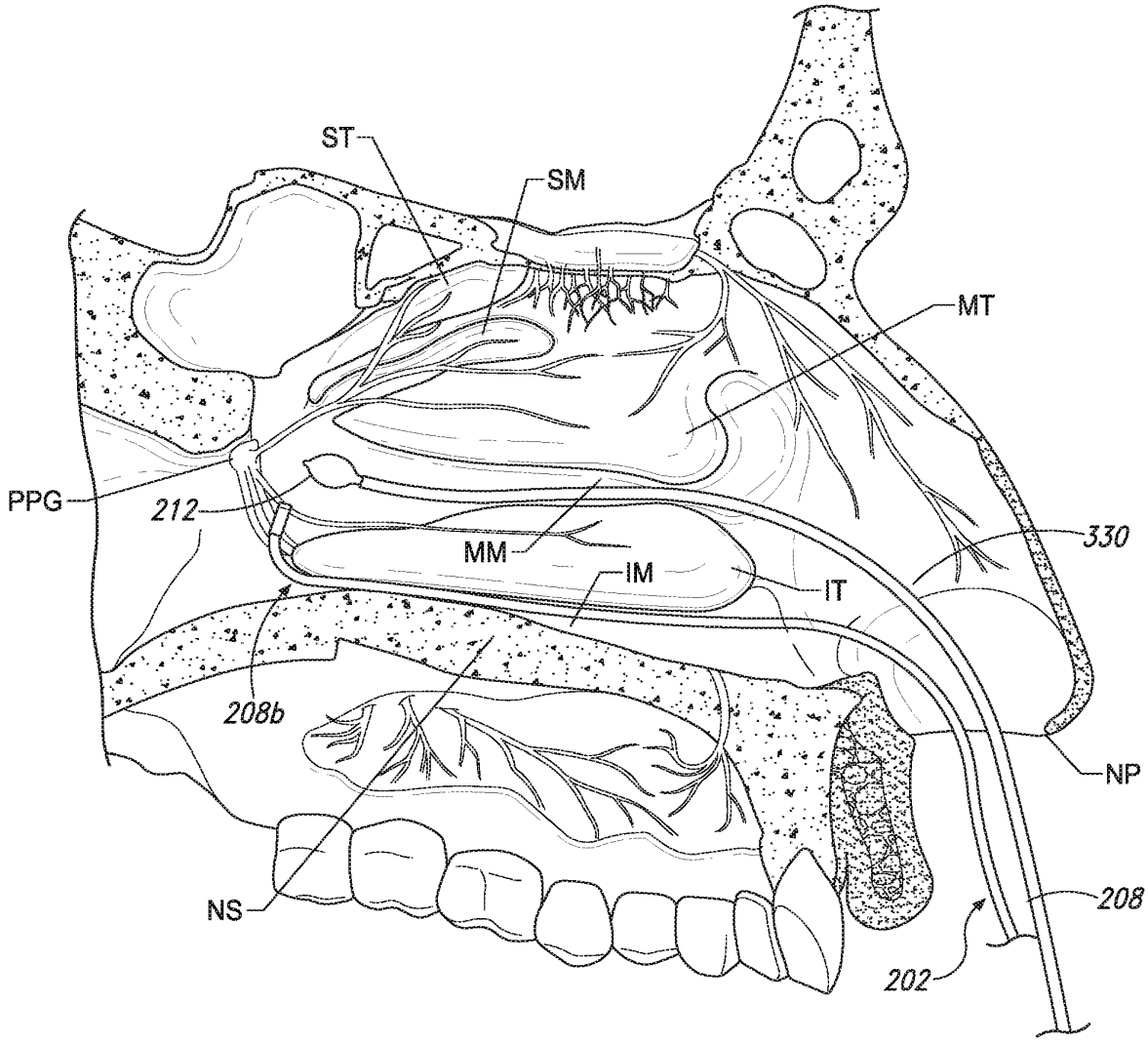


Fig. 3D

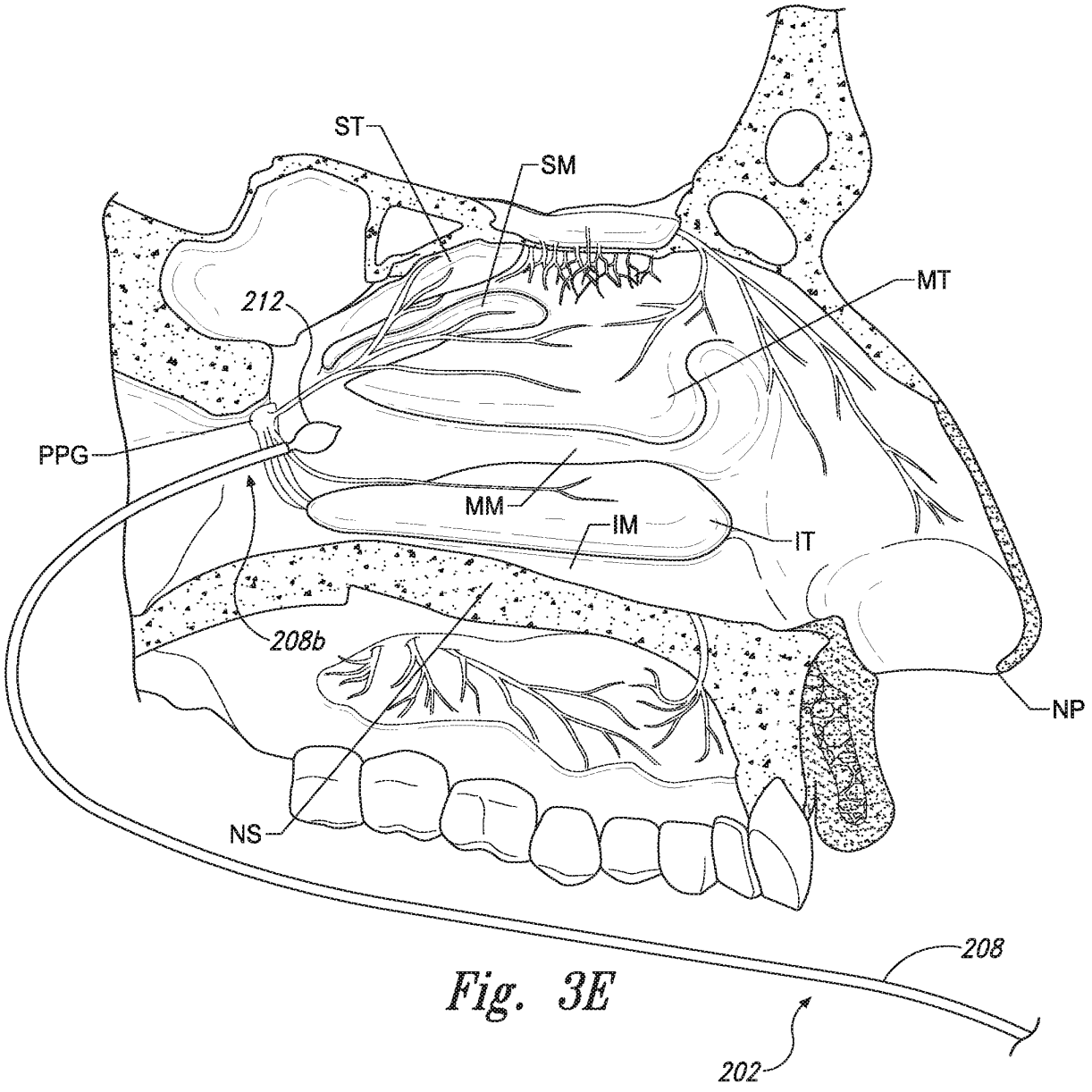


Fig. 3E

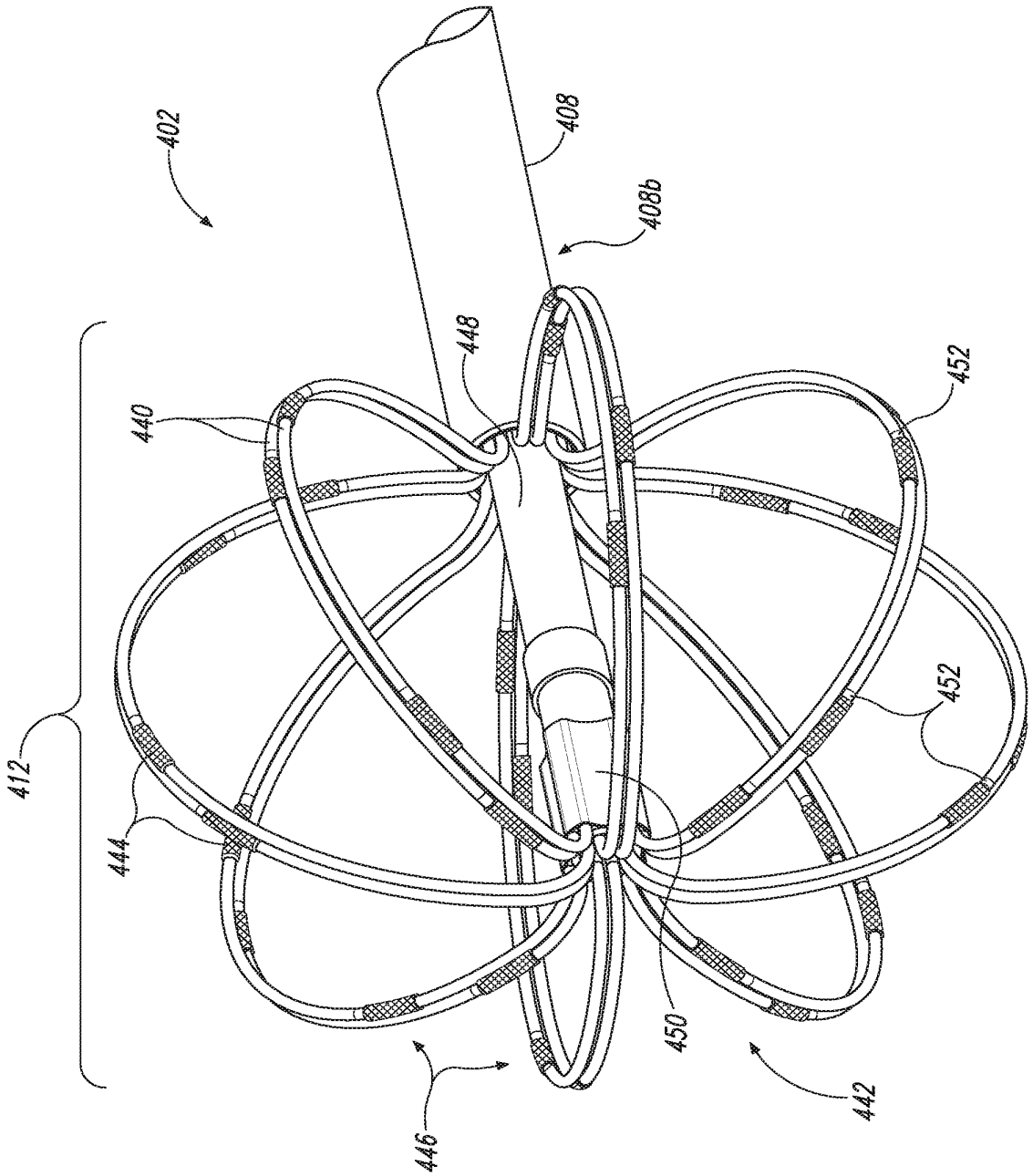


Fig. 4

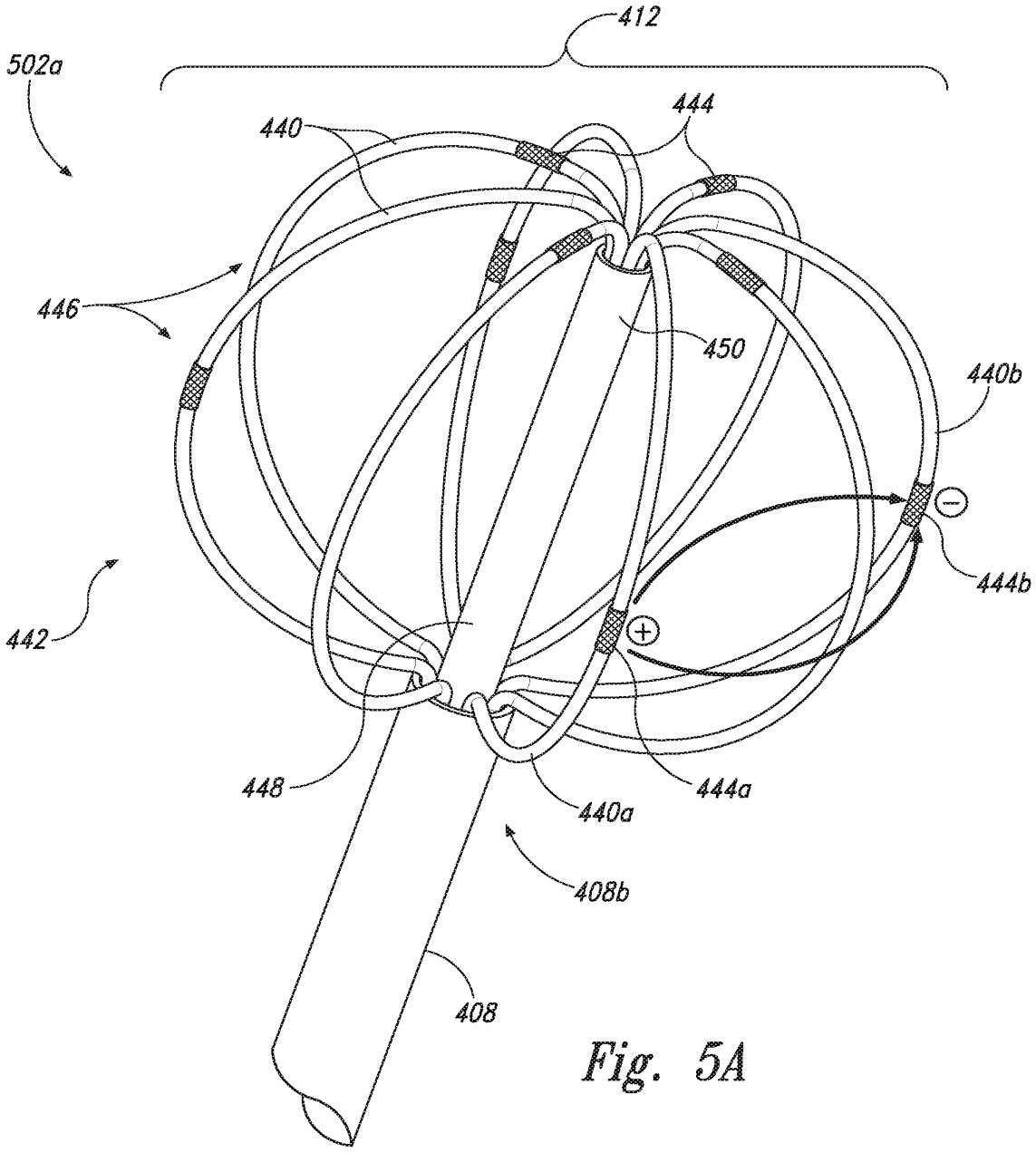


Fig. 5A

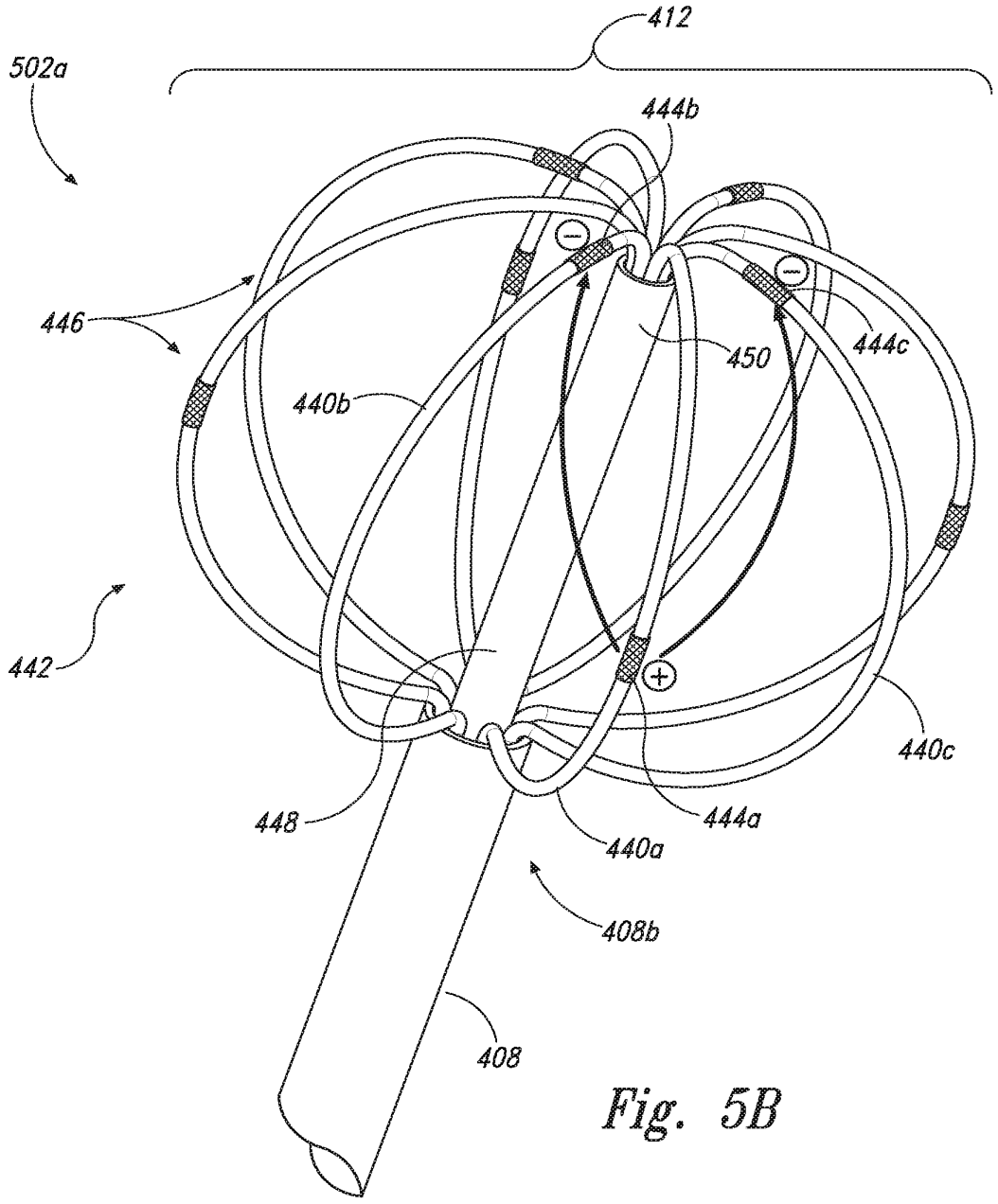

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Fig. 5B

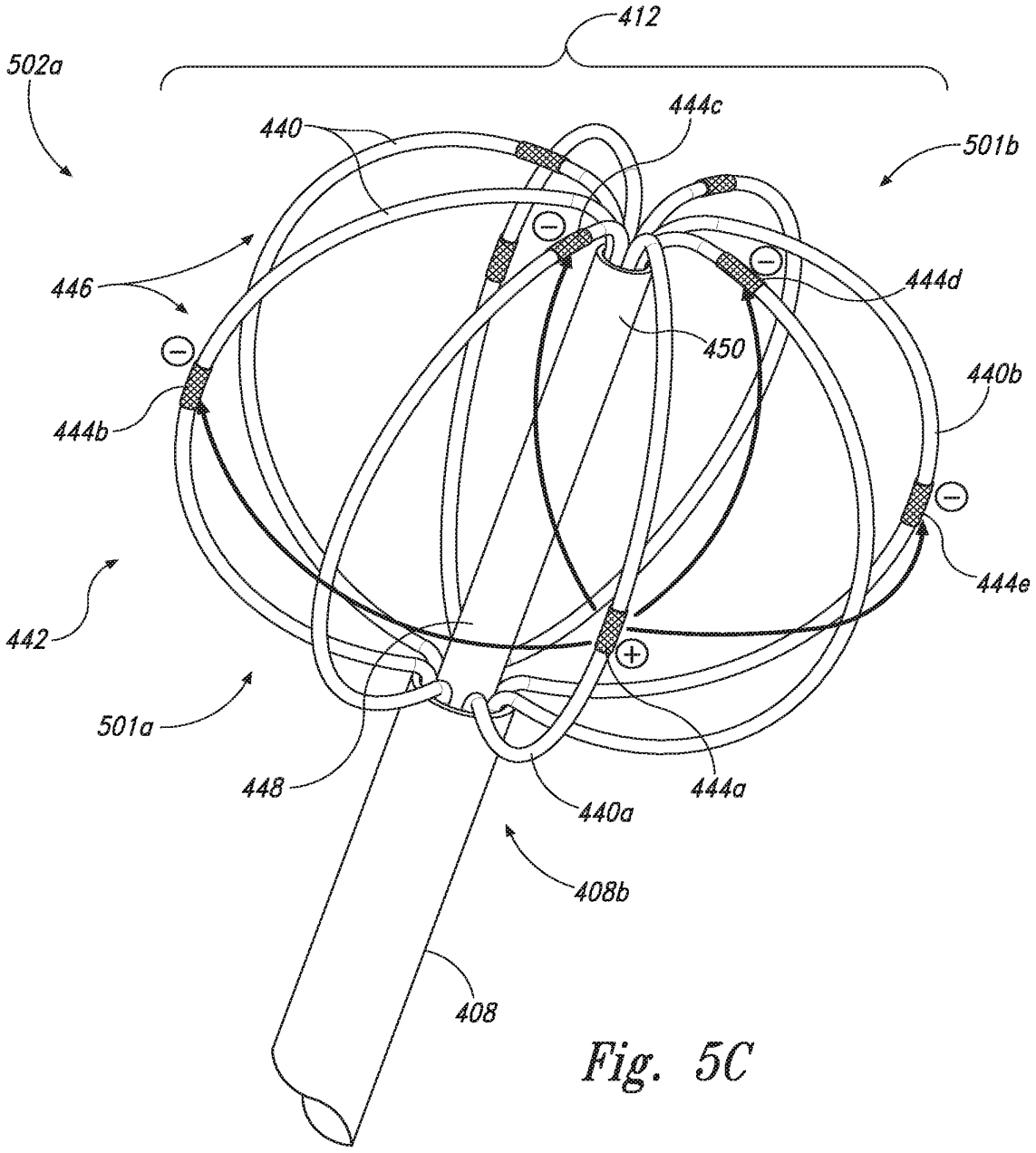

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Fig. 5C

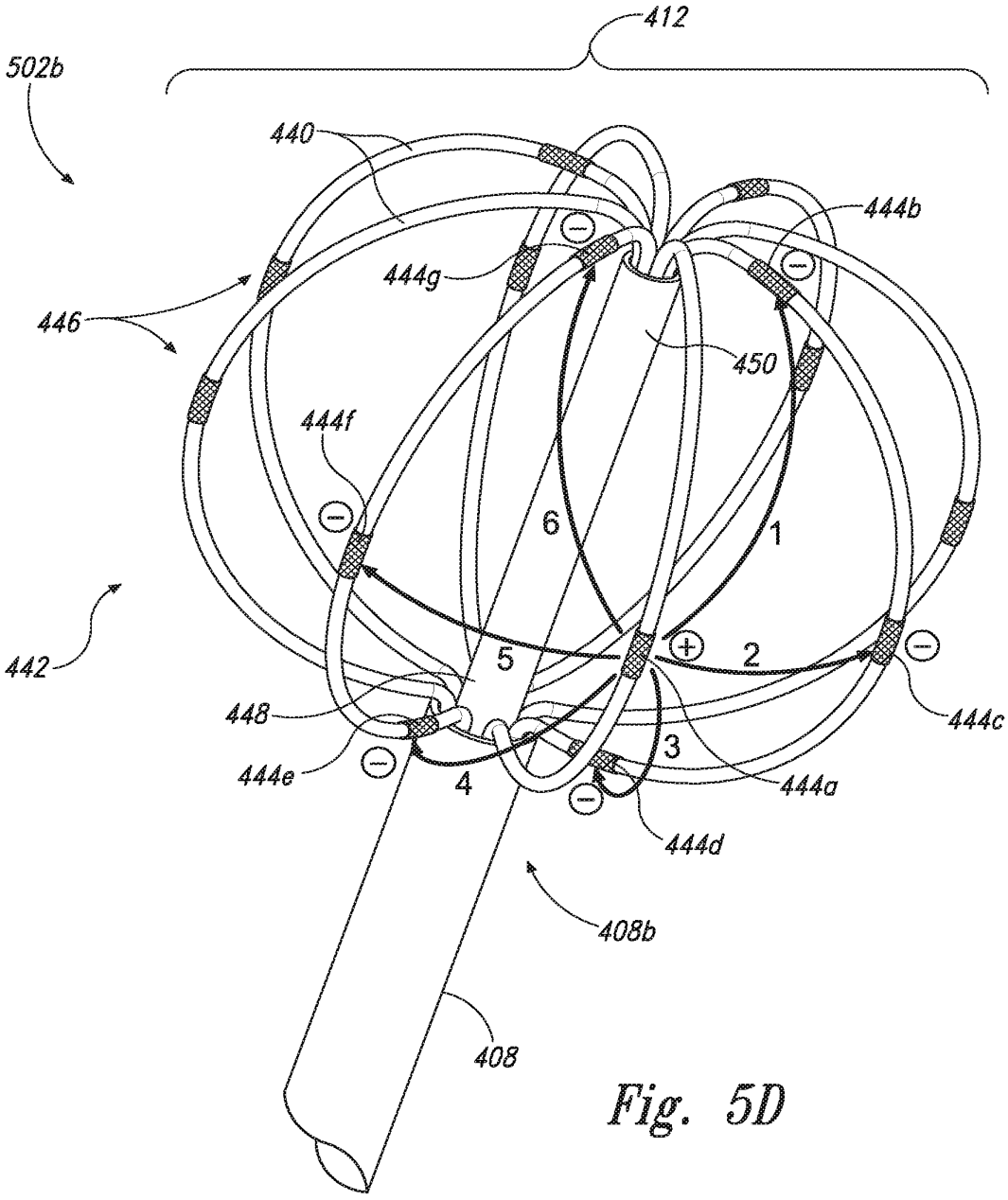

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Fig. 5D

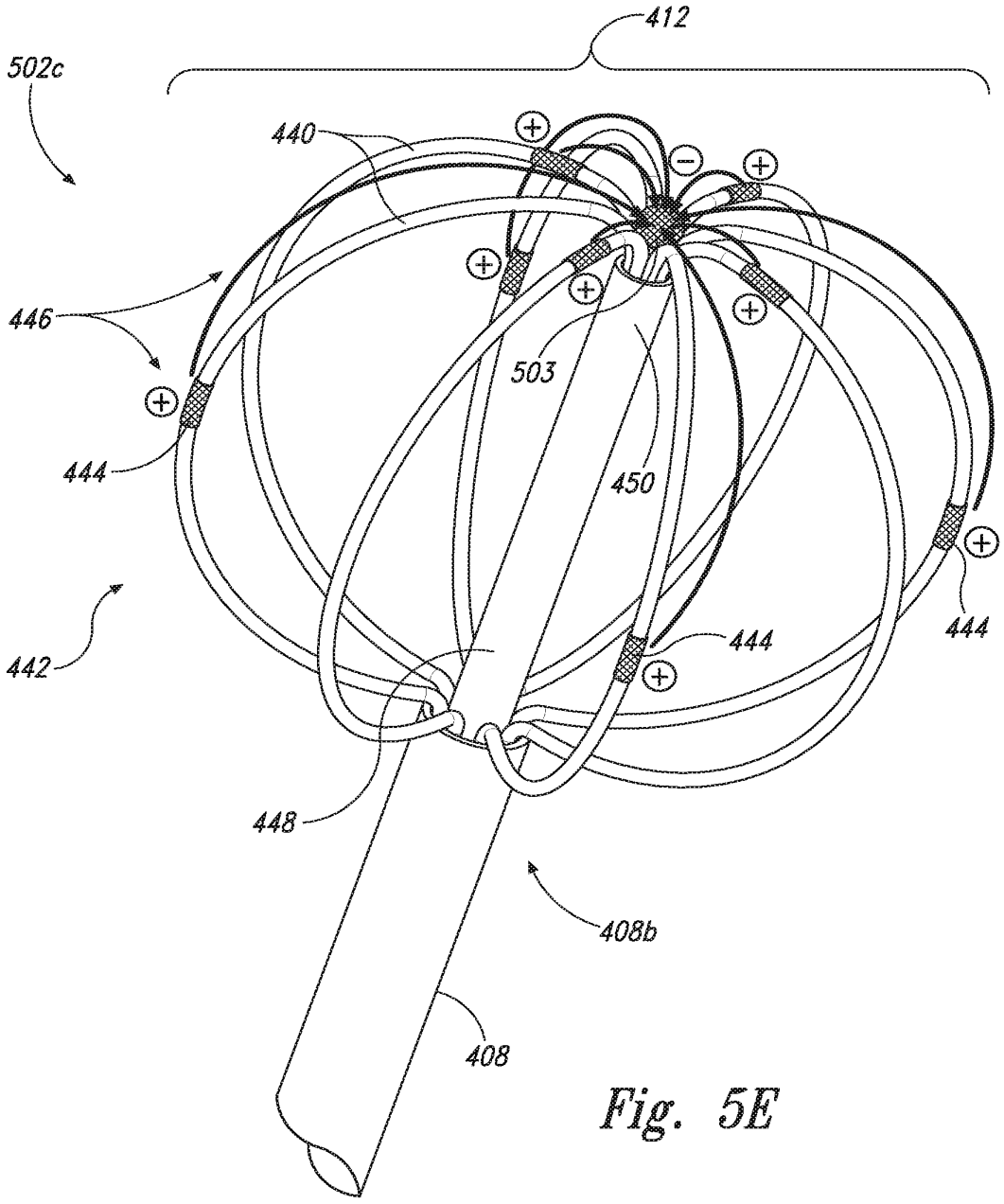


Fig. 5E

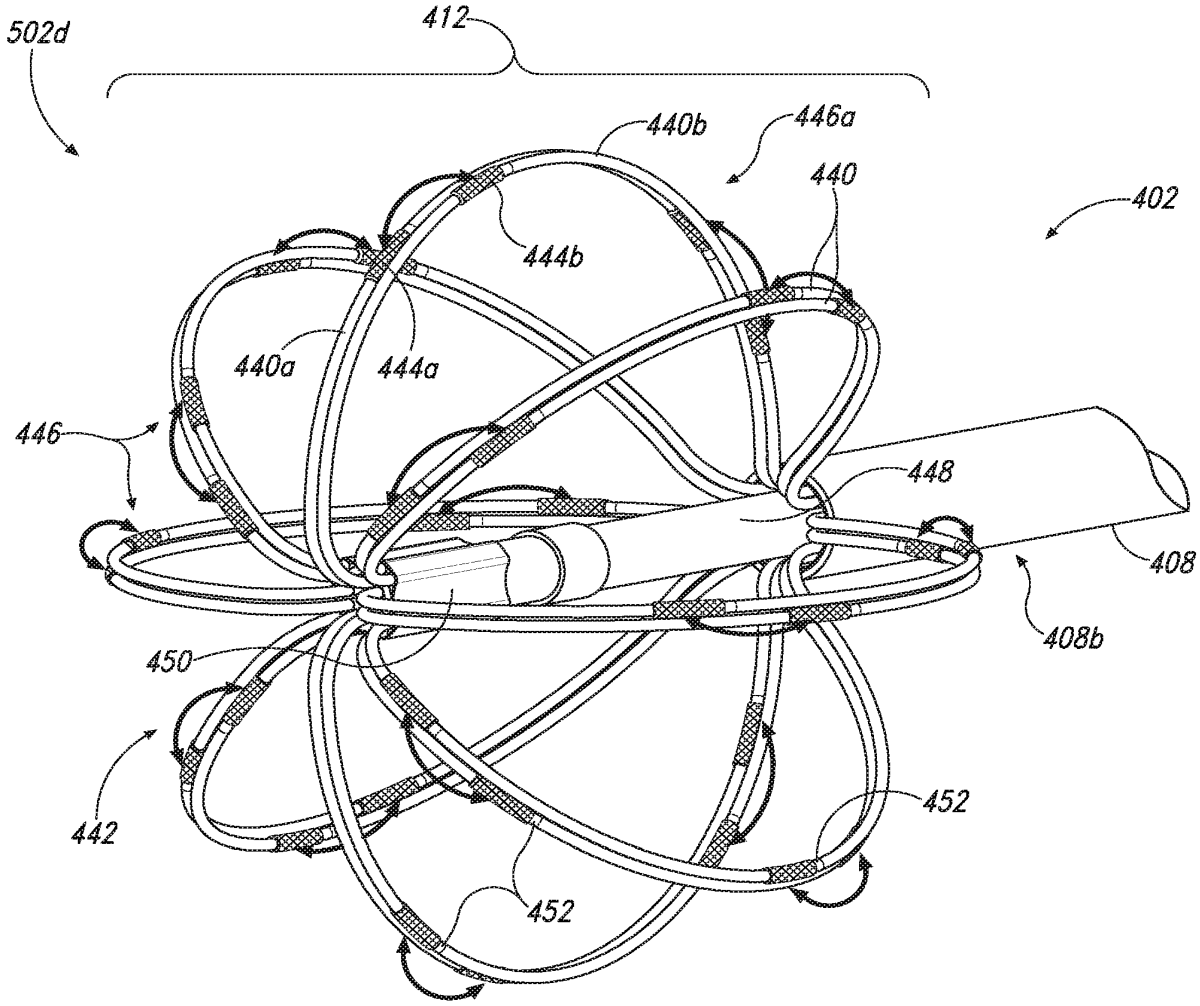

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452

Fig. 5F

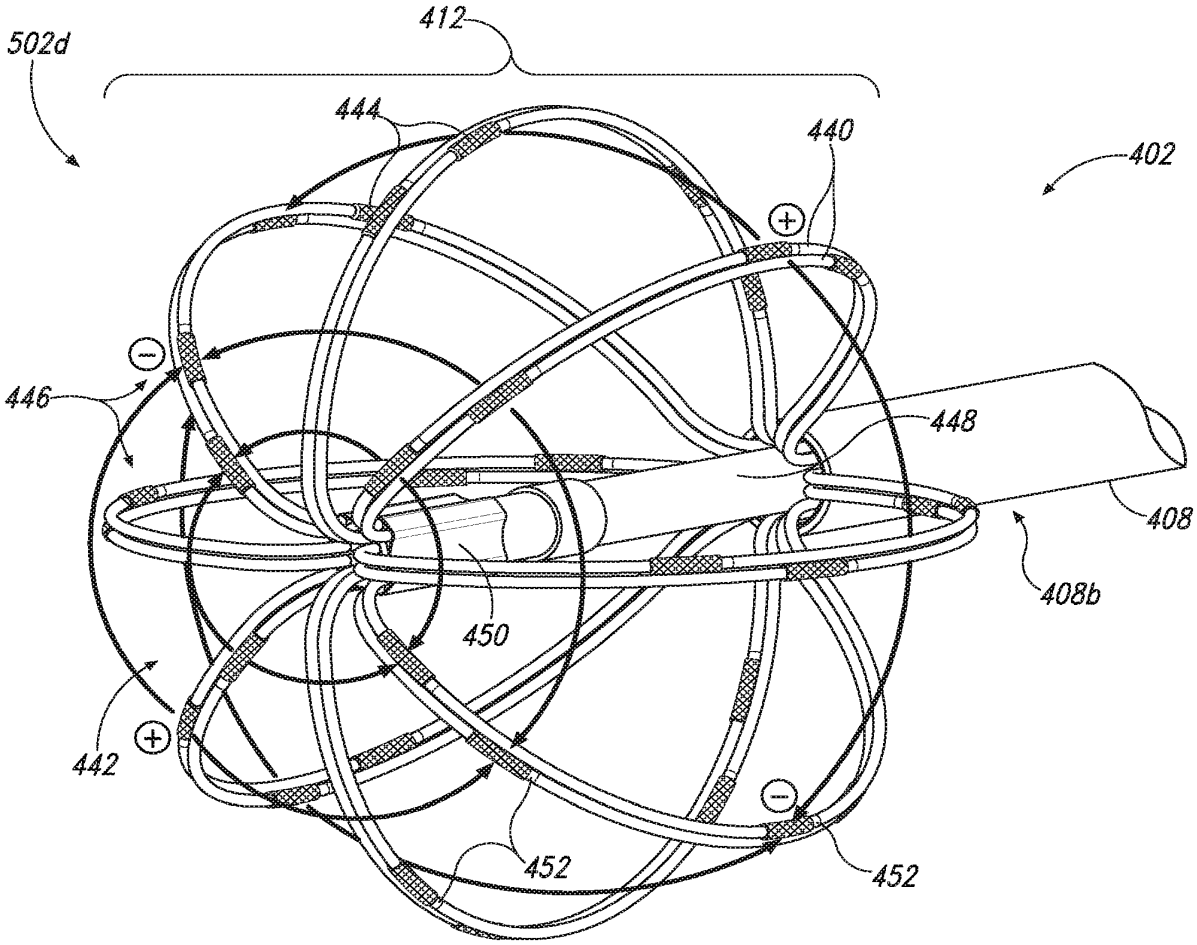


Fig. 5G

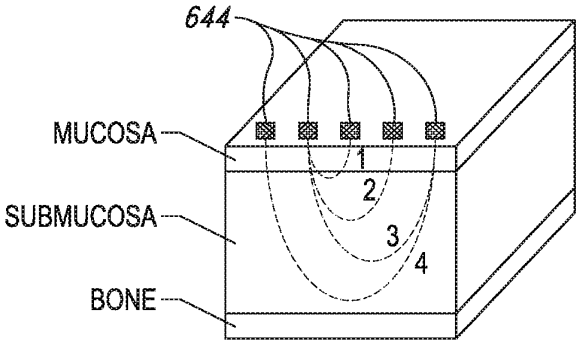


Fig. 6A

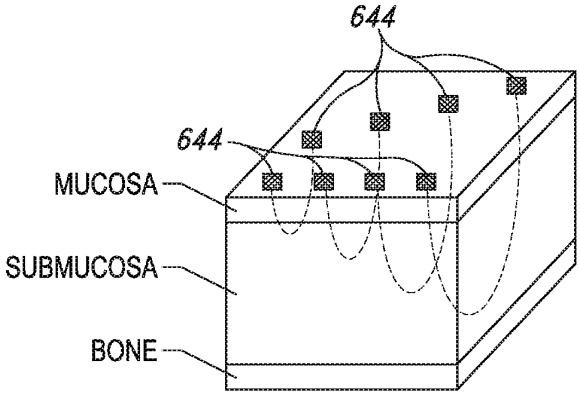


Fig. 6B

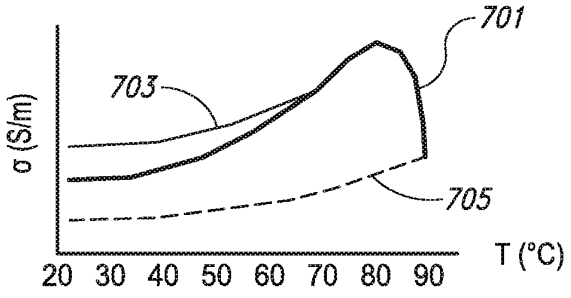


Fig. 7

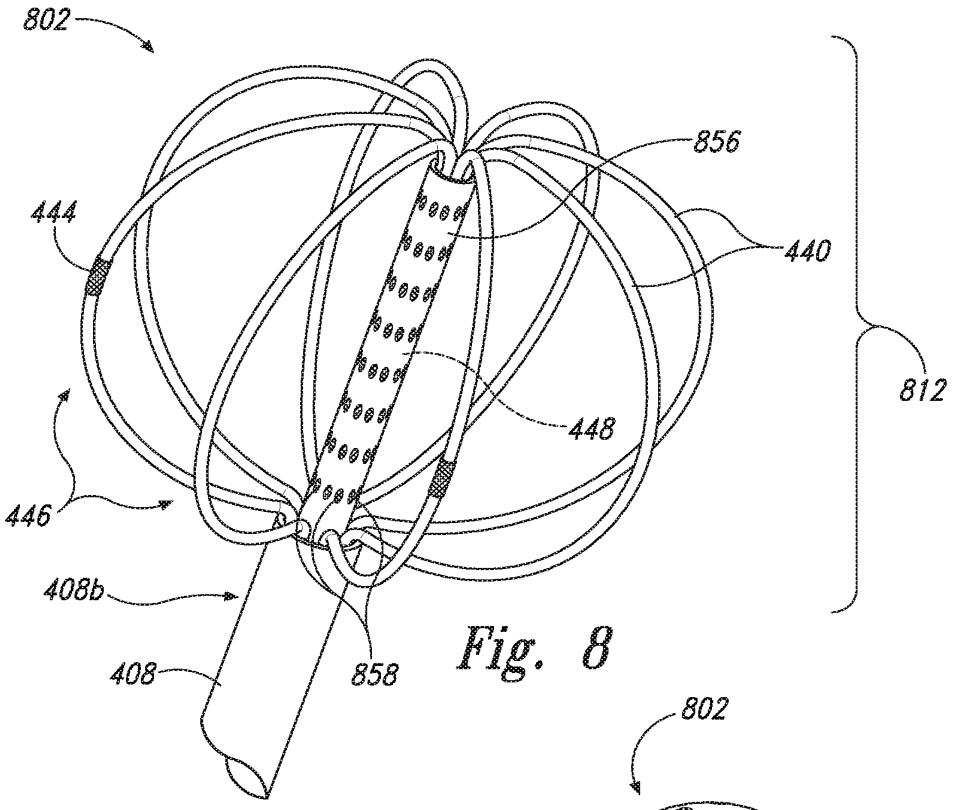

802
856
444
440
812
448
446
408b
858
408

Fig. 8

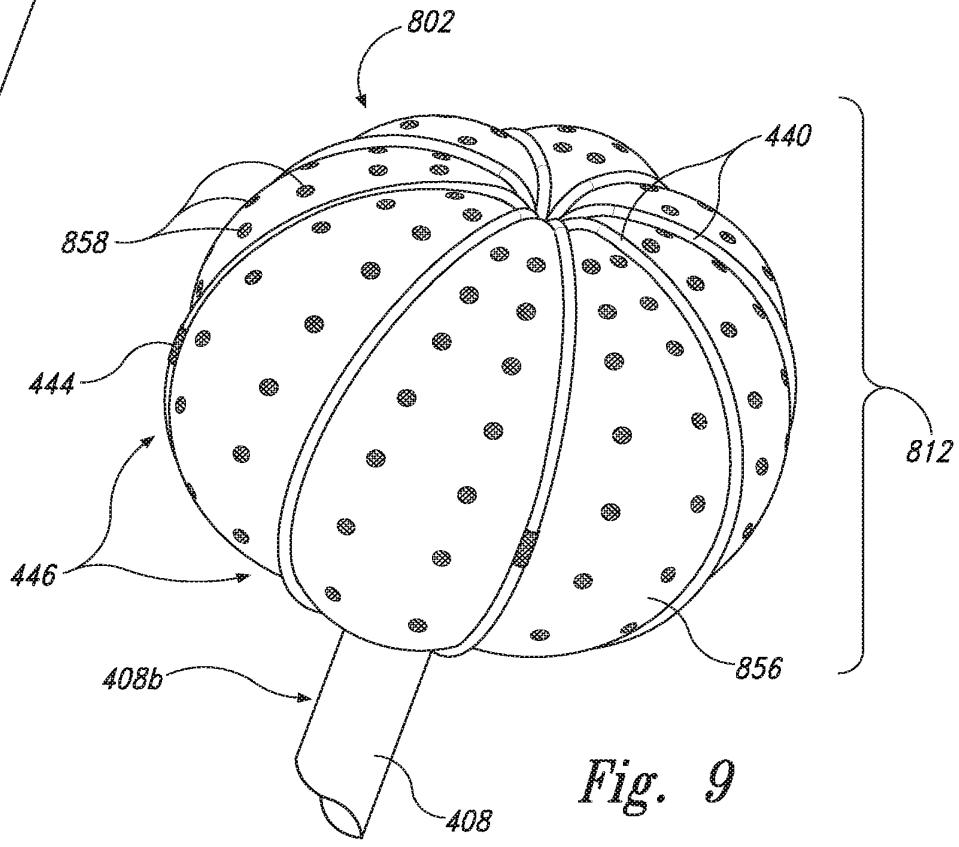

802
440
858
444
812
446
856
408b
408

Fig. 9

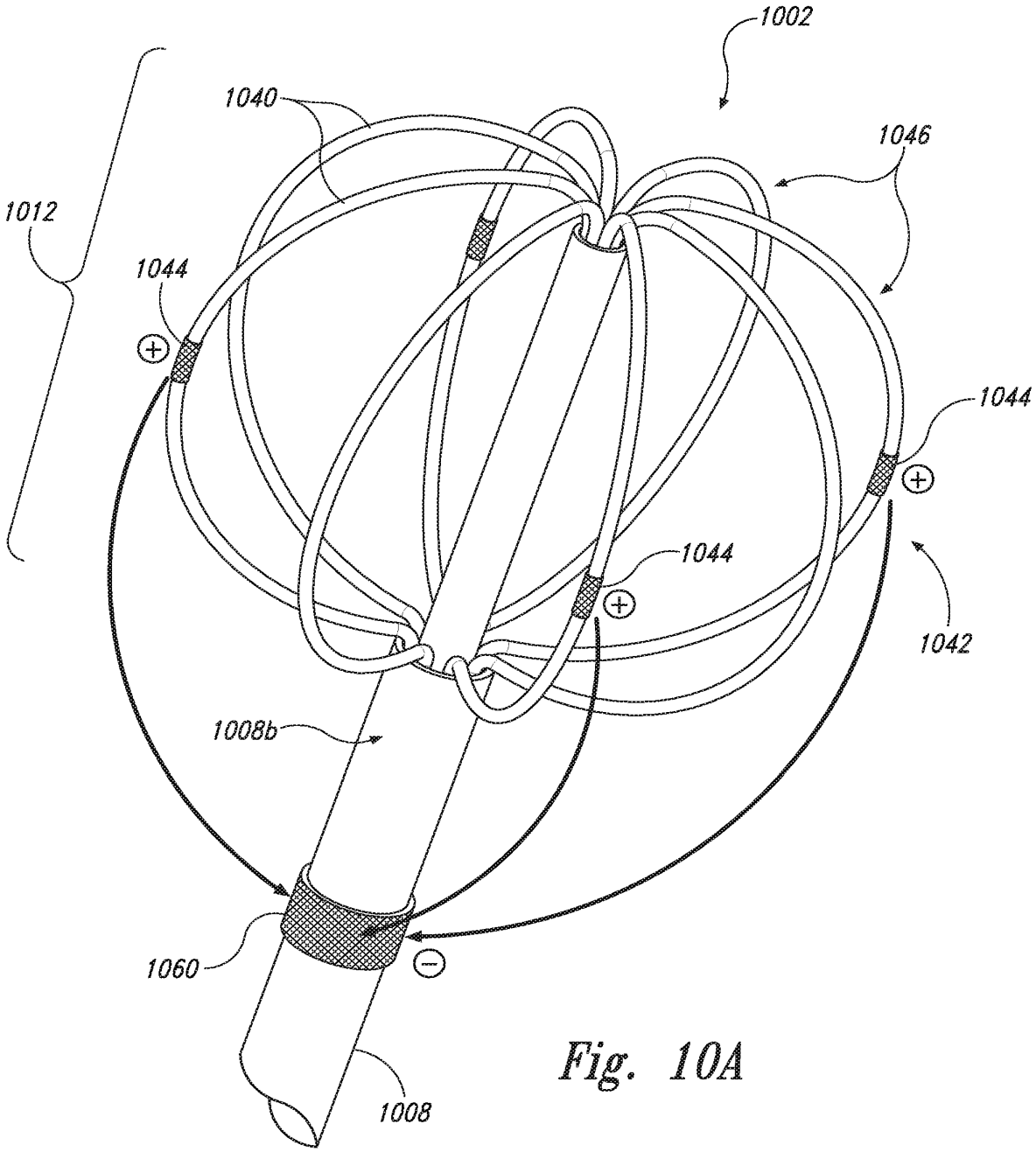


Fig. 10A

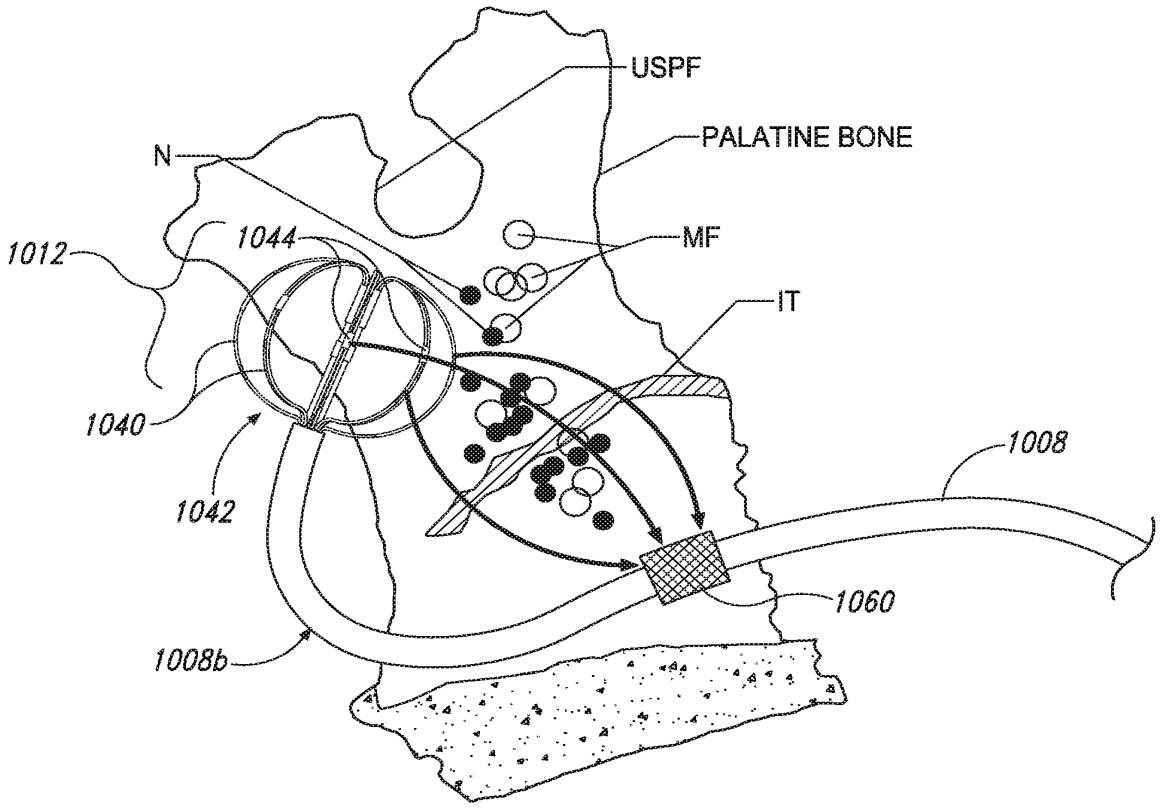

USPF
PALATINE BONE
N
1012
1044
MF
IT
1040
1042
1008
1060
1008b

Fig. 10B

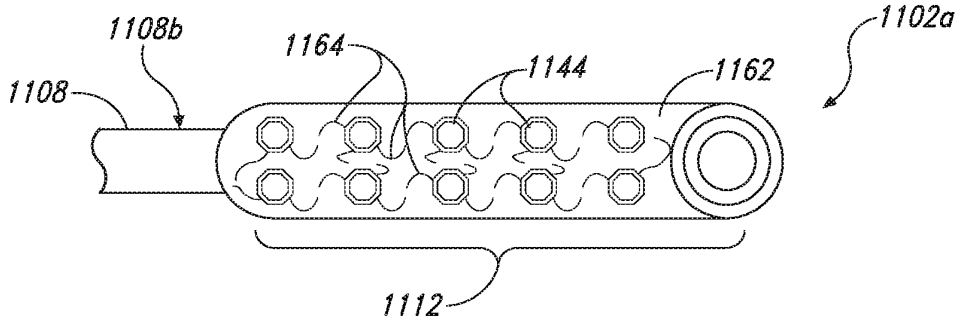


Fig. 11A

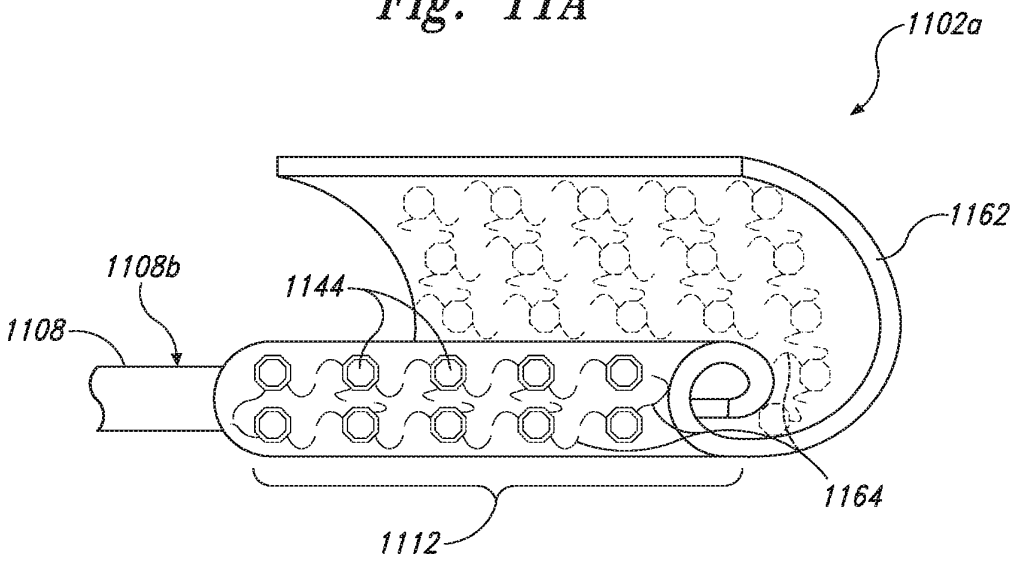


Fig. 11B

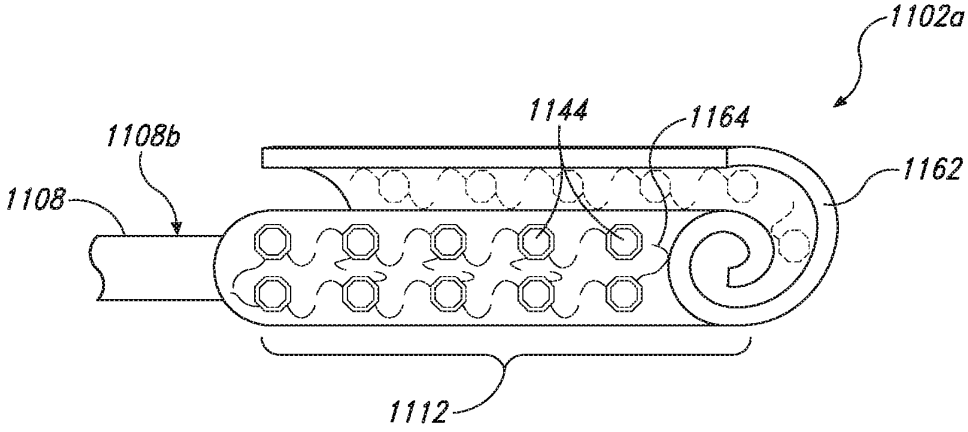


Fig. 11C

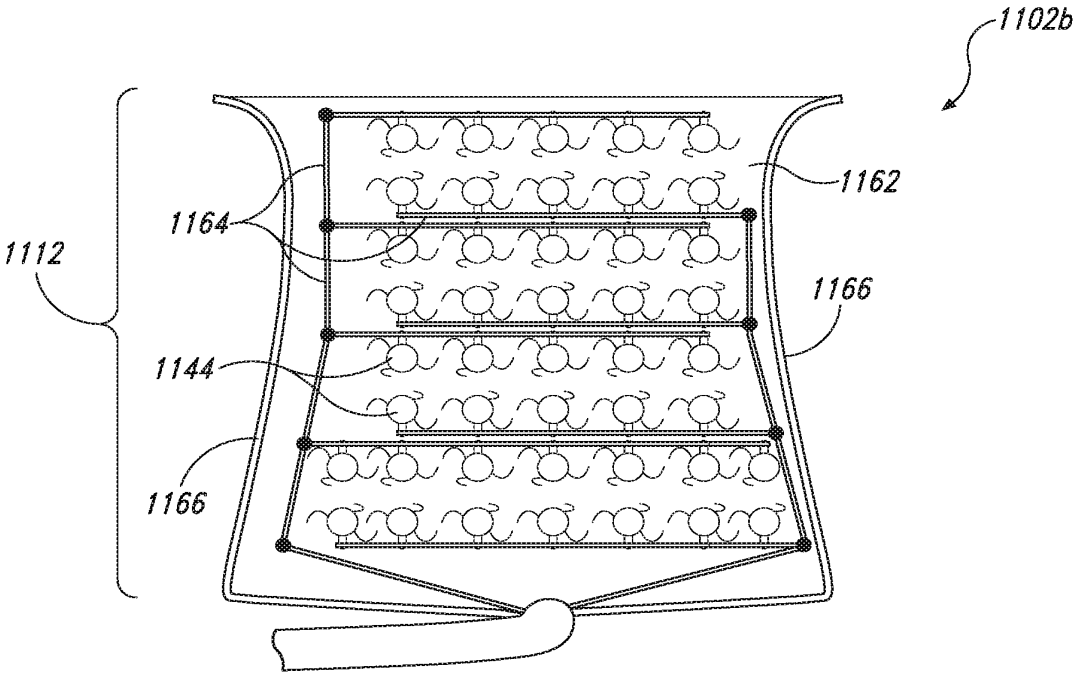


Fig. 11D

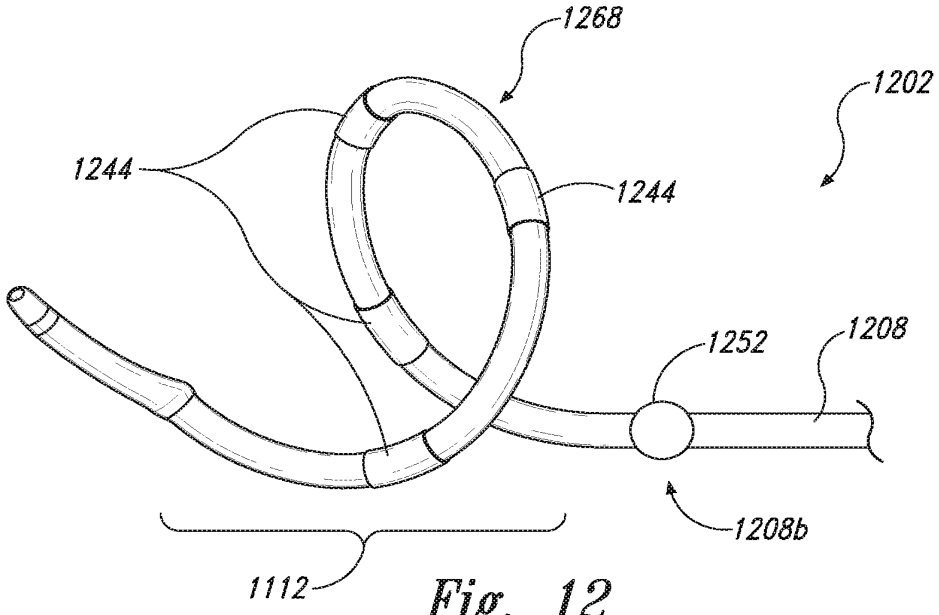


Fig. 12

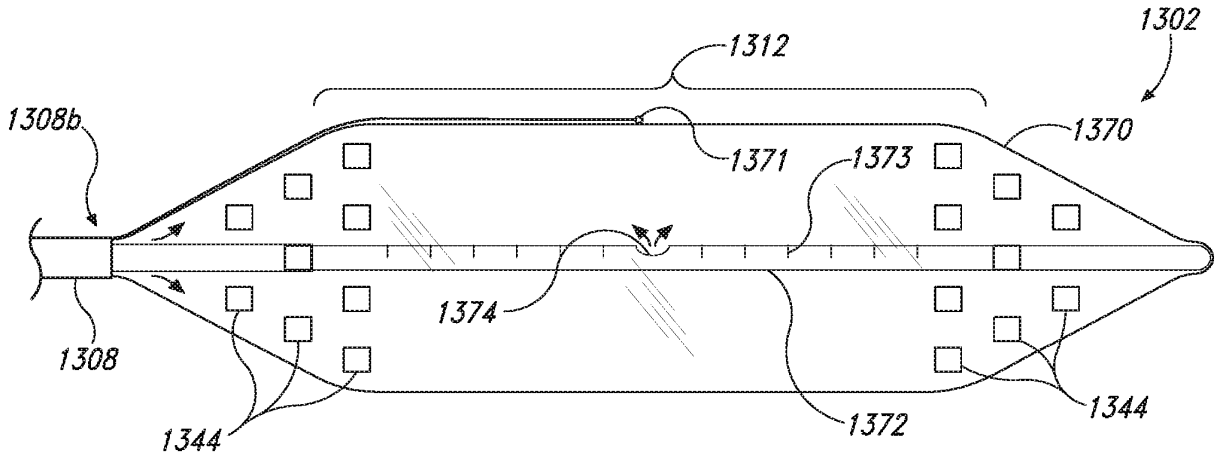

1302
1312
1308b
1371
1373
1370
1374
1308
1344
1372
1344

Fig. 13

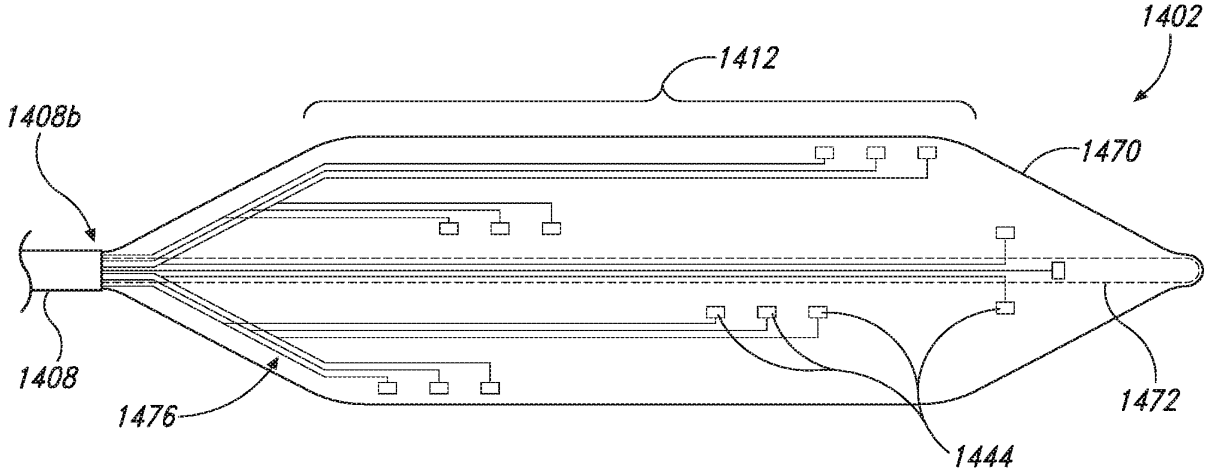

1402
1412
1408b
1470
1408
1476
1472
1444

Fig. 14

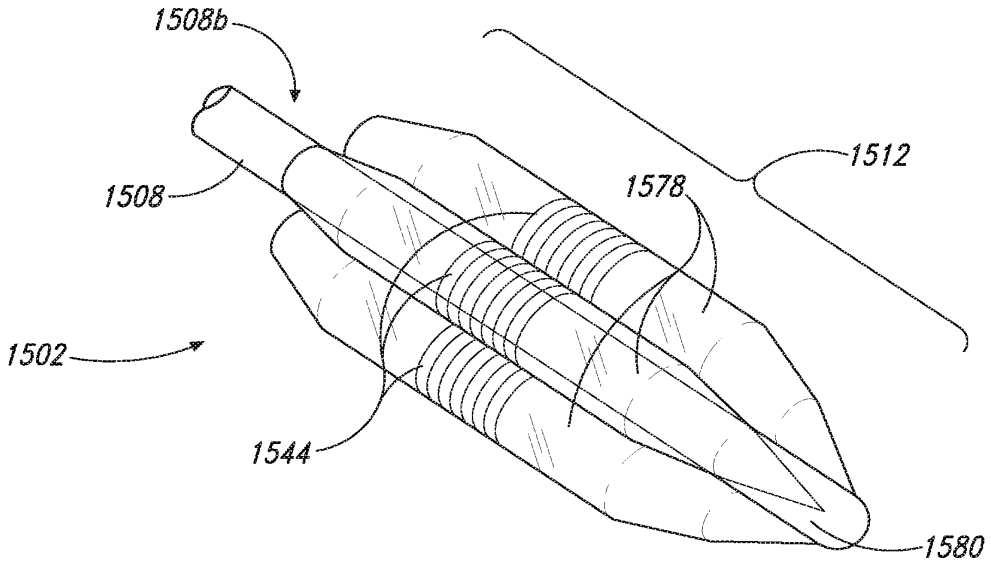

1508b
1512
1508
1578
1502
1544
1580

Fig. 15

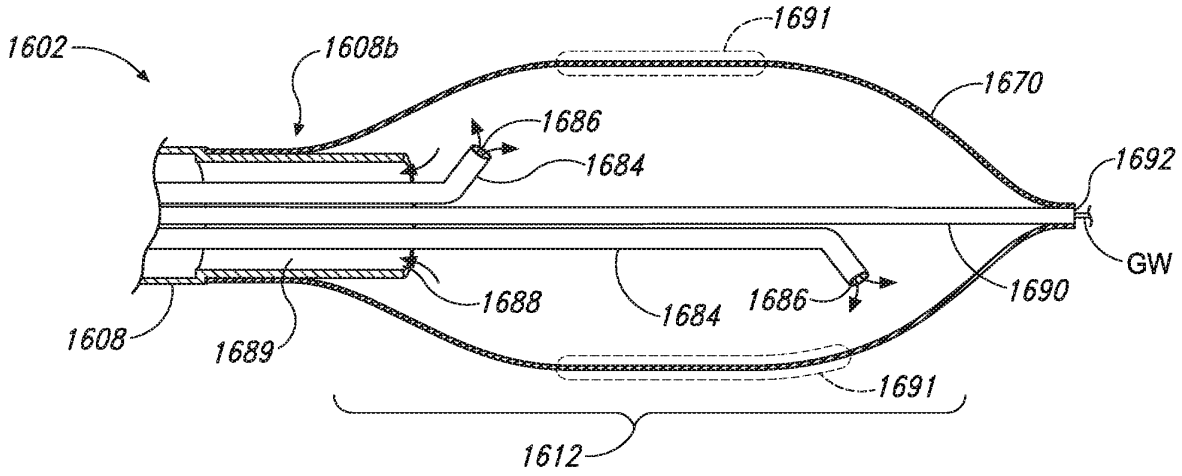

1691
1602
1608b
1670
1686
1684
1692
GW
1688
1684
1686
1690
1608
1689
1691
1612

Fig. 16

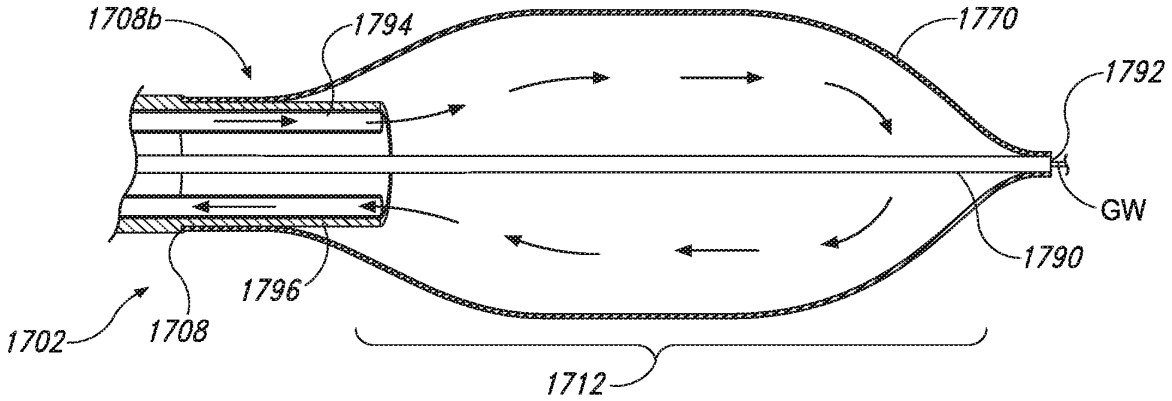

1708b
1794
1770
1792
GW
1790
1796
1702
1708
1712

Fig. 17

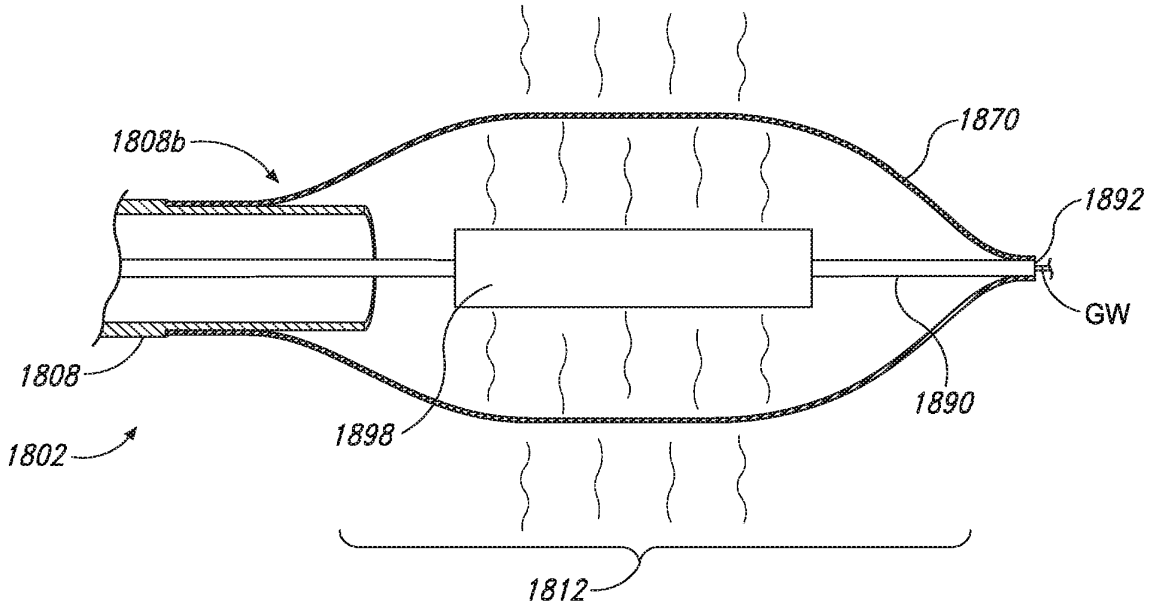

1808b
1870
1892
GW
1808
1802
1898
1890
1812

Fig. 18

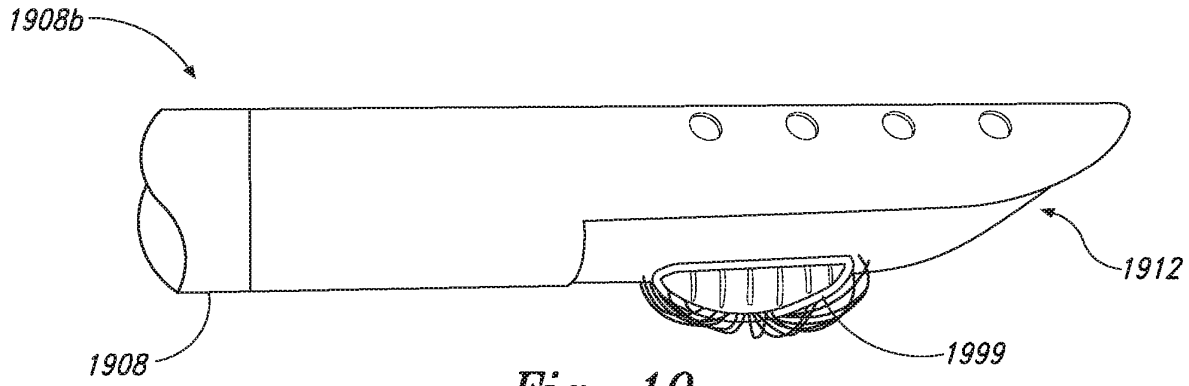

1908b
1912
1908
1999

Fig. 19

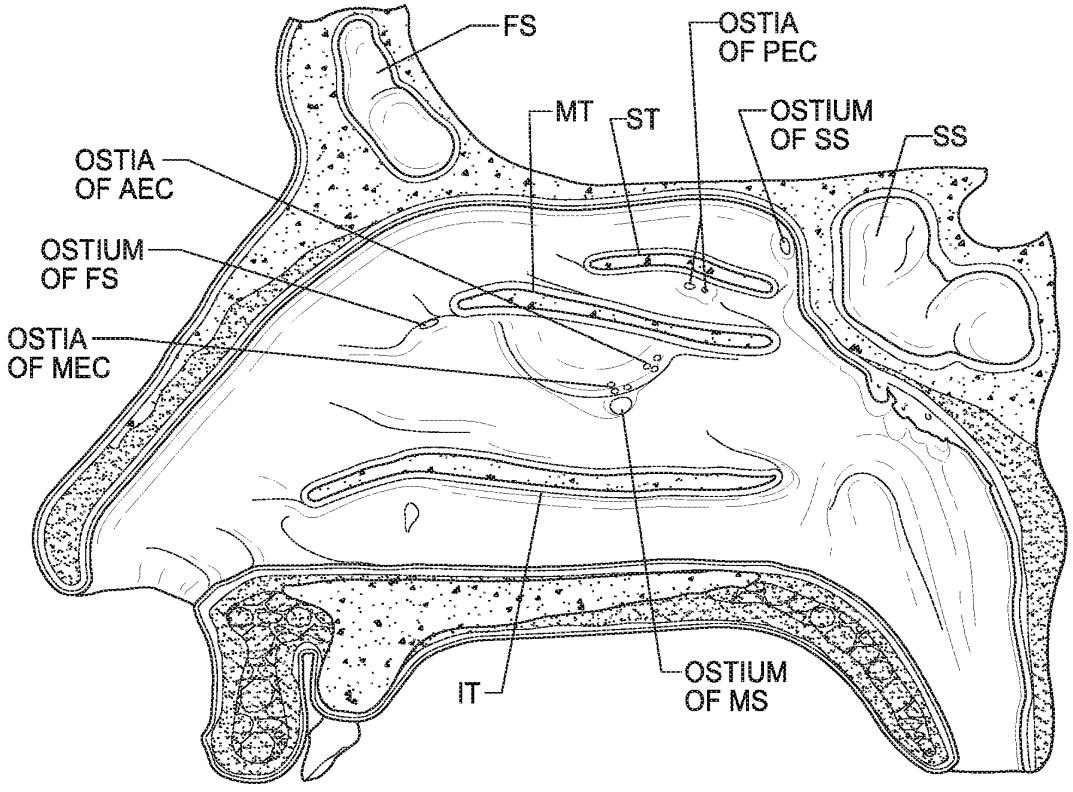

FS
OSTIA OF PEC
MT
ST
OSTIUM OF SS
SS
OSTIA OF AEC
OSTIUM OF FS
OSTIA OF MEC
IT
OSTIUM OF MS

Fig. 20