

**UNITED STATES PATENT AND TRADEMARK OFFICE**

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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NEURENT MEDICAL INC. & NEURENT MEDICAL LTD.

Petitioners,

v.

THE FOUNDRY, LLC,  
Patent Owner.

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Case No. IPR2024-00280

U.S. Patent No. 10,894,011

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**PETITIONERS' DEMONSTRATIVES FOR ORAL ARGUMENT**

***Neurent Medical Inc. et al. v. The Foundry, LLC***

**Petitioners' Oral Hearing Demonstratives**

**April 29, 2025**

**IPR2024-00279, IPR2024-00280, IPR2024-00669**

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# Agenda

1

Overview of the Grounds and Challenged Claims

2

Priority Date of the Asserted Patents Is  
October 22, 2019

3

The Challenged Claims Would Have Been Obvious

4

Patent Owner's Definition of a POSITA Is  
Incorrect and Irrelevant to Any Disputed Issue

# **Overview of the Grounds and Challenged Claims**

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

## Overview of Grounds: October 22, 2019 Priority

|               | October 22, 2019 Priority |                      |       |
|---------------|---------------------------|----------------------|-------|
|               | Ground                    | Claims               | Basis |
| IPR2024-00279 | I (Sadaat)                | 1-3, 7, 9-10, 17-25  | §102  |
|               | II (Sadaat)               | 24-25                | §103  |
|               | III (Deem)                | 1-3, 7, 9-10, 17-25  | §102  |
| IPR2024-00280 | I (Sadaat)                | 1-2, 5, 8-10, 12, 14 | §102  |
|               | II (Sadaat)               | 12, 14               | §103  |
|               | III (Deem)                | 1-2, 5, 8-10, 12, 14 | §102  |
| IPR2024-00669 | I (Sadaat)                | 1-3, 5-8, 11         | §102  |
|               | II (Sadaat)               | 3, 11                | §103  |
|               | III (Sadaat + Stern)      | 4                    | §103  |
|               | IV (Deem)                 | 1-3, 5-8, 11         | §102  |

POR did not contest unpatentability for October 22, 2019 priority date

# Overview of Grounds: July 21, 2006 Priority

|               | July 21, 2006 Priority                    |                      |       |
|---------------|-------------------------------------------|----------------------|-------|
|               | Ground                                    | Claims               | Basis |
| IPR2024-00279 | IV (Makower + Fang)                       | 1-3, 7, 9-10, 17-25  | §103  |
| IPR2024-00280 | IV (Makower + Fang + Edwards-535)         | 1-2, 5, 8-10, 12, 14 | §103  |
| IPR2024-00669 | V (Makower + Fang + Edwards-535)          | 1-3, 5-8, 11         | §103  |
|               | VI (Makower + Fang + Edwards-535 + Stern) | 4                    | §103  |

## Representative Independent Claim 1 of the '675 Patent

[illegible]

1. A method of treating a nasal condition of a patient comprising:

- positioning a distal portion of a treatment device proximate to target tissue in a nasopharyngeal passage of a patient; and
- administering therapy to the target tissue with the treatment device so as to disrupt neural activity such that mucus secretion is reduced in the nasopharyngeal passage;

wherein administering therapy comprises at least one of delivering energy to the target tissue and changing the temperature of the target tissue.

# Challenged Claims

## Representative Independent Claim 1 of the '011 Patent

US 10,894,011 B2

(12) United States Patent  
Decm et al.

(10) Patent No.: US 10,894,011 B2  
(43) Date of Patent: Jan. 19, 2021

(54) SYSTEMS AND METHODS FOR DELIVERY OF A THERAPEUTIC AGENT

(71) Applicant: The Foundry, LLC, Menlo Park, CA (US)

(72) Inventors: Mark E. Deane, Menlo Park, CA (US); Hassan Gifford, Woodside, CA (US)

(73) Assignee: The Foundry, LLC, Menlo Park, CA (US)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. (154b) by 9 days.

(21) Appl. No. 14/842,280

(22) Filed: Apr. 7, 2020

(65) Prior Publication Data  
US 2020/023964 A1 Jul. 30, 2020

(60) Continuation of application No. 16/639,893, filed on Oct. 12, 2019, now Pat. No. 10,636,073, which is a continuation of application No. 15/536,381, filed on Jul. 16, 2018, which is a continuation of application No. 15/553,187, filed on Nov. 22, 2016, now Pat. No. 10,022,529, which is a continuation of application No. 14/701,529, filed on Jan. 21, 2015, now Pat. No. 9,495,295, which is a continuation of application No. 13/661,629, filed on Oct. 25, 2012, now Pat. No. 8,460,191, which is a continuation of application No. 13/255,595, filed on Oct. 5, 2011, now Pat. No. 8,335,104, which is a continuation of application No. 12/550,278, filed on Sep. 14, 2009, now Pat. No. 8,133,497, which is a division of application No. 11/455,098, filed on Jul. 21, 2006, now Pat. No. 7,468,375.

(60) Provisional application No. 69/702,077, filed on Jul. 22, 2005.

(51) Int. Cl.  
A61M 27/00 (2006.01)  
A61K 9/08 (2006.01)  
A61K 36/06 (2006.01)  
A61K 36/08 (2006.01)  
A61K 47/00 (2006.01)  
A61K 61/12 (2006.01)  
A61N 6/00 (2006.01)  
A61N 6/10 (2006.01)  
A61N 7/00 (2006.01)  
A61B 16/14 (2006.01)  
A61B 16/18 (2006.01)  
A61N 5/10 (2006.01)  
A61M 5/14 (2006.01)  
A61B 1/00 (2006.01)

(52) U.S. Cl.  
CNC — A61K 9/0021 (2015.01); A61B 16/102 (2015.01); A61K 16/115 (2015.01); A61K 36/06 (2015.01); A61K 36/08 (2015.01); A61K 47/00 (2015.01); A61N 6/00 (2015.01); A61N 6/10 (2015.01); A61N 7/00 (2015.01); A61B 16/14 (2015.01); A61B 16/18 (2015.01); A61N 5/10 (2015.01); A61M 5/14 (2015.01); A61B 1/00 (2015.01).

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(Continued)

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"Acetaminophen, Nomenclature (from Wikipedia)" Retrieved from <http://en.wikipedia.org/w/index.php?title=Acetaminophen&redirected=paracetamol> Apr. 2, 2015, 21 pages.  
(Continued)

Primary Examiner: Albert M. Nguyen  
(74) Attorney, Agent, or Firm: Patterson Thibodeau Pedersen, P.A.

(57) ABSTRACT  
Methods and apparatus are provided for applying, as fragment of a neuropeptide such as the active light chain (LC) of the botulinum toxin (BoNT), such as one of the serotype A, B, C, D, E, F, or G botulinum toxins, the permeabilization of targeted cell membranes to enable translocation of the botulinum serotype light chain (BoNT-LC) molecule across the targeted cell membrane in the cell cytosol where a therapeutic response is produced in a mammalian system. The methods and apparatus include use of carrier based delivery systems, non-invasive delivery systems, and transdermal delivery systems.

29 Claims, 27 Drawing Sheets  
NEURENT 1001

1. Apparatus for treatment of a nasal condition by altering function of a nasopharyngeal passage of a patient, the apparatus comprising:

a hand-held elongate body having proximal and distal portions, the distal portion being configured for positioning in a nasopharyngeal passage of a patient with the proximal portion positioned outside the nasopharyngeal passage;

an energy transmission element in the distal portion configured to deliver energy to target tissue in the nasopharyngeal passage; and

an energy source operatively coupled to the energy transmission element for supplying energy thereto according to one or more parameters selected so as to alter nasopharyngeal cells in the target tissue such that nasal congestion is reduced.

'280 Ex.1001 ('011 Patent), Cl. 1

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Representative Independent Claim 1 of the '077 Patent

NEURENT 1001

'669 Ex.1001 ('077 Patent), Cl. 1

## Challenged Claims: “Lateral” Limitations

|                                                                            |  |                                                                                                   |  |
|----------------------------------------------------------------------------|--|---------------------------------------------------------------------------------------------------|--|
| <p>(12) <b>United States Patent</b></p> <p>Deem et al.</p>                 |  | <p>(36) Patent No. <b>US 10,610,675 B2</b></p> <p>(45) Date of Patent: <b>Apr. 7, 2020</b></p>    |  |
| <p>(54) <b>SYSTEMS AND METHODS FOR DELIVERY OF A THERAPEUTIC AGENT</b></p> |  | <br>US10610675B2 |  |
| <p>(71) Applicant: <b>The University, LLC, Maricopa, AZ, USA</b></p>       |  |                                                                                                   |  |

**22.** The method of claim **18**, wherein the energy delivery element is configured to concentrate energy **laterally** relative to the distal portion of the treatment device.

(60) Continuation of application No. 16/955,381, filed on Jul. 16, 2018, which is a continuation of application Ser. 15/338,367, filed on Dec. 22, 2016, now Pat. No. 10,022,529, which is a continuation of application No. 14/681,870, filed on Jan. 21, 2015, now Pat. No. 9,408,285, which is a continuation of application No. 13/000,626, filed on Oct. 25, 2012, now Pat. No. 8,561,397, which is a continuation of application No. 12/755,278, filed on Sep. 14, 2009, now Pat. No. 8,316,164, which is a continuation of application No. 12/759,278, filed on Sep. 14, 2009, now Pat. No. 8,150,497, which is a division of application No. 11/420,690, filed on Jul. 21, 2006, now Pat. No. 7,618,275.

(60b) Provisional application No. 60/002,077, filed on Jul. 22, 2005.

(71) **Int. Cl.**  
*A61B 19/02* (2006:01)  
*A61M 5/00* (2006:01)  
*A61B 1/00* (2006:01)  
*A61B 5/10* (2006:01)  
*A61B 18/00* (2006:01)  
*A61B 18/12* (2006:01)  
*A61M 5/00* (2006:01)  
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| <br>US 11,679,072 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| (12) <b>United States Patent</b><br><b>Deem et al.</b>                                               | (10) Patent No.: <b>US 11,679,072 B2</b><br>(45) Date of Patent: <b>*Jun. 20, 2023</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| (54) <b>SYSTEMS AND METHODS FOR DELIVERY OF A THERAPEUTIC AGENT</b>                                  | (52) <b>U.S. CL.</b><br>C1C <b>2011.01, 461K 00/02 (2013.01), 461K 10/7492 (2013.01), 461K 30/02 (2013.01), 461K 30/0978 (2013.01), 461K 30/1044 (2013.01), 461K 30/1054 (2013.01), 461K 30/1056 (2013.01), 461K 30/1058 (2013.01), 461K 30/1060 (2013.01), 461K 30/1062 (2013.01), 461K 30/1064 (2013.01), 461K 30/1066 (2013.01), 461K 30/1068 (2013.01), 461K 30/1070 (2013.01), 461K 30/1072 (2013.01), 461K 30/1074 (2013.01), 461K 30/1076 (2013.01), 461K 30/1078 (2013.01), 461K 30/1080 (2013.01), 461K 30/1082 (2013.01), 461K 30/1084 (2013.01), 461K 30/1086 (2013.01), 461K 30/1088 (2013.01), 461K 30/1090 (2013.01), 461K 30/1092 (2013.01), 461K 30/1094 (2013.01), 461K 30/1096 (2013.01), 461K 30/1098 (2013.01), 461K 30/1100 (2013.01), 461K 30/1102 (2013.01), 461K 30/1104 (2013.01), 461K 30/1106 (2013.01), 461K 30/1108 (2013.01), 461K 30/1110 (2013.01), 461K 30/1112 (2013.01), 461K 30/1114 (2013.01), 461K 30/1116 (2013.01), 461K 30/1118 (2013.01), 461K 30/1120 (2013.01), 461K 30/1122 (2013.01), 461K 30/1124 (2013.01), 461K 30/1126 (2013.01), 461K 30/1128 (2013.01), 461K 30/1130 (2013.01), 461K 30/1132 (2013.01), 461K 30/1134 (2013.01), 461K 30/1136 (2013.01), 461K 30/1138 (2013.01), 461K 30/1140 (2013.01), 461K 30/1142 (2013.01), 461K 30/1144 (2013.01), 461K 30/1146 (2013.01), 461K 30/1148 (2013.01), 461K 30/1150 (2013.01), 461K 30/1152 (2013.01), 461K 30/1154 (2013.01), 461K 30/1156 (2013.01), 461K 30/1158 (2013.01), 461K 30/1160 (2013.01), 461K 30/1162 (2013.01), 461K 30/1164 (2013.01), 461K 30/1166 (2013.01), 461K 30/1168 (2013.01), 461K 30/1170 (2013.01), 461K 30/1172 (2013.01), 461K 30/1174 (2013.01), 461K 30/1176 (2013.01), 461K 30/1178 (2013.01), 461K 30/1180 (2013.01), 461K 30/1182 (2013.01), 461K 30/1184 (2013.01), 461K 30/1186 (2013.01), 461K 30/1188 (2013.01), 461K 30/1190 (2013.01), 461K 30/1192 (2013.01), 461K 30/1194 (2013.01), 461K 30/1196 (2013.01), 461K 30/1198 (2013.01), 461K 30/1200 (2013.01), 461K 30/1202 (2013.01), 461K 30/1204 (2013.01), 461K 30/1206 (2013.01), 461K 30/1208 (2013.01), 461K 30/1210 (2013.01), 461K 30/1212 (2013.01), 461K 30/1214 (2013.01), 461K 30/1216 (2013.01), 461K 30/1218 (2013.01), 461K 30/1220 (2013.01), 461K 30/1222 (2013.01), 461K 30/1224 (2013.01), 461K 30/1226 (2013.01), 461K 30/1228 (2013.01), 461K 30/1230 (2013.01), 461K 30/1232 (2013.01), 461K 30/1234 (2013.01), 461K 30/1236 (2013.01), 461K 30/1238 (2013.01), 461K 30/1240 (2013.01), 461K 30/1242 (2013.01), 461K 30/1244 (2013.01), 461K 30/1246 (2013.01), 461K 30/1248 (2013.01), 461K 30/1250 (2013.01), 461K 30/1252 (2013.01), 461K 30/1254 (2013.01), 461K 30/1256 (2013.01), 461K 30/1258 (2013.01), 461K 30/1260 (2013.01), 461K 30/1262 (2013.01), 461K 30/1264 (2013.01), 461K 30/1266 (2013.01), 461K 30/1268 (2013.01), 461K 30/1270 (2013.01), 461K 30/1272 (2013.01), 461K 30/1274 (2013.01), 461K 30/1276 (2013.01), 461K 30/1278 (2013.01), 461K 30/1280 (2013.01), 461K 30/1282 (2013.01), 461K 30/1284 (2013.01), 461K 30/1286 (2013.01), 461K 30/1288 (2013.01), 461K 30/1290 (2013.01), 461K 30/1292 (2013.01), 461K 30/1294 (2013.01), 461K 30/1296 (2013.01), 461K 30/1298 (2013.01), 461K 30/1300 (2013.01), 461K 30/1302 (2013.01), 461K 30/1304 (2013.01), 461K 30/1306 (2013.01), 461K 30/1308 (2013.01), 461K 30/1310 (2013.01), 461K 30/1312 (2013.01), 461K 30/1314 (2013.01), 461K 30/1316 (2013.01), 461K 30/1318 (2013.01), 461K 30/1320 (2013.01), 461K 30/1322 (2013.01), 461K 30/1324 (2013.01), 461K 30/1326 (2013.01), 461K 30/1328 (2013.01), 461K 30/1330 (2013.01), 461K 30/1332 (2013.01), 461K 30/1334 (2013.01), 461K 30/1336 (2013.01), 461K 30/1338 (2013.01), 461K 30/1340 (2013.01), 461K 30/1342 (2013.01), 461K 30/1344 (2013.01), 461K 30/1346 (2013.01), 461K 30/1348 (2013.01), 461K 30/1350 (2013.01), 461K 30/1352 (2013.01), 461K 30/1354 (2013.01), 461K 30/1356 (2013.01), 461K 30/1358 (2013.01), 461K 30/1360 (2013.01), 461K 30/1362 (2013.01), 461K 30/1364 (2013.01), 461K 30/1366 (2013.01), 461K 30/1368 (2013.01), 461K 30/1370 (2013.01), 461K 30/1372 (2013.01), 461K 30/1374 (2013.01), 461K 30/1376 (2013.01), 461K 30/1378 (2013.01), 461K 30/1380 (2013.01), 461K 30/1382 (2013.01), 461K 30/1384 (2013.01), 461K 30/1386 (2013.01), 461K 30/1388 (2013.01), 461K 30/1390 (2013.01), 461K 30/1392 (2013.0</b> |

7. The apparatus of claim 1, wherein the multiple radiofrequency electrodes are configured to deliver energy laterally relative to the distal portion of the elongate body.

'279 IPR, Ex.1001 ('675 Patent), Cl. 22

'669 Ex.1001 ('077 Patent), Cl. 7



**Priority Date of the Asserted Patents Is  
October 22, 2019**

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

# Applicant Claims Priority to '090 Utility Application Based on Content From '771 Prov.

Challenged Patents Claim Priority  
to '090 Utility App. Not '771 Prov.

## Related U.S. Application Data

(60) Continuation of application No. 16/036,381, filed on Jul. 16, 2018, which is a continuation of application No. 15/358,187, filed on Nov. 22, 2016, now Pat. No. 10,022,529, which is a continuation of application No. 14/601,529, filed on Jan. 21, 2015, now Pat. No. 9,498,283, which is a continuation of application No. 13/660,629, filed on Oct. 25, 2012, now Pat. No. 8,961,391, which is a continuation of application No. 13/253,595, filed on Oct. 5, 2011, now Pat. No. 8,338,164, which is a continuation of application No. 12/559,278, filed on Sep. 14, 2009, now Pat. No. 8,133,497, which is a division of application No. 11/459,090, filed on Jul. 21, 2006, now Pat. No. 7,608,275.

'279 Ex.1001 ('675 patent), Cover;  
see also '280 Ex.1001 ('011 patent), Cover; '669 Ex.1001 ('011 patent), Cover

'090 Utility App. Incorporates  
'771 Prov. by Reference

## CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims the benefit of provisional application 60/702,077, filed Jul. 22, 2005, and of provisional application 60/747,771, filed on May 19, 2006, the full disclosures of which are incorporated herein by reference.

Ex.1012, 1:4-10

See '279 Petition, 20-21; '280 Petition, 22-23; '669 Petition, 21;  
'279 POR, 20-21; '280 POR, 20-22; '669 POR, 20-21;  
'279 Reply, 2; '280 Reply, 2; '669 Reply, 2

## Priority: Written Description



### *Ariad Pharms. v. Eli Lilly & Co.*

For priority, must show written description that “reasonably conveys to [POSITAs] the inventor had possession of the claimed subject matter.”

\* \* \*

Disclosure that “merely renders the invention obvious” is insufficient.

*Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351-52 (Fed. Cir. 2010)

'279 Reply, 3, 5; '280 Reply, 3, 5; '669 Reply, 3, 5

## The Challenged Claims Recite Energy-Only Treatment

- '675 Patent Claim 1: “administering **therapy** comprises ... **delivering energy** to the target tissue”
- '011 Patent Claim 1: “an energy source operative coupled to the energy transmission element for **supplying energy** thereto according to one or more parameters selected **so as to alter nasopharyngeal cells in the target tissue such that nasal congestion is reduced**”
- '077 Patent Claim 1: “supplying **radiofrequency energy** to the multiple radiofrequency electrodes **to treat a target tissue...**”

'279 Ex.1001 ('675 Patent), Cl. 1; '280 Ex.1001 ('011 Patent), Cl. 1; '669 Ex.1001 ('077 Patent), Cl. 1; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 3; '280 Reply, 3; '669 Reply, 3

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# The Specification Describes Neurotoxin Treatment

## SYSTEMS AND METHODS FOR DELIVERY OF A THERAPEUTIC AGENT

'279 Ex.1001 ('675 Patent), Title

### Field of the Invention

The present invention relates to methods and apparatus for the control of autonomic nerve function comprising delivery via permeabilization of targeted cell membranes a therapeutically effective amount of a portion or fragment of a neurotoxin such as botulinum toxin (BoNT), the active portion known as the light chain (LC), to cause a clinical benefit in various regions within the body. More particularly, the present invention relates to methods and systems for delivering toxins, such as botulinum toxin light chain fragments, to target cells in a nasal cavity.

'279 Ex.1001 ('675 Patent), 1:33-42

Recently, a longer term therapy for rhinitis which relies on the use of botulinum toxin ("BoNT") for blocking mucus production by mucus-producing cells in the nasal membrane has been proposed. Botulinum and other neurotoxins are capable of disabling adrenergic cells, including epithelial or goblet cells which are responsible for the majority of mucus production in the nasal cavity membrane. Dr. Ira Sanders has demonstrated that introduction of intact botulinum toxin molecules into the nasal passages of canines can reduce mucus secretion by a significant amount.

'279 Ex.1001 ('675 Patent), 3:25-34

For these reasons, it would be desirable to provide improved methods and systems for delivering toxins, such as botulinum and active botulinum fragments, to the nasal membrane of a patient, particularly a patient suffering from rhinitis or other conditions associated with nasal inflammation and conditions, such as sinus headaches and migraine headaches. The methods and systems should be capable of

'279 Ex.1001 ('675 Patent), 3:50-56

The toxin to be delivered may comprise any neurotoxin capable of disabling mucus secretion in epithelial or goblet cells and other mucus-producing nasal cells. Preferably, the

'279 Ex.1001 ('675 Patent), 8:38-40

See '280 Ex.1001 ('011 Patent), Title, 1:35-44, 3:27-36, 3:52-58, 8:40-42;  
'669 Ex.1001 ('077 Patent), Title, 1:38-47, 3:31-40, 3:56-62, 8:45-47  
'279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26;  
'279 Reply, 4; '280 Reply, 4; '669 Reply, 4-5

## Discussion of Energy Is to “Enhance” Neurotoxin Delivery

(57)

### ABSTRACT

Methods and apparatus are provided for applying an fragment of a neurotoxin such as the active light chain (LC) of the botulinum toxin (BoNT), such as one of the serotype A, B, C, D, E, F or G botulinum toxins, via permeabilization of targeted cell membranes to enable translocation of the botulinum neurotoxin light chain (BoNT-LC) molecule across the targeted cell membrane to the cell cytosol where a therapeutic response is produced in a mammalian system. The methods and apparatus include use of catheter based delivery systems, non-invasive delivery systems, and transdermal delivery systems.

'279 Ex.1001 ('675 Patent), Abstract;  
'280 Ex.1001 ('011 Patent), Abstract;  
'669 Ex.1001 ('077 Patent), Abstract

See '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26;  
'279 Reply, 4-6; '280 Reply, 4-6; '669 Reply, 4-6

According to the present invention, botulinum toxin, ricin, exotoxin A, diphtheria toxin, cholera toxin, tetanus toxin, other neurotoxins, and active fragments thereof are delivered to a patient's nasal membrane while applying energy to target cells within the membrane under conditions which cause a reversible (or in some instances non-reversible) poration of the cell membranes to enhance delivery of the toxin into the cells. The region where the toxin is introduced may comprise any portion of the nasal cavity, such as a single paranasal sinus or portion thereof, a main nasal passage, two or more paranasal sinuses, or in some cases may comprise substantially the entire nasal cavity of the patient. A particular target region for the toxin may comprise the nasopharynx which is at the back of the nasal passage. The nasopharynx comprises a cluster of goblet cells which are responsible for mucus secretion and which are susceptible to the disabling mechanism of the botulinum toxin and other neurotoxins.

'279 IPR, Ex.1001 ('675 Patent), 8:4-21; '279 Ex.1002, ¶71;  
'280 Ex.1001 ('011 Patent), 8:6-23; '280 Ex.1002, ¶74;  
'669 Ex.1001 ('077 Patent), 8:10-28; '669 Ex.1002, ¶70

## Discussion of Energy Is to “Enhance” Neurotoxin Delivery

target cells. The systems further comprise an energy applicator for applying energy to the target cells under condition which cause poration of the cell membranes to enhance delivery of the toxins and/or their active fragments. The

greatly reduced. Delivery of the active or light chain fragments into the target cells, according to the present invention, is mediated and enhanced by the selective application of an energy which porates the cell membrane to allow entry of the light chain or active fragment. The presently preferred

Botulinum toxin blocks acetylcholine release from cells, such as the epithelial or goblet cells in the nasal membranes responsible for mucus hypersecretion, and can thus be effective even without energy-mediated delivery in accordance with the principles of the present invention. The use of energy to permeablize or porate the cell membranes of the epithelial or goblet cells or other mucus-secreting cells of the nasal lining, in accordance with the present invention, allows botulinum and other toxins to be preferentially delivered to the targeted epithelial or goblet and other mucus-producing cells. Additionally, it allows use of the active or light chains of these toxins (having the heavy chains removed or inactivated) for treatments in accordance with the present invention. Normally, the light chains when

'279 Ex.1001 ('675 Patent), 5:13-16, 8:54-56, 21:43-56; '280 Ex.1001 ('011 Patent), 5:15-18, 8:56-60, 21:43-56; '669 Ex.1001 ('077 Patent), 5:20-23, 8:61-65, 21:46-59; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 4-6; '280 Reply, 4-6; '669 Reply, 4-6

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# PO Pursued Neurotoxin, Not Energy Claims From '771 Prov.

(12) United States Patent  
Deem et al.

(19) Patent No.: US 7,655,243 B2  
(45) Date of Patent: Feb. 2, 2010

(54) METHODS AND SYSTEMS FOR TOXIN

DELIVERY TO THE NASAL CAVITY

(75) Inventors: Mark E. Deem, Mountain View, CA

(US); Hanson Clifford, Woodside, CA

(US)

(73) Assignee: The Foundry, LLC, Menlo Park, CA

(US)

(\*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35

U.S.C. 154(b) by 341 days.

This patent is subject to a terminal dis-

claimer.

(21) Appl. No.: 11/758,063

(22) Filed: May 18, 2007

(56) Prior Publication Data

US 2008/0021469 A1 Jan. 24, 2008

Related U.S. Application Data

(63) Continuation-in-part of application No. 11/451,601,

filed on Jul. 21, 2006.

(60) Provisional application No. 60/747,773, filed on May

19, 2006; provisional application No. 60/907,872,

filed on Jul. 22, 2005.

(51) Int. Cl.

A61K 35/00 (2006.01)

A61K 35/00 (2006.01)

(52) U.S. Cl.

424/236.1; 424/239.1; 424/247.1

(53) Table of Classification Search

See application file for complete search history.

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2004/0000250 A1 12/2004 Brooks et al.

1. A method for delivering toxins to target cells in a nasal membrane of a patient, said method comprising: introducing a toxin to a region proximate the target cells, said toxin comprising a light chain fragment of a neurotoxin and being substantially free of heavy chain fragments of the neurotoxin; and applying energy to the target cells to enhance delivery of the toxin to the cells.

Ex.1026, Cl. 1; '279 Petition, 25; '280 Petition, 26-27; '669 Petition, 25; '279 Reply, 3; '280 Reply, 3; '669 Reply, 4

DEMONSTRATIVE EXHIBIT - NOT EVIDENCE

# Patent Owner's Response

UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEURENT MEDICAL INC. & NEURENT MEDICAL LTD.  
Petitioners

v.

THE FOUNDRY, LLC  
Patent Owner

U.S. Patent No. 10,610,675

Case No.: IPR2024-00279

PATENT OWNER RESPONSE

## B. The '675 Patent Discloses and Claims a Two-Step Therapy for Treating a Nasal Condition

The '675 patent relates to a two-step therapeutic treatment method, with the first step being delivery of energy and the second being delivery of an agent, such as a neurotoxin. Indeed, the '675 patent explains that an “aspect of the invention is

'279 POR, 22; *see also* '280 POR, 22; '669 POR, 23

## The Specification Does Not Describe Energy-Only Treatment

According to the present invention, botulinum toxin, ricin, exotoxin A, diphtheria toxin, cholera toxin, tetanus toxin, other neurotoxins, and active fragments thereof are delivered to a patient's nasal membrane while applying energy to target cells within the membrane under conditions which cause a reversible (or in some instances non-reversible) poration of the cell membranes to enhance delivery of the toxin into the cells. The region where the toxin is introduced may comprise any portion of the nasal cavity, such as a single paranasal sinus or portion thereof, a main nasal passage, two or more paranasal sinuses, or in some cases may comprise substantially the entire nasal cavity of the patient. A particular target region for the toxin may comprise the nasopharynx which is at the back of the nasal passage. The nasopharynx comprises a cluster of goblet cells which are responsible for mucus secretion and which are susceptible to the disabling mechanism of the botulinum toxin and other neurotoxins.

'279 Ex.1001 ('675 Patent), 8:4-21; '280 Ex.1001 ('011 Patent), 8:6-23; '669 Ex.1001 ('077 Patent), 8:10-28; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 4-6; '280 Reply, 4-6; '669 Reply, 4-6

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## The Specification Does Not Describe Energy-Only Treatment

When the energy applicator is incorporated with or within the catheter, the delivery pattern of the energy will usually be at least partially overlapping with the toxin delivery pattern of the catheter. For example, when a porous balloon is used for toxin delivery, the acoustic transducer, electroporation electrodes, or the like, will usually be disposed to deliver energy which at least partly overlaps with the dispersion pattern of the toxin. In some instances, the region of applied energy will be coextensive with the region of toxin dispersion. In other instances, the two regions will only partially overlap. In the latter case, the delivery of the toxin will be enabled or enhanced principally within the regions of overlap.

'279 Ex.1001 ('675 Patent), 9:58-10:3; '280 Ex.1001 ('011 Patent), 9:60-10:5; '669 Ex.1001 ('077 Patent), 9:65-10:10; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 6-7; '280 Reply, 6-7; '669 Reply, 6-8

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## The Specification Does Not Describe Energy-Only Treatment

In addition to the methods described above, the present invention further provides systems for delivering toxins to goblet and other target cells as defined above in a nasal membrane. The systems may typically comprise a catheter adapted to introduce a toxin to a region adjacent to the target cells. An energy applicator is further provided for applying energy to the target cells under conditions which cause a reversible poration of the cell membranes to enhance delivery of the toxin. Systems may still further comprise a source of the toxin suitable for introduction from or through the catheter. The energy applicator may be mounted on or incorporated within the catheter, or may be a separate or intrabronchial external source. In an exemplary embodiment illustrated below, an external applicator may comprise a mask or other structure which fits over the nose and/or sinus region of the patient and which is capable of delivering acoustic to the target cells within the target regions.

'279 Ex.1001 ('675 Patent), 9:41-57; '280 Ex.1001 ('011 Patent), 9:43-59;  
'669 Ex.1001 ('077 Patent), 9:48-64

When the energy applicator is incorporated with or within the catheter, the delivery pattern of the energy will usually be at least partially overlapping with the toxin delivery pattern of the catheter. For example, when a porous balloon is used for toxin delivery, the acoustic transducer, electroporation electrodes, or the like, will usually be disposed to deliver energy which at least partly overlaps with the dispersion pattern of the toxin. In some instances, the region of applied energy will be coextensive with the region of toxin dispersion. In other instances, the two regions will only partially overlap. In the latter case, the delivery of the toxin will be enabled or enhanced principally within the regions of overlap.

'279 Ex.1001 ('675 Patent), 9:58-10:3; '280 Ex.1001 ('011 Patent), 9:60-10:5;  
'669 Ex.1001 ('077 Patent), 9:65-10:10

'279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 6-7; '280 Reply, 6-7; '669 Reply, 6-8

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## The Specification Does Not Describe Energy-Only Treatment

The energy is preferably selectively applied to a targeted region containing a variety of cell types, including goblet cells, epithelial cells, ciliated and non-ciliated columnar cells, basal cells, and less or no energy applied to untargeted regions. It will be appreciated that the energy may be applied to regions of the nasal membrane which are the same or different from the regions to which the toxin has been introduced. By controlling the delivery area of both the toxin delivery and the energy delivery, the methods and apparatus of the present invention can more specifically target the epithelial or goblet and other recipient cells of interest while minimizing the amount of toxin which enters non-targeted cells. That is, only those cells in the nasal membrane which are exposed to both the toxin and the applied energy will preferentially be permeablized or porated to receive the toxin within the cytoplasm of the cell.

'279 Ex.1001 ('675 Patent), 8:22-37; '280 Ex.1001 ('011 Patent), 8:24-39; '669 Ex.1001 ('077 Patent), 8:29-44; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26; '279 Reply, 6-7; '280 Reply, 6-7; '669 Reply, 6-8

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# The Specification Does Not Describe Energy-Only Treatment



**Dr. Nicolas Bu-Saba**

*Petitioners' Expert*

*Harvard Medical School  
Mass. Eye & Ear*

72. Disclosure of the use of energy (e.g., RF energy) in the '771 Provisional relating to using energy to porate cells to enhance the delivery of toxins is different than the use of energy in the Challenged Claims. The '771 Application (and the '675 patent) does not describe using energy *without a neurotoxin* to treat any conditions—in each instance, energy is exclusively used to facilitate and enhance the delivery of toxins. *E.g.*, Ex.1011-FH771, [0075]-[0083], FIGs.10-16; Ex.1001-USP675, 22:23-24:12, FIGs.18-24. As I discussed above, using energy for poration

'279 Ex.1002 at ¶172; see also '280 Ex.1002, ¶175; '669 Ex.1002, ¶171; '279 Petition, 24-25; '280 Petition, 26-27; '669 Petition, 24-26

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# PO's Arguments Do Not Show Written Description

## PO Argument

nasal membrane, respectively). A POSITA would have appreciated based on at least these teachings of the '675 patent that applying irreversible energy to such tissues disrupts and/or alters target tissue such that mucus secretion or congestion is reduced in the nasopharyngeal passageway. Thus, the '675 patent “reasonably conveys to

'279 POR, 30; see also '280 POR, 30; '669 POR, 30-31



## Impact Engine, Inc. v. Google LLC

Testimony POSITA “would have understood” element insufficient.

Impact Engine, Inc. v. Google LLC, 2024 WL 3287126, at \*10 (Fed. Cir. July 3, 2024)

'279 Reply, 5; '280 Reply, 5; '669 Reply, 5

# The Specification Does Not Describe Energy-Only Treatment



## *Idenix Pharms. LLC v. Gilead Scis. Inc.*

“[T]he '597 patent is invalid for lack of written description...[T]he specification provides no indication that [claimed] nucleosides outside of those disclosed in its formulas could be effective to treat HCV.”

*Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1164-65 (Fed. Cir. 2019)

'279 Reply, 5; '280 Reply, 5; '669 Reply, 5

# The Specification Does Not Describe Energy-Only Treatment



**Dr. Marom Bikson**

*PO's Declarant*

**Q.** And are the wave forms that are used for reversible electroporation different from the wave forms used for irreversible electroporation?

**A.** **Generally speaking, whether reversible electroporation is produced or irreversible electroporation is produced is going to depend on a lot of things, but one of those things is going to be the nature of the energy that the tissue is exposed to. And so by designing the energy to have certain features, you could attempt to preferentially produce either reversible electroporation or irreversible electroporation.**

**Q.** For example, if you design the device that is intended to preferentially produce reversible electroporation, is there the risk that you will also produce irreversible electroporation?

**A.** **Yes.**

**Q.** If you design a device that's intended to preferentially cause reversible electroporation, do you know how many cells would undergo irreversible electroporation?

**A.** **I think that would very much depend on the device and the use case, to even start to answer that question.**

Ex.1091, 55:9-21, 57:15-19, 59:17-60:2; '279 Reply, 6-7; '280 Reply, 6-7; '669 Reply, 6-7

## The Specification Does Not Describe Energy-Only Treatment



**Dr. Howard Levine**

*PO's Declarant*

**Q.** Do the patents provide any data regarding the use of irreversible electroporation energy without the use of neurotoxins?

**A.** They do not.

\* \* \*

**Q.** You haven't identified any example of anybody using irreversible electroporation alone to destroy tissue to achieve a therapeutic result before The Foundry patents, have you?

**A.** I have not.

Ex.1089, 186:3-7, 197:1-6; '279 Reply, 6; '280 Reply, 6; '669 Reply, 6-7

# Aerin: The Specification Describes Neurotoxin Treatment

## RPI Aerin Medical Statement to PTO

Appl. No. 15/686,265

Dkt. No. 17713.0001US11

### REMARKS

Claims 1-12 are pending and stand rejected by the Office Action of January 18, 2019. This Amendment amends claims 1-12 and adds new claims 13-16. The amendments add no new matter. For example, support for the amendments may be found in, *Ex. 1034, '279, '280, '669, '279 Reply, 3; '280 Reply, 3; '669 Reply, 3-4*. paragraphs [0151]-[0154]. Support for new claims 13 and support for new claims 14 and 16 may be found in requests examination and consideration of claims 1-16.

### Rejection under 35 U.S.C. 102

Claims 1-12 stand rejected under 35 U.S.C. § Patent No. 7,655,243, to Deem et al. (hereinafter "Deem") rejection.

Although Applicant disagrees with the Office claims 1-12 as originally filed, in an effort to expedite claims 1-12 to specify that the method involves using energy (claim 1) or deliver a cryotherapy treatment (c using cryotherapy. In fact, the sole purpose of applying target cells to enhance uptake of a nerve toxin. It is doubtful that cryogenic cooling would work for such a purpose, but in any event, Deem does not teach the use of cryotherapies.

For at least this reason, Applicant respectfully over Deem. Applicant thus respectfully requests with 35 U.S.C. § 102

### No Disclaimers or Disavowals

Although the present communication may include or characterizations of claim scope or referenced art, application, that previously pending claims are not part any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue, at a later date, any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior

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Claims 1-12 stand rejected under 35 U.S.C. § 102, as allegedly being anticipated by U.S. Patent No. 7,655,243, to Deem et al. (hereinafter "Deem"). Applicant respectfully traverses this rejection.

using cryotherapy. In fact, the sole purpose of applying energy described by Deem is to porate target cells to enhance uptake of a nerve toxin. It is doubtful that cryogenic cooling would work

Ex.1034, 786; '279 Petition, 25; '280 Petition, 26-27; '669 Petition, 25-26; '279 Reply, 3; '280 Reply, 3; '669 Reply, 3-4

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# The Claims Lack Written Description

## The Board Correctly Evaluated the Specification at Institution

Trials@uspto.gov  
571-272-7822

Paper 9  
Entered: July 23, 2024

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NEURENT MEDICAL INC. & NEURENT MEDICAL LTD.,  
Petitioner,

v.

THE FOUNDRY, LLC,  
Patent Owner.

IPR2024-00279  
Patent 10,610,675 B2

Before SHERIDAN K. SNEDDEN, SUSAN L. C. MITCHELL, and  
TIMOTHY G. MAJORS, *Administrative Patent Judges*,

SNEDDEN, *Administrative Patent Judge*,

DECISION  
Granting Institution of *Inter Partes* Review  
35 U.S.C. § 314

On the record before us, however, we do not discern how the Specification of the '675 patent provides written description support for the challenged claims. The challenged claims are purportedly directed to treating a nasal condition comprising “delivering energy to the target tissue” to reduce mucus secretion or congestion. Ex. 1001, claims 1 and 17. As noted by Petitioner, the '675 patent Specification does not describe the use to energy to treat a nasal condition in the manner recited in the claims. Pet. 24–25. Rather, the '675 patent Specification discloses the use of neurotoxins to treat nasal conditions, and, more specifically, that neurotoxins are used to disrupt neural signals in the targeted tissue and, therein, disable mucus secretion by such tissues. Ex. 1001, 3:25–34, 8:18–21, 8:38–60, 21:43–53.<sup>4</sup> In the '675 patent Specification, energy is applied only to achieve cell membrane permeabilization or poration and effectuate the delivery of neurotoxin into to target cells. *See, e.g., id.* at 4:49–51, 8:4–21. Here, we note that the challenged claims do not recite administering neurotoxins, but instead only require the delivery of energy to the target tissue to administer therapy.

<sup>4</sup>279 Institution Decision, 15–16; *see also* '280 Institution Decision, 16–17; '669 Institution Decision, 23–24

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## PO Cannot Claim Priority to Material in '771 Prov.

### Essential Material Cannot Be Incorporated From Provisional

#### 35 U.S.C. §1.57(d)

“(d) “Essential material” may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference. “Essential material” is material that is necessary to:

(1) Provide a written description of the claimed invention...”



'279 Petition, 23; '280 Petition, 25; '669 Petition, 23-24; '279 Reply, 8-9; '280 Reply, 8-9; '669 Reply, 8-9

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## PO Cannot Claim Priority to Material in '771 Prov.

### Essential Material Cannot Be Incorporated From Provisional



#### ***NRG Energy, Inc. v. Midwest Energy Emissions Corp.***

“37 C.F.R. § 1.57(c) (2005) permitted the incorporation by reference of essential material, which included material necessary to provide a written description of the claimed invention, but it is critical to note that it limited such incorporations to U.S. patents and U.S. patent application publications.”

\* \* \*

“Therefore, to the extent the provisional application provides support for the challenged claims, the incorporation by reference of the provisional application by the '595 and '163 applications cannot cure the deficiencies [in written description].”

*NRG Energy, Inc. v. Midwest Energy Emissions Corp.*, IPR2020-00832, Paper 17, 29-30 (P.T.A.B. Oct. 26, 2020)

'279 Petition, 23-24; '280 Petition, 25-26; '669 Petition, 23-24; '279 Reply, 8-9; '280 Reply, 8-9; '669 Reply, 8-9

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## PO Cannot Claim Priority to Material in '771 Prov.

### PO Cannot Rely on Nested Incorporation



#### ***Focal Therapeutics, Inc. v. Senorx, Inc.***

“[I]f **any** application in the priority chain fails to meet either (1) the written description requirement under § 112, or (2) the “specific reference” requirement under § 120, the later-filed application is not entitled to the benefit of the filing date of any applications preceding the break in the priority chain. *Hollmer*, 681 F.3d at 1355; *Medtronic CoreValve*, 741 F.3d at 1363. Because the ’718 application (and its issued ’226 patent) failed to meet both (1) and (2) at the same time, i.e., failed to meet either (1) or (2) at a given point in time, a break in the priority chain occurred at this point. *In re Hogan*, 559 F.2d 595, 609 (CCPA 1977) (stating “[t]here must be continuing disclosure through the chain of applications, without hiatus, to ultimately secure the benefit of the earliest filing date”).”

*Focal Therapeutics, Inc. v. Senorx, Inc.*, IPR2014-00116, Paper 8, 11-12 (P.T.A.B. Apr. 22, 2014)

’279 Petition, 23-24; ’280 Petition, 25-26; ’669 Petition, 23-24; ’279 Reply, 8-9; ’280 Reply, 8-9; ’669 Reply, 8-9

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## PO Cannot Claim Priority to Material in '771 Prov.

### PO Cannot Rely on Nested Incorporation



#### ***Hollmer v. Harari***

“[I]f **any** application in the priority chain fails to make the requisite disclosure of subject matter, the later-filed application is not entitled to the benefit of the filing date of applications preceding the break.”

*Hollmer v. Harari*, 681 F.3d 1351, 1355 (Fed. Cir. 2012)

'279 Petition, 21-23; '280 Petition, 23-24; '669 Petition, 22-23; '279 Reply, 9; '280 Reply, 9; '669 Reply, 9

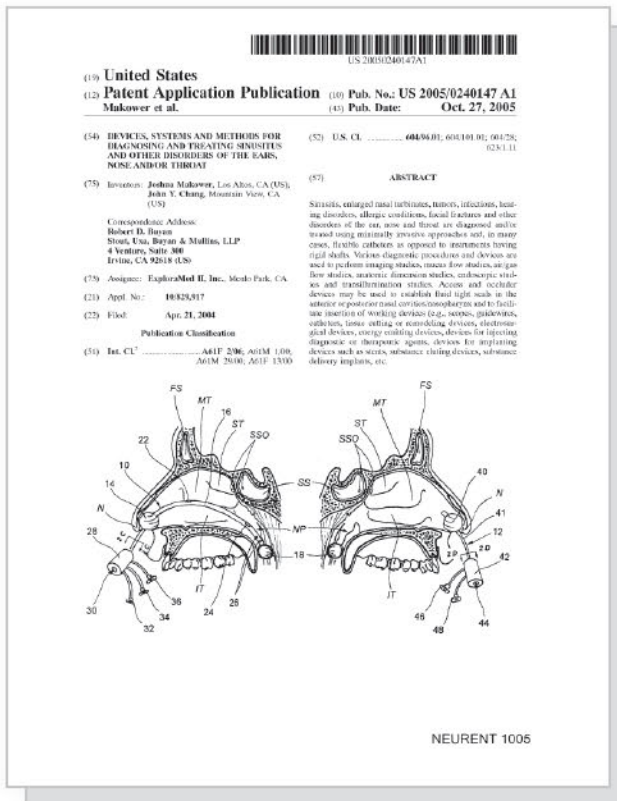
DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# **The Challenged Claims Would Have Been Obvious**

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

# Makower (Ex.1005)

## DEVICES, SYSTEMS AND METHODS FOR DIAGNOSING AND TREATING SINUSITIS AND OTHER DISORDERS OF THE EARS, NOSE AND/OR THROAT



[0001] The present invention relates generally to medical devices and methods and more particularly to minimally invasive, catheter based devices, systems and methods for treating sinusitis and other ear, nose & throat disorders.

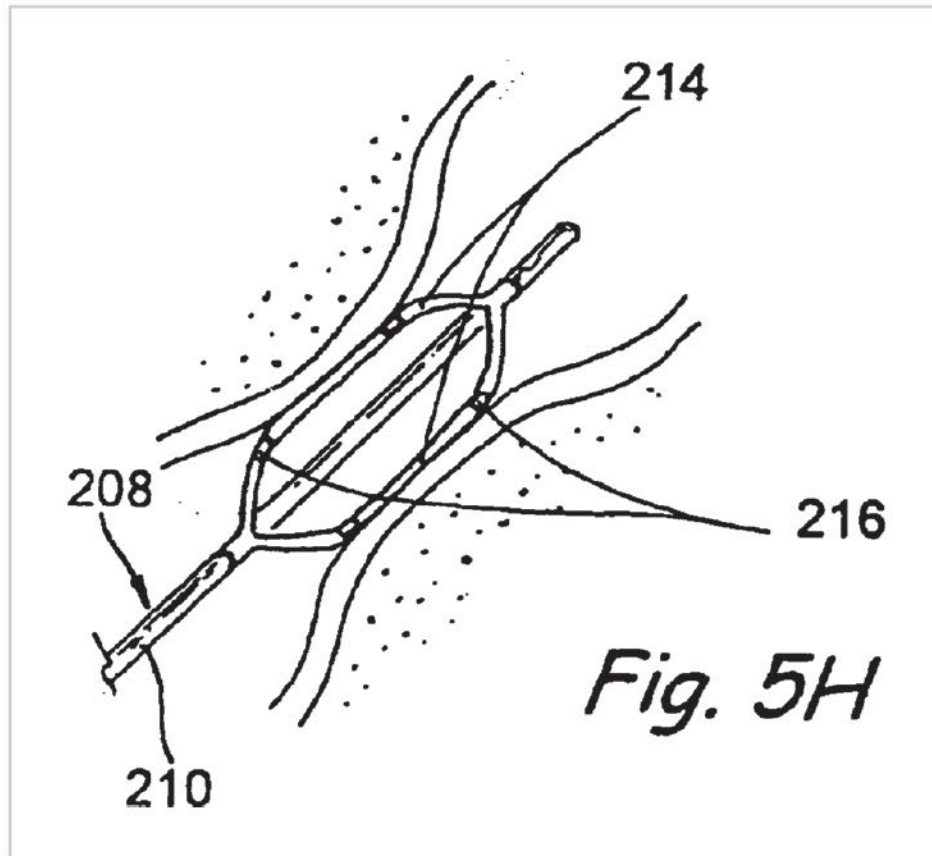
[0160] C. Working Devices for Delivering Substances or for Cutting, Ablating, Remodeling or Expanding Bone or Soft Tissue

[0161] The present invention provides a variety of apparatus that may be inserted into the nasal cavity, paranasal sinus, nasopharynx or middle ear to perform diagnostic or therapeutic procedures. These devices may be delivered through or incorporated into flexible catheters or flexible rod-like shafts. Such flexible construction allows these

Ex.1005, [0001], [0160], [0161]; '279 Petition, 27-28, 73; '280 Petition, 29, 79-80; '669 Petition, 29-30, 78-79

DEMONSTRATIVE EXHIBIT - NOT EVIDENCE

## Makower (Ex.1005)

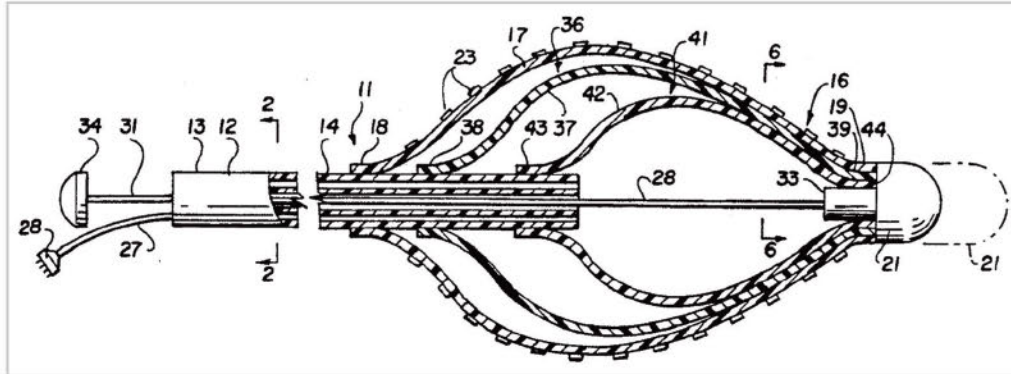


[0187] FIG. 5H shows an electro-surgical device 208 comprising a flexible shaft 210 (e.g., a catheter or solid shaft) having arched strut members 214 attached thereto. Electrodes 216 are located on the strut members 214. In some cases, the strut members may be of fixed configuration and in other cases the strut members 214 may be collapsible and expandable. In operation, the device 208 is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. Thereafter, current is applied to the electrodes 216 causing tissue adjacent to the struts 214 to be cauterized or heated. The electrodes 216 may be bipolar, monopolar or facilitated by any other suitable form of energy such as a gas or plasma arc. Additionally, sensing elements may also be attached to the catheter and/or strut members to monitor various parameters of the catheter and/or surrounding tissue (e.g., temperature, etc.). In instances where monopolar electrodes are used, a separate antenna electrode (not shown) will be applied to the patient's body in accordance with processes and techniques that are well known in the art.

Ex.1005, Fig.5H, [0187]; '279 Petition, 27-28; '280 Petition, 29; '669 Petition, 29-30

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Makower (Ex.1005)



[0164] Also, some of the working devices shown in FIGS. 5A-5Y''' and described herein incorporate assemblies, components or mechanisms (e.g., rotating cutters, radiofrequency electrodes, electrocautery devices, receptacles for capturing matter, cryosurgical apparatus, balloons, stents, radioactive or substance-eluting coatings, snares, electro-anatomical mapping and guidance, optical fibers, lenses and other endoscope apparatus, seals, hemostatic valves, etc. The designs and constructions of such components and assemblies are well known in the art. Non-limiting examples of some such designs and constructions are set forth in U.S. Pat. No. 5,722,984 (Fischell et al.), U.S. Pat. No. 5,775,327 (Randolph et al.), U.S. Pat. No. 5,685,838 (Peters, et al.), U.S. Pat. No. 6,013,019 (Fischell et al.), U.S. Pat. No. 5,356,418 (Shturman), U.S. Pat. No. 5,634,908 (Loomas), U.S. Pat. No. 5,255,679 (Imran), U.S. Pat. No. 6,048,299 (Hoffman), U.S. Pat. No. 6,585,794 (Wright et al.), U.S. Pat. No. 6,503,185 (Waksman), U.S. Pat. No. 6,669,689 (Lehmann et al.), U.S. Pat. No. 6,638,233 (Corvi et al.), U.S. Pat. No. 5,026,384 (Farr et al.), U.S. Pat. No. 4,669,469 (Gifford et al.), U.S. Pat. No. 6,685,648 (Flaherty et al.), U.S. Pat. No. 5,250,059 (Andreas et al.), U.S. Pat. No. 4,708,834 (Tsuno), U.S. Pat. No. 5,171,233 (Amplatz), U.S. Pat. No. 6,468,297 (Williams et al.) and U.S. Pat. No. 4,748,869 (Wardle).

Ex.1068, Fig.1; Ex.1005, [0164]; '279 Petition, 86; '280 Petition, 89; '669 Petition, 89; '279 Ex.1002 at ¶1206; '280 Ex.1002, ¶1202; '669 Ex.1002, ¶1209

DEMONSTRATIVE EXHIBIT - NOT EVIDENCE

## Fang (Ex.1006)

**Abstract:** **Objective** To evaluate the therapeutic effects of nasal endoscopic surgery combined with multiple radiofrequency in the treatment of perennial allergic rhinitis. **Methods** Sixty-three patients with perennial allergic rhinitis whose symptoms failed to be controlled by medication received nasal endoscopic surgery for submucous resection of the nasal septum combined with radiofrequency ablation of the bilateral sphenopalatine foramen, anterior ethmoidal nerve, and inferior nasal concha. **Result** At 1 month after operation, the rate of excellent recovery was 92.1% (58/63), the efficacy rate was 7.9% (5/63), and the total efficacy rate was 100%. At 1 year after operation, the rate of excellent recovery was 88.9% (56/63), the efficacy rate was 7.9% (5/63), the rate of no efficacy was 3.2% (2/63), and the total efficacy rate was 96.8% (61/63). At 2 years after operation, the rate of excellent recovery was 82.6% (52/63), the efficacy rate was 12.7% (8/63), the rate of no efficacy was 4.8% (3/63), and the total efficacy rate was 95.2% (60/63). Compared with patients in the control group who underwent only nasal endoscopic surgery for submucous resection of the nasal septum, the total efficacy rate ( $P < 0.01$  for excellent recovery + Efficacy) at 1 and 2 years after the surgery was significantly improved, with statistical significance. **Conclusion** Nasal endoscope combined with radio frequency may achieve good therapeutic effects on perennial allergic rhinitis with less adverse effects.

The patients in the treatment group were put in the supine position and treated with 2% dicaine and 1/1000 adrenaline cotton pad for surface anesthesia and contraction of the nasal mucosa. Under nasal endoscopy, the SHP-I five-organ radiofrequency therapy instrument (manufactured by Guangzhou Medical Instrument Factory) was firstly used, with the Level 3 intensity selected, and the firing head aligned with the sphenopalatine foramen on both sides, to carry out radiofrequency at the anterior upper part of the nasal septum on both sides (the radiofrequency points on both sides were staggered by 5 mm to prevent perforation of the nasal septum), and at the anterior upper part of the lateral wall of the nasal cavity, the nasal ridge, and the anterior part of the inferior nasal turbinate (for those with severe hypertrophy of the inferior turbinate, partial resection of the inferior turbinate was performed). It was advisable to have a white ring around

Ex.1006, Abstract, 876; '279 Petition, 28-29; '280 Petition, 30-31; '669 Petition, 30

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Fang (Ex.1006)

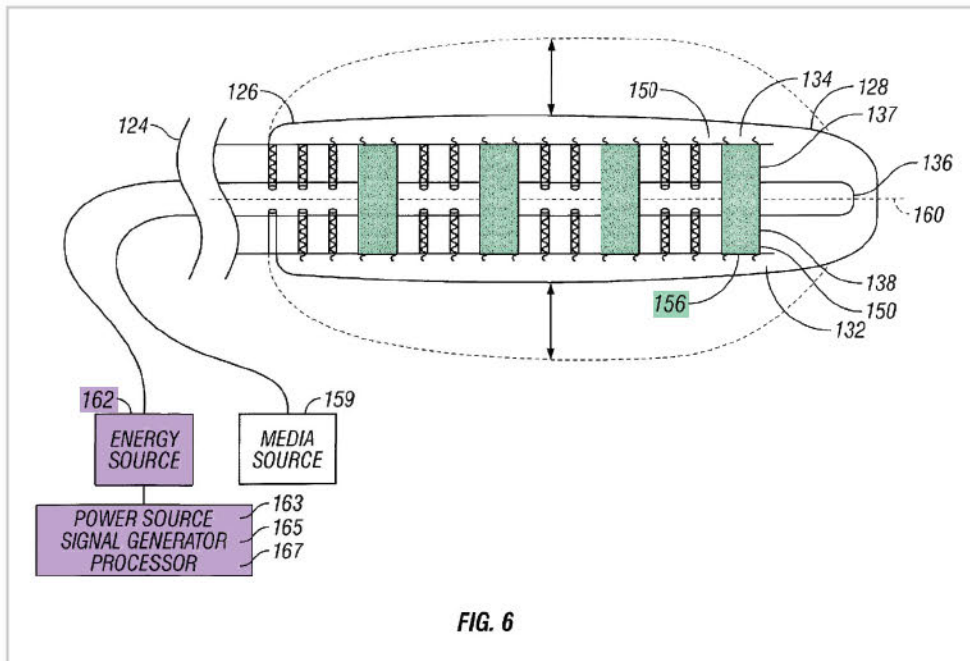
Numerous studies have shown that the parasympathetic nerves in the nasal cavity include the parasympathetic fibers of the pterygoid canal nerves and anterior ethmoidal nerves, independent cholinergic ganglia in the inferior turbinate mucosa, and some neurovascular peptides (vasoactive peptides and substance P) in the unmyelinated sensory nerve fiber endings of the nasal cavity, which regulate the vascular dilation and contraction of the nasal mucus membrane and the secretion of glands [2-4]. The treatment of perennial allergic rhinitis mainly relies on medication, but for cases with abnormal nasal structures, medication alone often has poor efficacy. Reasonable surgical interventions should be carried out based on the specific structural characteristics. Due to the complex innervation of the nasal mucosal nerves, radiofrequency technique was used to process multiple parts in the nasal cavity. In two cases, the radiofrequency ablation of sphenopalatine foramen was used to block the posterior parasympathetic fibers of the sphenopalatine nerve, and the medial and lateral branches of the anterior ethmoidal nerve were damaged by radiofrequency ablation of the anterior upper part of the nasal septum and the lateral wall of the nasal cavity [3, 5]. In addition, the inferior turbinate contains cholinergic nerves and their parasympathetic plexus [6], so 3-5 points were selected for radiofrequency ablation at the anterior part of the inferior turbinate.

The use of radiofrequency technique completely blocks the parasympathetic pathway of the nasal mucosa, reduces the vascular tension, reduces glandular secretion, and thus achieves the therapeutic purposes [7]. Pterygoid canal neurotomy alone or/and anterior ethmoidal neurotomy or inferior turbinate treatment preserves 1-2 parasympathetic pathways in the source and distribution of parasympathetic nerves in the nasal mucosa. However, due to the presence of allergic reaction arcs, the postoperative effect is poor and the recurrence rate is high [8, 9]. For the patients in this group, all the nasal mucosal parasympathetic pathways, including the posterior ganglionic fibers of the sphenopalatine nerve, the parasympathetic fibers of the anterior ethmoidal nerve, and the cholinergic ganglia within the inferior turbinate mucosa were blocked. The allergic reflex arc was completely relieved, thus achieving stable and reliable results.

Ex.1006, 877; '279 Petition, 28-29, 73-75; '280 Petition, 30-31, 79-81; '669 Petition, 30, 80-81

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Edwards (Ex.1008)

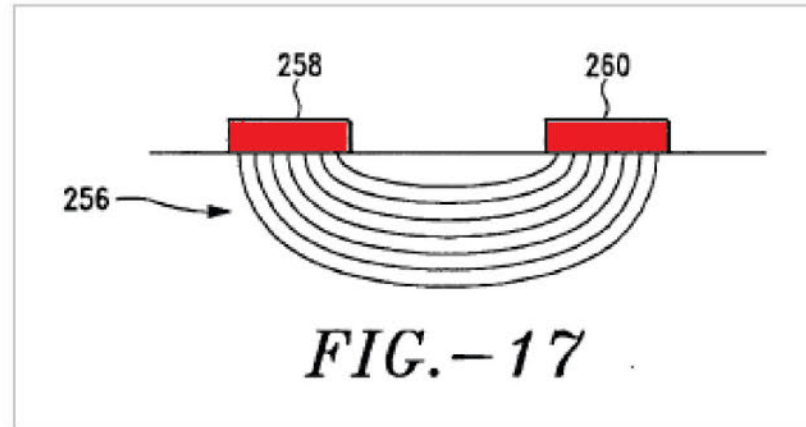
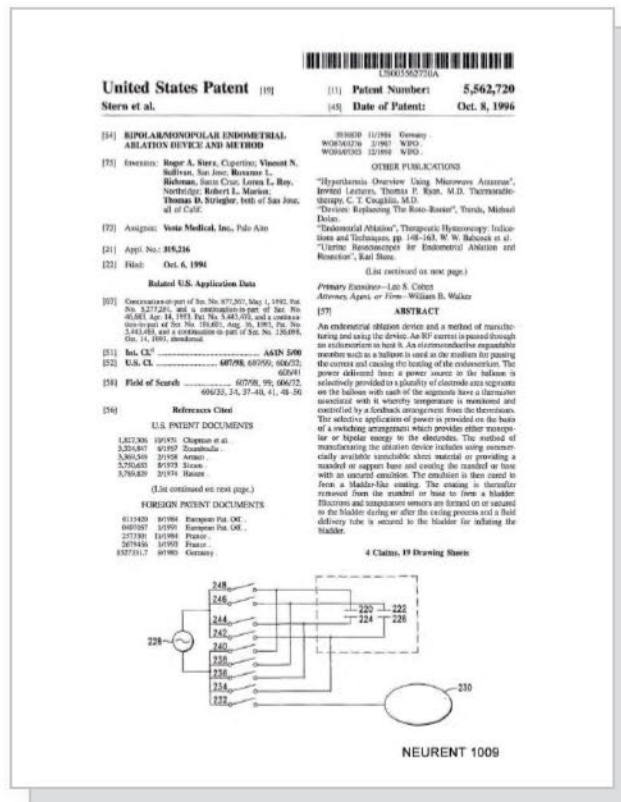


In one embodiment, illustrated in FIG. 6, the energy delivery device includes one or more ring electrodes 156 disposed on the surface of the expandable member 132. As illustrated, the plurality of ring electrodes 156 may be disposed in parallel with their axes aligned with a long axis 160 of the catheter body 126. As noted above, energy may be delivered to all of the energy delivery devices or may be independently delivered to each energy delivery device.

As illustrated in FIG. 5, ablative energy is supplied to the energy delivery device by an energy source 162. As discussed above, a variety of forms of ablative energy may be used in the present invention. Accordingly, the energy source is selected to provide the desired form of energy. The energy used is preferably RF energy which ablates the turbinate by heat and cell destruction.

Ex.1008, Fig.6, 8:18-25, 8:47-53; '280 Petition, 31-32; '669 Petition, 30-31

## Stern (Ex.1009)



Ex.1009, Fig.17; '699 Petition, 51

It is a further object of the present invention to provide a system of selective delivery of either monopolar RF energy to a single electrode or bipolar RF energy to chosen pairs of an array of separate electrodes which are used to bring the endometrial temperature to a desired level.

Ex.1009, 2:36-40; '669 Petition, 28, 51-53

# Stern (Ex.1009)

United States Patent [19]  
Stern et al.

(11) Patent Number: 5,562,720  
(12) Date of Patent: Oct. 8, 1996

(54) **BIPHASINOPOLAR ENDOMETRIAL ABLATION DEVICE AND METHOD**  
(57) **Abstract**  
Burger A. Stern, Capetown, Vincent N. Hoffman, Santa Cruz, Larry L. Roy, Norridge, Robert L. Martin, Thomas D. Burkhart, both of San Jose, all of Calif.

(72) **Assignee:** Yonit Medical, Inc., Palo Alto  
(21) **Appl. No.:** 08/328  
(22) **Filed:** Oct. 6, 1994

**Related U.S. Application Data**  
(32) **Continuation-in-part of:** Ser. No. 077,302, May 3, 1992, Pat. No. 5,277,201, and a continuation-in-part of Ser. No. 06,481, Apr. 14, 1993, Pat. No. 5,443,033, and a continuation-in-part of Ser. No. 06,202, Aug. 16, 1993, Pat. No. 5,443,033, and a continuation-in-part of Ser. No. 06,202, Aug. 16, 1993, Pat. No. 5,443,033, and a continuation-in-part of Ser. No. 06,202, Aug. 16, 1993, Pat. No. 5,443,033.  
(51) **Int. Cl.** A61B 18/00  
(52) **U.S. Cl.** 606/98, 606/99, 606/102  
(53) **Field of Search** 606/98, 606/99, 606/102, 606/103, 24, 27-40, 41, 48-51

**References Cited**  
**U.S. PATENT DOCUMENTS**  
1,827,306 (1931) Chapman et al.  
3,253,447 (1967) Zuckerman  
3,569,549 (1972) Aronson  
3,750,622 (1974) Rosen  
3,789,629 (1974) Rosen  
(List continued on next page.)  
**FOREIGN PATENT DOCUMENTS**  
0135429 (1984) European Pat. Off.  
0675227 (1991) European Pat. Off.  
2773381 (1994) France  
2678452 (1994) France  
5373317 (1995) Germany

4 Claims, 19 Drawing Sheets

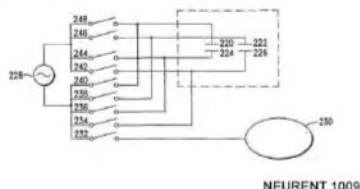
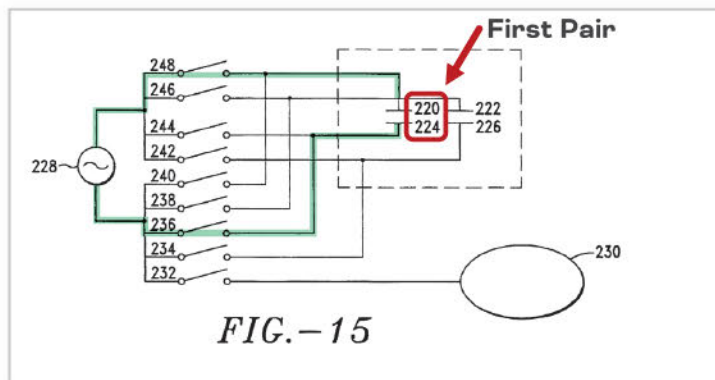
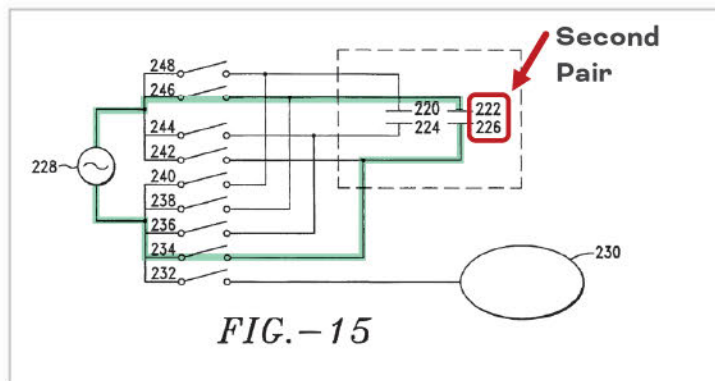


FIG. 15 illustrates the use of four electrodes 220, 222, 224 and 226 and a voltage source 228 with the same patient grounding pad or patch or return electrode 230 as in, for example the FIG. 5 unipolar arrangement. The essence of the FIG. 15 monopolar/bipolar switching arrangement is that the physician or operator has the ability to provide either monopolar or bipolar operation. When switch 232 is closed and the switches 234, 236, 238 and 240 remain open, the device functions essentially the same as the FIG. 5 embodiment. That is, it provides monopolar operation. On the other hand, if the switch 232 is opened and if pairs of switches, with one of the pair being selected from the switches 242, 244, 246 and 248 and the other being selected from switches 234, 236, 238 and 240, are operated in proper conjunction, the electrodes 220, 222, 224 and 226 will provide a bipolar operation. As an example, if switch 248 is closed as well as switch 236, then the current will pass from electrode 220 to electrode 224. In a similar manner, if switch 246 is closed as well as switch 234, there will be a bipolar operation with current flowing between electrodes 222 and 226. Clearly bipolar operation is not limited to these 220-224 and 222-226 pair couplings. If switch 248 and switch 238 are closed there will be bipolar operation between the electrodes 220 and 222.

The embodiment of FIG. 15 not only provides a choice between monopolar and bipolar operation but also provides flexibility within the bipolar operation so that any pair or any combination of pairs of electrodes may be utilized together. Obviously, if both switches 248 and 240 were closed nothing would occur because there would be a short circuit.



Ex.1009, 12:46-13:2, 13:39-44;  
'669 Petition, 52-53; '669 Reply, 24-25

## All Claim Elements Were Taught in the Prior Art

| Claim Element                                                             | Prior Art |
|---------------------------------------------------------------------------|-----------|
| Treatment Device (e.g., with Bipolar RF Electrodes)                       | ✓         |
| Use in Nasal Cavity/Nasopharynx                                           | ✓         |
| Delivering Energy to Target Tissue to Disrupt Neural Activity/Alter Cells | ✓         |
| Treating Nasal Condition/Rhinitis Symptoms                                | ✓         |
| Energy Source                                                             | ✓         |
| Multiple Pairs of Bipolar Electrodes                                      | ✓         |

# Prosecution History ('675 Patent)

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Application Number: 16659893 Document Date: 10/22/2019

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Page 1 of 650

The closest prior art is Makower et al (US Publication 2005/0240147) of record. Makower et al teach of treating disorders of the ear, nose and throat via inserting an energy emitting device into the nasopharynx. (See abstract). However, Makower et al do not teach or fairly suggest treating nasal conditions with a device so as to disrupt neural activity such that mucus secretion is reduced in the nasopharyngeal passage, and wherein the target tissue has a change in temperature.

Ex.1022, 122; '279 Petition, 72; '280 Petition, 78; '669 Petition, 79

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Motivation to Combine with Reasonable Expectation of Success

- References are analogous art to the challenged claims
- Electrodes in Makower (Fig. 5H) and Fang (generic device) operate in same way (radiofrequency energy delivery)
- Motivation to use Makower device to achieve well-known results from Fang/others in same location in the body
- Makower teaches additional details of its device were known in the art
  - Edwards & Stern teach routine design and implementation details
  - Stern teaches known configuration of bipolar electrodes
  - Challenged Patents assume implementation details

'279 Petition, 71-77; '280 Petition, 77-81, 83-84; '669 Petition, 78-84; '279 Reply, 10-22; '280 Reply, 10-23; '669 Reply, 10-23

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# Additional References Taught Ablation of Nerves to Treat Rhinitis Symptoms

Chen (Ex.1044)

## 3 Discussions

Although the pathogenesis of allergic rhinitis is mainly antigen-antibody reactions, the occurrence of its three main symptoms is closely related to the imbalance of the sensory nerves innervating the nasal mucosa and the two types of vegetative nerves, that is, it is related to parasympathetic hyperfunction. The parasympathetic nerves in the nasal cavity mainly originate from the sphenopalatine nerves (which branch into the nasal cavity along with the posterior inferior nasal nerves in the pterygopalatine canal) and the medial branch of the anterior ethmoidal nerves. In the inferior turbinate, there are cholinergic nerves and parasympathetic nerve plexus.<sup>[3]</sup> The use of radiofrequency thermocoagulation of the posterior inferior nasal nerve, anterior ethmoidal nerves, and inferior turbinate under nasal endoscopy for the treatment of PAR can widely block the source of the parasympathetic nerves in the nasal cavity and reduce the excitability of the parasympathetic nerves, the sensitivity of the nasal mucosa to sensitive areas, and the sensory-parasympathetic reflex. This can disrupt the sneezing reflex arc input pathway, reduce the sensitivity of the nasal mucosa to external stimuli, reduce vascular dilation, reduce the gland secretion, and reduce the swelling of the nasal mucosa, which can thereby alleviate or eliminate symptoms such as nasal itching, sneezing, nasal congestion, and runny nose in...

...patients, achieving the objective of treating PAR. The pterygoid canal nerve, as the main parasympathetic nerve innervating the nasal mucosa, can effectively control the symptoms of watery nasal discharge and congestion in allergic rhinitis after being cut off, which has been confirmed by domestic and foreign scholars.<sup>[1,4]</sup> The posterior inferior nasal nerve is derived from the postganglionic fibers of the pterygoid canal nerve and the sensory fibers of the maxillary nerve in the sphenopalatine ganglion. Therefore, cutting off the nerve can not only achieve a similar therapeutic effect as that of the pterygoid canal nerve cutting surgery, but also effectively alleviate symptoms of sneezing and nasal itching. Moreover, the posterior inferior nasal nerve does not contain parasympathetic nerve fibers that innervate the lacrimal gland, so it will not cause dry eye symptoms like those of pterygoid canal nerve cutting surgery.<sup>[5]</sup> The anterior ethmoidal nerve contains both the sensory nerve fibers of the first branch of the trigeminal nerve and the parasympathetic nerve fibers originating from the oculomotor nucleus. Therefore, cutting off this nerve can also play a certain role in alleviating the three major nasal symptoms. In the opinions of the authors, the mechanism of radiofrequency thermocoagulation of the inferior turbinate mucosa is not only related to the reduction of inferior turbinate volume and improvement of nasal ventilation, but also to the destruction of the microganglia and parasympathetic plexus in the inferior turbinate, resulting in a decrease in acetylcholine release.<sup>[6]</sup>

Ex.1044, 240, 243; '279 Petition, 14, 76; '280 Petition, 14, 83; '669 Petition, 15, 83; '279 Reply, 18; '280 Reply, 18-19; '669 Reply, 18-19; '279 Ex.1002, ¶146; '280 Ex.1002, ¶146; '669 Ex.1002, ¶146; '279 Ex.1098, ¶1107; '280 Ex.1098, ¶1107; '669 Ex.1098, ¶1107

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# Additional References Taught Ablation of Nerves to Treat Rhinitis Symptoms

Arora (Ex.1054)

**Cryodestruction of the nasal branches of the Vidian nerve in the region of the sphenopalatine foramen has been done in cases of vasomotor rhinitis.**

Ex.1054, 80

Liang (Ex.1045)

For radiofrequency, radiofrequency electromagnetic waves are mainly used to generate strong endogenous heat effects in local cells, causing thermal coagulation of protein, vascular occlusion, tissue degeneration, and atrophy to treat diseases. Radiofrequency treatment can not only cause degeneration and atrophy of the sensitive mucosa on the nasal ridge and corresponding nasal septum, as well as damage to the glands, but also can cause varying degrees of damage to the deep ethmoidal nerve, reducing its sensitivity to adverse external physical and chemical stimuli, reducing the secretion of vasoactive peptides, inhibiting sneezing reflex, reducing runny nose, and improving nasal ventilation, thus achieving the goal of treating allergic rhinitis<sup>[1, 2]</sup>.

Ex.1045, 341-342

Kong (Ex.1043)

**[Abstract] Objective:** To observe the role of low-temperature ablation plasma surgery system in the treatment of perennial allergic rhinitis. **Method:** After surface anesthesia of the nasal cavity and submucosal infiltration anesthesia of the inferior turbinate, 35 patients with perennial allergic rhinitis were treated with endoscopic ablation of the inferior turbinate. **Results:** The patients were followed up with for more than 6 months, and the total effective rate was 94.3% (33/35), and the excellent rate was 85.75% (30/35). **Conclusion:** With a good short-term effect, low-temperature plasma ablation of the inferior turbinate in the treatment of perennial allergic rhinitis is simple in operation, and safe and reliable, and has high clinical application values.

Ex.1043, 214

'279 Petition, 13-14, 74; '280 Petition, 14-15, 79-80; '669 Petition, 14-15, 80-81; '279 Reply, 18; '280 Reply, 18-19; '669 Reply, 18-19; '279 Ex.1002, ¶146; '280 Ex.1002, ¶146; '669 Ex.1002, ¶146; '279 Ex.1098, ¶1107; '280 Ex.1098, ¶1107; '669 Ex.1098, ¶1107

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Dr. Nicolas Bu-Saba



Dr. Nicolas Bu-Saba

*Petitioners' Expert*

- **Instructor, Assistant Professor, Associate Professor  
Department of Otolaryngology**  
**1996-Present** | Harvard Medical School
- **Otolaryngology Surgeon**  
**1996-Present** | Massachusetts Eye and Ear
- **M.D. (*with distinction*)**  
**June 1985** | American University of Beirut
- **B.Sc. (*with distinction*) in Biology-Chemistry**  
**June 1981** | American University of Beirut



**HARVARD**  
MEDICAL SCHOOL



Mass General Brigham  
**Mass Eye and Ear**



'279 Ex.1002, ¶¶3-7; '280 Ex.1002, ¶¶3-7; '669 Ex.1002, ¶¶3-7

## Dr. Gregory Martin



Dr. Greg Martin

*Principal,  
Tremont Consulting LLC*

**25 years' experience developing and commercializing medical devices, focusing on energy-based devices**

- **Senior Lecturer, Department of Medical Engineering**  
**2013-2017, 2019-2020** | Boston University
- **Ph.D. in Mechanical Engineering**  
**June 1995** | Massachusetts Institute of Technology
- **M.S. in Mechanical Engineering**  
**June 1991** | Massachusetts Institute of Technology
- **B.S. in Mechanical Engineering**  
**June 1988** | Massachusetts Institute of Technology



'669 Ex.1007, ¶¶13-7

# **Disputed Issues Regarding Obviousness**

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

# Makower Teaches “Working Devices” and Is Not Limited to Flexible Catheters

## PO Argument

*First*, Makower is not directed to RF energy delivery devices. Instead, it is directed to the use of flexible catheters attached to numerous potential medical devices, only one of which is an RF energy delivery device. *See* §VII.B, *infra*. Thus,

'279 POR, 34; *see also* '280 POR, 35; '669 POR, 34

## Makower

[0161] The present invention provides a variety of apparatus that may be inserted into the nasal cavity, paranasal sinus, nasopharynx or middle ear to perform diagnostic or therapeutic procedures. These devices may be delivered through or incorporated into flexible catheters or flexible rod-like shafts. Such flexible construction allows these

[0162] Also, in some but not necessarily all procedures, these working devices (and/or the catheters used to deliver them) may be inserted through lumens of the occluder &



**Dr. Howard Levine**

*PO's Declarant*

- Q. And flexible catheters can be used with ablation devices, correct?
- A. Yes.

Ex.1005, [0161], [0162]; '279 Reply, 10-11; '280 Reply, 10-11; '669 Reply, 10-11

Ex.1089 172:16-18; '279 Reply, 10; '280 Reply, 11; '669 Reply, 11

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# PO's Demand for a Prior Art Commercial Device is Contrary to Law



## PO Argument

*Second*, the RF energy device of Makower FIG. 5H is entirely hypothetical.

'279 POR, 34; *see also* '280 POR, 35; '669 POR, 35



### ***Galderma Laboratories, L.P. v. Tolmar, Inc.***

“Nothing in the statute or our case law requires Tolmar to prove obviousness by starting with a prior art commercial embodiment and then providing motivation to alter that commercial embodiment.”

*Galderma Laboratories, L.P. v. Tolmar, Inc.*, 737 F.3d 731, 737 (Fed. Cir. 2013)

'279 Reply, 11; '280 Reply, 11; '669 Reply, 11

# Makower Teaches a Device Capable of Delivering Energy to Target Tissue to Achieve Therapeutic Results



## *Amgen Inc. v. Hoechst Marion Roussel, Inc.*

“[W]e hold a presumption arises that both the claimed and unclaimed disclosures in a prior art patent are enabled.”

*Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354-55 (Fed. Cir. 2003)

expandable. In operation, the device **208** is advanced into a passageway such as a nostril, nasal cavity, meatus, ostium, interior of a sinus, etc. Thereafter, current is applied to the electrodes **216** causing tissue adjacent to the struts **214** to be cauterized or heated. The electrodes **216** may be bipolar, monopolar or facilitated by any other suitable form of energy such as a gas or plasma arc. Additionally, sensing

Ex.1005, [0187]

'279 Reply, 12; '280 Reply, 12; '669 Reply, 12

# Makower Teaches a Device Capable of Delivering Energy to Target Tissue to Achieve Therapeutic Results

## PO Argument

or bipolar—in either case, the application of current to Makower’s electrodes would not result in the treatment of target tissue. (Ex-2003-Levine at ¶¶96-97; Ex-2005-Bikson at ¶69.) Instead, due to the presence of electrolytic fluid within Makower’s hollow interior, ions would preferentially flow into this electrolytic fluid and not the target tissue:

*'279 POR, 38; see also '280 POR, 39; '669 POR, 39*



**Dr. Howard Levine**

*PO's Declarant*

**A. [G]enerally speaking, the mucus isn't the issue...It's there, and it's fine.**

**\*\*\***

**Q. Do you respect [Dr. Makower's] work as an engineer?**

**A. I respect his work as an engineer as high or beyond anyone that I know.**

*Ex.1089, 83:15-16, 47:4-6; '279 Reply, 11, 13; '280 Reply, 12, 14; '669 Reply, 12, 14*

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

# Makower Teaches a Device Capable of Delivering Energy to Target Tissue to Achieve Therapeutic Results



**Dr. Nicolas Bu-Saba**

*Petitioners' Expert*

slightly.”).<sup>24</sup> The patient is positioned in a seated or slightly reclined position to not only allow the physician to physically see the treatment area, but also to help facilitate the flow of any mucus or fluids away from the nasal cavity and nasopharynx and to the nasal floor and back of the patient's throat. For example, if the nasal cavity is irrigated to remove mucus or blood during the procedure, by virtue of gravity, the fluid would fall to the nasal floor and throat, i.e., away from the nasal cavity and nasopharynx. Ex.1089-Levine-Tr., 86:1-87:2. Additionally, while decongestants are used (*see* next step) to reduce mucus production, positioning the patient in this manner allows any mucus that may be secreted during the procedure to fall to the nasal floor and throat, i.e., away from the surgical site.

<sup>24</sup>279 Ex.1098 ¶181; *see also* '280 Ex.1098 ¶181; '669 Ex.1098 ¶181; '279 Reply, 13-14; '280 Reply, 14-15; '669 Reply, 14-15

# Makower Teaches a Device Capable of Delivering Energy to Target Tissue to Achieve Therapeutic Results



**Dr. Nicolas Bu-Saba**

*Petitioners' Expert*

85. As a result, a person of ordinary skill in the art would have understood that prior to performing ablation procedures in the nasal cavity or nasopharynx, blood and mucus (or any electrolyte fluid) would be removed or would not be present in the nasal cavity or nasopharynx. And in non-emergency circumstances where blood or mucus could not be removed, the procedure would either be halted or rescheduled and the patient would return on a future date for treatment to ensure that the treatment could be safely performed.

86. It is for all of these reasons I agree with Dr. Levine that mucus is typically not an issue. Ex.1089-Levine-Tr., 83:3-16 (“[G]enerally speaking, the mucus isn’t the issue.”). That is, I agree that mucus and blood is not an issue during radiofrequency procedures in the nasal cavity and nasopharynx, and if it was, the procedure would be halted or rescheduled.

'279 Ex.1098 ¶¶85-86; *see also* '280 Ex.1098 ¶¶85-86; '669 Ex.1098 ¶¶85-86; '279 Reply, 13-14; '280 Reply, 14-15; '669 Reply, 14-15

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# PO's Motivation Argument Misapplies the Law



**Dr. Howard Levine**

*PO's Declarant*

71. Fang's study is also inconclusive as to the effects of RF energy on perennial allergic rhinitis. Specifically, to determine whether Fang actually teaches that ablating tissue in the nasopharyngeal passage achieves the result of reduced mucus secretion or congestion, as Petitioners allege, a POSITA would need to see conclusive proof that RF energy alone was responsible for the improvement in perennial allergic rhinitis. Fang cannot provide such proof.

'279 Ex.2003 ¶171; '280 Ex.2003 ¶171; '669 Ex.2003 ¶171

## ***Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.***

"This court has long rejected a requirement of [c]onclusive proof of efficacy for obviousness."

*Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1333 (Fed. Cir. 2018) (citations omitted)

## ***In re Longi***

"Only a reasonable expectation of success, not absolute predictability, is necessary for a conclusion of obviousness."

*In re Longi*, 759 F.2d 887, 896 (Fed. Cir. 1985) (citations omitted)

'279 Reply, 17; '280 Reply, 17-18; '669 Reply, 17-18



# A POSITA Would Have Considered Fang

## PO Argument

Section 1.1.) Yet, a careful review shows that no conclusions regarding RF energy can be made because Fang conducted multiple operations on an unidentified number of patients in the experimental group, rendering Fang's hypothesis unsupported.

'279 POR, 46; see also '280 POR, 47; '669 POR, 47

## Fang

not satisfactory. The 63 patients were randomly selected as the treatment group according to the admission period, and another 20 patients with the same disease who underwent nasal septum surgery alone were selected as the control group. The patients in both groups were inpatients.

According to statistical analysis, there was a significant difference in the total efficacy rate between the two groups at 1 and 2 years after the surgery ( $P < 0.01$ ).

The use of radiofrequency technique completely blocks the parasympathetic pathway of the nasal mucosa, reduces the vascular tension, reduces glandular secretion, and thus achieves the therapeutic purposes<sup>[7]</sup>. Pterygoid canal neurectomy alone or/and anterior ethmoidal

Ex.1006 at 876-877; '279 Reply, 17-18; '280 Reply, 18-19; '669 Reply, 18-19

# Disabling Nerves to Treat Rhinitis Was Well Known

## The Challenged Patents

*Clostridium botulinum* neurotoxins (BoNTs) block the release of acetylcholine from peripheral cholinergic nerve endings thereby disabling the release of neurotransmitters from the cells (Bigalke, H. and Shoer, L. F. (1999) Clostridial Neurotoxins in Handbook of Experimental Pharmacology 45, 407-443). This mechanism of action is well defined. Seven immunologically distinct serotypes of neu-

Recently, a longer term therapy for rhinitis which relies on the use of botulinum toxin ("BoNT") for blocking mucus production by mucus-producing cells in the nasal membrane has been proposed. Botulinum and other neurotoxins are capable of disabling adrenergic cells, including epithelial or goblet cells which are responsible for the majority of mucus production in the nasal cavity membrane. Dr. Ira Sanders has demonstrated that introduction of intact botulinum toxin molecules into the nasal passages of canines can reduce mucus secretion by a significant amount.

'279 Ex.1001 ('675 Patent), 1:60-66, 3:25-34; '280 Ex.1001 ('011 Patent), 1:62-2:1, 3:27-36; '669 Ex.1001 ('077 Patent), 1:65-2:4, 3:31-40; '279 Reply, 18; '280 Reply, 19; '669 Reply, 19

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Disabling Nerves to Treat Rhinitis Was Well Known



**Dr. Howard Levine**

*PO's Declarant*

**Q.** So Dr. Sanders had already used neurotoxin in the nose to treat rhinitis before The Foundry patents?

**A. Yes.**

**Q.** And the effect of disabling nerve cells on rhinitis was already known before The Foundry patents?

**A. Yes.**

Ex.1089, 199:12-19; '279 Reply, 18; '280 Reply, 19; '669 Reply, 19

## Disabling Nerves to Treat Rhinitis Was Well Known

| Reference         | Teaching Regarding Function of Nerves in Rhinitis                                                                                                                                                                                                       |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chen (Ex.1044)    | “allergic rhinitis...is related to parasympathetic hyperfunction.” “[R]adiofrequency thermocoagulation...can thereby alleviate or eliminate symptoms...achieving the objective of treating PAR [perennial allergic rhinitis]”                           |
| Arora (Ex.1054)   | “Cryodestruction of the nasal branches of the Vidian nerve...in cases of vasomotor rhinitis”                                                                                                                                                            |
| Liang (Ex.1045)   | “Radiofrequency treatment...can cause varying degrees of damage to the deep ethmoidal nerve...thus achieving the goal of treating allergic rhinitis”                                                                                                    |
| Kong (Ex.1043)    | “ablation plasma surgery in the treatment of perennial allergic rhinitis”                                                                                                                                                                               |
| Windsor (Ex.1051) | “Post-ganglionic parasympathetic neurons from this ganglion then distribute to the lacrimal gland and glands of the nasal cavity, paranasal sinuses, palate, and upper pharynx where they promote secretion....”                                        |
| Fenton (Ex.1052)  | “The first line of defense is the covering of mucous secretion on the epithelium, as produced by the goblet cells and glands of the mucous membrane....Mucous glands and goblet cells are found in the walls of the nasopharynx and also in the lungs.” |

'279 Petition, 13-14, 74; '280 Petition, 14-15, 79-80; '669 Petition, 14-15, 80-81; '279 Reply, 18; '280 Reply, 18-19; '669 Reply, 18-19; '279 Ex.1002, ¶¶46, 173; '280 Ex.1002, ¶¶46, 182; '669 Ex.1002, ¶¶46, 184; '279 Ex.1098, ¶107; '280 Ex.1098, ¶107; '669 Ex.1098, ¶107

## Fang Relied on Standard Diagnostic Criteria

| Diagnostic Criteria | Fang (Haikou, Ex.1113)                                                                                                                      | Dr. Levine                                                                                                                            |
|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------|
| Symptoms            | “Clinical manifestations” including “sneezing,...runny nose, and nasal mucosa swelling.”                                                    | Symptoms including “nasal obstruction, nasal congestion, secretions...”                                                               |
| History             | “[c]lear sign of inhaled allergens, personal and/or family history of allergic diseases, and typical signs and symptoms during onset.”      | “various triggers”, assessment of “foods, ...environmental factors, ...exposure to animals, industrial factors”                       |
| Testing             | “positive specific IgE antibody test or positive nasal allergen challenge (NAC) test, and consistent with skin test and medical history[.]” | “I would typically send the patient to an allergist” for testing including “skin testing,” “scratch testing,” or “IGE...blood tests.” |

Ex.1113, 134

Ex.1089, 97:8-16, 97:22-98:15, 99:7-101:8, 104:11-22

'279 Reply, 18; '280 Reply, 19; '669 Reply, 19; '279 Ex.1098, ¶¶112-115; '280 Ex.1098, ¶¶112-115; '669 Ex.1098, ¶¶112-115

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# Makower and Fang Share Objectives

## Fang

for surface anesthesia and contraction of the nasal mucosa. Under nasal endoscopy, the SHP-I five-organ radiofrequency therapy instrument (manufactured by Guangzhou Medical Instrument Factory) was firstly used, with the Level 3 intensity selected, and the firing head aligned with the sphenopalatine foramen on both sides, to carry out radiofrequency at the anterior upper part of the nasal septum on both sides (the radiofrequency points on both sides were staggered by 5 mm to prevent perforation of the nasal septum), and at the anterior upper part of the lateral wall of the nasal cavity, the nasal ridge, and the anterior part of the inferior nasal turbinate (for those with severe hypertrophy of the inferior turbinate, partial resection of the inferior turbinate was performed). It was advisable to have a white ring around the radiofrequency head. The anterior part of the inferior turbinate could undergo radiofrequency at 3-5 points, and the nasal ridge and lateral wall of the nasal cavity could be cut to the periosteum using a radiofrequency knife. Further submucosal resection of the nasal septum was performed, and uncinate process resection, sinus opening, lateral part resection of the middle turbinate or nasal polypectomy were performed for those who had hypertrophy of the uncinate process, sinusitis, hypertrophy or polypoid lesion of the middle turbinate, or nasal polyps. After the surgery, both nasal cavities were filled with

Ex.1006, 876

## Makower

[0043] In accordance with the present invention, there are provided methods wherein one or more flexible catheters or other flexible elongate devices as described herein are inserted in to the nose, nasopharynx, paranasal sinus, middle ear or associated anatomical passageways to perform an interventional or surgical procedure. Examples of procedures that may be performed using these flexible catheters or other flexible elongate devices include but are not limited to: delivering contrast medium; delivering a therapeutically effective amount of a therapeutic substance; implanting a stent, tissue remodeling device, substance delivery implant or other therapeutic apparatus; cutting, ablating, debulking, cauterizing, heating, freezing, lasing, dilating or otherwise modifying tissue such as nasal polyps, aberrant or enlarged tissue, abnormal tissue, etc.; grafting or implanting cells or

[0161] The present invention provides a variety of apparatus that may be inserted into the nasal cavity, paranasal sinus, nasopharynx or middle ear to perform diagnostic or therapeutic procedures. These devices may be delivered through or incorporated into flexible catheters or flexible rod-like shafts. Such flexible construction allows these devices to be delivered and positioned to perform the desired diagnostic or therapeutic procedures with minimal trauma to other tissues, as can result from the insertion of rigid scopes and rigid instruments in accordance with the methodology of the prior art. It is within the scope of this approach that these

Ex.1005, [0043], [0161]

'279 Reply, 21-22; '280 Reply, 22; '669 Reply, 22

## Makower and Fang Share Objectives



**Dr. Howard Levine**

*PO's Declarant*

- Q.** And so what are types of procedures that you might perform concurrently?
- A.** So there are many things that need to be done, and that really comes down to proper diagnosis, evaluation and then doing what needs to be done for that particular patient. But it's not unusual to combine several procedures.

\* \* \*

- Q.** So if I understood your testimony just now, if a patient had multiple different problems in the nose that you needed to fix, you would typically try to fix all of them in the same time, rather than doing –
- A.** If possible.
- Q.** – separate procedures?
- A.** Yes, yes.

Ex.1089, 89:20-91:8, 91:19-92:5; '279 Reply, 21-22; '280 Reply, 22; '669 Reply, 22

# Stern Teaches Multiple Pairs of Bipolar Electrodes

## PO Argument

*Second*, Stern's statement that "any combination of pairs of electrodes may be utilized together" (Reply, 24) does not disclose claim 4. When read in isolation, the above quote from Stern is at best ambiguous. A POSITA could have (and would have) read the above sentence as teaching that any combination of pairs of electrodes may be utilized together *sequentially* (i.e., one pair at a time). (Ex-1091, 110:14-116:20, *id.*, 131:13-21.) It is improper to read portions of the prior art in isolation

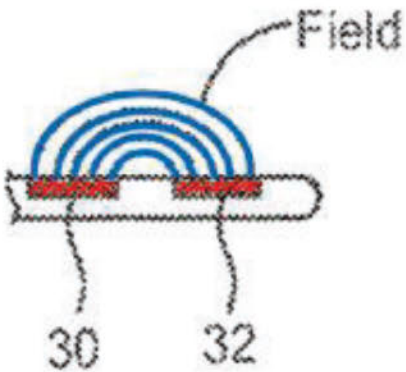
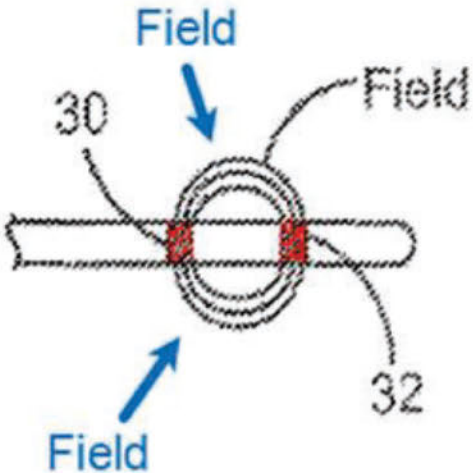
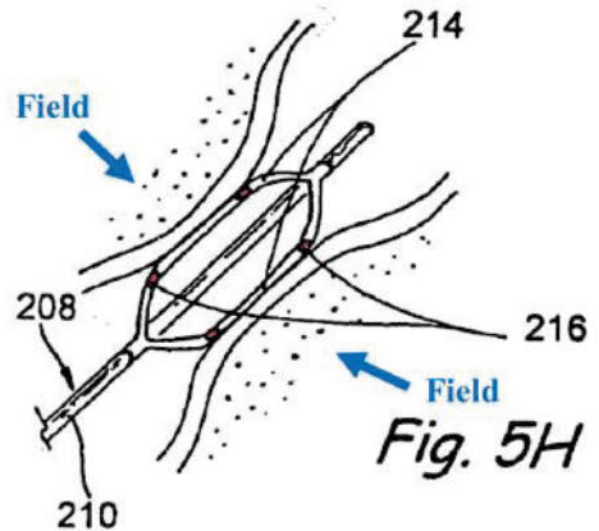
'669 POR, 23

## '077 Patent

electrodes. Further, it may be desirable to incorporate multiple pairs of electrodes that may be activated in pairs, in groups, or in a sequential manner in order to maximize the desired shape of the energy field (EF) while minimizing the field strength requirements.

'669 Ex.1001 ('077 Patent), 18:42-46; '669 Reply, 23-24

# Makower Teaches Lateral Energy Delivery

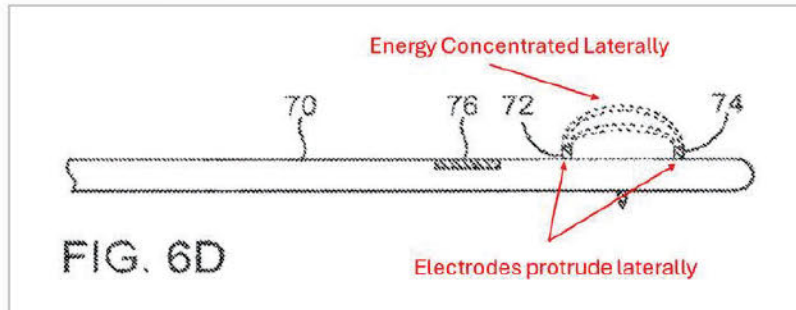
| Challenged Patents, FIG.5A                                                                        | Challenged Patents, FIG.5B                                                                         | Makower, FIG.5H                                                                                     |
|---------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|
|  <p>FIG. 5A</p> |  <p>FIG. 5B</p> |  <p>Fig. 5H</p> |

'279 Ex.1001 ('675 Patent), Figs.5A, 5B; '280 Ex.1001 ('011 Patent), Figs.5A, 5B; '669 Ex.1001 ('077 Patent), Figs.5A, 5B; Ex.1005, Fig.5H  
 '279 Petition, 85-87; '280 Petition, 88-90; '669 Petition, 88-90; '279 Reply, 23-26; '280 Reply, 23-26; '669 Reply, 25-27

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

# Makower Teaches Lateral Energy Delivery

## '011 Patent

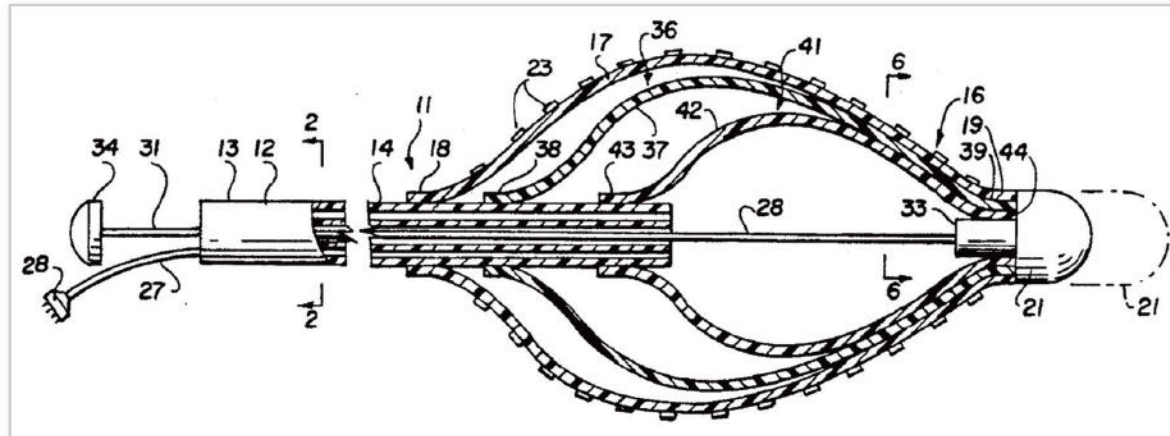


9. The apparatus of claim 8, wherein the energy transmission element is configured to deliver energy laterally relative to the distal portion of the body.

10. The apparatus of claim 9, wherein the energy transmission element is configured to extend laterally from the distal portion of the body.

'280 Ex.1001 ('011 Patent), Fig.6D, Cls. 9-10; '279 & '669 Ex.1023 ('011 Patent), Fig.6D, Cls. 9-10

## Imran



Ex.1068, Fig.1

'279 Petition, 85-87; '280 Petition, 88-90; '669 Petition, 88-90; '279 Reply, 23-26; '280 Reply, 23-26; '669 Reply, 25-27

DEMONSTRATIVE EXHIBIT - NOT EVIDENCE



**Patent Owner's Definition of a POSITA Is Incorrect  
and Irrelevant to Any Disputed Issue**

*DEMONSTRATIVE EXHIBIT – NOT EVIDENCE*

## Petitioners' POSITA Definition is Correct

### Petitioners' Definition

- (1) A Doctor of Medicine (M.D.) or at least a bachelor of science degree in engineering or a related discipline and
- (2) At least three years of experience in the **clinical use, design, development, and/or testing of medical devices**, including **medical devices** that deliver energy to **tissue**.

A higher level of education may compensate for less work experience, and vice versa.

### Patent Owner's Definition

- (1) A Doctor of Medicine (M.D.) or at least a bachelor of science degree in engineering or a related discipline; and
- (2) At least three years of experience in the **design and development, of nasal medical devices**, including **nasal medical devices** that deliver energy to the **nasopharyngeal passage**.

'279 Petition, 17; '280 Petition, 18-19; '669 Petition, 17-18; '279 POR, 18; '280 POR, 19; '669 POR, 18

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

## Dr. Bu-Saba and Dr. Martin Are POSITAs



**Dr. Nicolas Bu-Saba**

*Harvard Medical School  
Massachusetts Eye & Ear*

- Board-certified otolaryngologist and surgeon with over 28 years' experience
- Chief, Division of Comprehensive Otolaryngology, Mass. Eye & Ear
- Positions with American Academy of Otolaryngology, Massachusetts Society of Otolaryngology, and others
- Used and taught use of RF energy devices in the nose for decades

'279 Ex.1002, ¶¶3-7; '280 Ex.1002, ¶¶3-7; '669 Ex.1002, ¶¶3-7



**Dr. Greg Martin**

*Principal  
Tremont Consulting LLC*

- Ph.D. in mechanical engineering, MIT
- Designed and developed energy-based medical devices since 1998
- Senior Lecturer at Boston University
- Vice President of R&D for 4 different companies
- Chief Technology Officer for Hemedex, Inc.

'669 Ex.1007, ¶¶3-7

## Patent Owner's Definition is Irrelevant as to Any Contested Issue



**Dr. Howard Levine**

*PO's Declarant*

**Q.** And you're aware of Dr. Bu-Saba's credentials and experience?

**A.** I am.

\* \* \*

**Q.** You don't dispute that he's an expert on the anatomy of the nasal cavity and the nasopharynx, do you?

**A.** I do not.

Ex.1089, 170:12-171:2; '279 Reply, 27; '280 Reply, 27; '669 Reply, 29

## Patent Owner's Definition is Irrelevant as to Any Contested Issue



**Dr. Marom Bikson**

*PO's Declarant*

39. I have been asked to apply Patent Owner's definition of POSITA, which I agree with. My opinions would not change if Petitioner's definition of POSITA is adopted.

'279 Ex.2005 ¶139; '280 Ex.2005 ¶139; '699 Ex.2005 ¶141; '279 Reply, 30; '280 Reply, 30; '669 Reply, 32

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

***Neurent Medical Inc. et al. v. The Foundry, LLC***

**Petitioners' Oral Hearing Demonstratives**

**April 29, 2025**

**IPR2024-00279, IPR2024-00280, IPR2024-00669**

DEMONSTRATIVE EXHIBIT – NOT EVIDENCE

U.S. Patent No. 10,894,011  
Petitioners' Demonstratives for Oral Argument  
Case No. IPR2024-00280

Respectfully,

Date: April 22, 2025

/Gilbert T. Smolenski/  
Gilbert T. Smolenski  
Registration No. 78,549

Counsel for Petitioners

**CERTIFICATE OF SERVICE**

I hereby certify that, on April 22, 2025, I caused a true and correct copy of  
Petitioners' Demonstratives for Oral Argument to be served on Patent Owner via  
electronic mail to:

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