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.

Case No. IPR2024-00279

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

REPLY DECLARATION OF DR. NICOLAS BU-SABA REGARDING CLAIMS 1-3, 7, 9-10, AND 17-25 OF U.S. PATENT NO. 10,610,675

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I, Nicolas Y. Bu-Saba, M.D., declare as follows:

I. INTRODUCTION

1. My name is Nicolas Y. Bu-Saba.

2. I am making this declaration at the request of Neurent Medical Inc. and Neurent Medical Ltd. ("Neurent" or "Petitioners") as an independent expert consultant in this proceeding before the United States Patent and Trademark Office and to address and respond to the arguments made in the Patent Owner's Patent Owner Response ("POR") and the declarations submitted by Dr. Howard Levine ("Levine Declaration") (Ex. 2003) and Dr. Marom Bikson ("Bikson Declaration") (Ex. 2005) in support of the POR. I previously submitted a Declaration in support of the Petition, dated January 17, 2024 (Ex.1002) ("First Declaration").[1]

[1] In my First Declaration, I inadvertently suggested that I am a named inventor on patents. Ex.1002-Decl., ¶3. For the avoidance of doubt, I am not a named inventor on any patent applications. Otherwise, the rest of the description of my background and experience, as well as my CV that is attached to my First Declaration, is correct. Ex.1002-Decl., ¶¶3-7. For example, as reflected in my CV, I have numerous peer reviewed publications, academic and hospital appointments, funded and unfunded

3. As stated in the First Declaration, I am being compensated for my work on this matter at my standard hourly consulting rate of $750 per hour, but my opinions are based on my own views and understanding of the prior art, the knowledge of a person of ordinary skill in the art, and the patented technology. My compensation is not dependent on and in no way affects the substance of my statements, opinions, or conclusions in my First Declaration and this Reply Declaration nor is it dependent on any testimony I give or on the outcome of this proceeding.

4. As also stated in my First Declaration, I have no financial interest in Petitioners or Patent Owner. I similarly have no financial interest in the ’675 patent and have had no contact with the named inventors of the ’675 patent.

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research projects, teaching responsibilities, presentations, reviews, chapters, editorials, and clinical innovations. *See generally*, Ex.1002-Decl., Appendix A.

II. MATERIALS CONSIDERED

5. In forming my opinions, in addition to my knowledge and experience, I have considered the materials cited in my First Declaration and the documents cited herein, which are listed in **Appendix D.**[2]

6. Since preparing my First Declaration, I have reviewed Patent Owner's Preliminary Response ("POPR"), the Board's Institution Decision ("ID"), the POR, the Levine Declaration, and the Bikson Declaration. I have also reviewed and considered the documents cited by Dr. Levine and Dr. Bikson in their declarations, and the transcript of Dr. Levine's deposition held on January 7, 2025 ("Levine Deposition") (Ex.1093) and the transcript of Dr. Bikson's deposition held on January 9, 2025 ("Bikson Deposition") (Ex.1094).[3]

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[2] Similar to my First Declaration, various annotations have been added to the figures and diagrams in this report. All of these annotations are added unless noted otherwise.

[3] I also signed an errata with respect to the transcript from previous deposition regarding my First Declaration. *See* Ex.1100.

III. SUMMARY OF OPINIONS

7. For the reasons discussed at length in my First Declaration, it is my opinion that there is nothing inventive about claims 1-3, 7, 9-10, and 17-25 of the ’675 patent. As detailed below, it remains my opinion that the prior art anticipates and renders obvious claims 1-3, 7, 9-10, and 17-25 of the ’675 patent.

8. Nothing in the POR, the Levine Declaration, the Levine Deposition, the Bikson Declaration, or the Bikson Deposition changes my opinions set forth in my First Declaration. As stated in my First Declaration and in this Reply Declaration, I have interpreted the ’675 patent, the ’675 patent’s priority applications, and the prior art references consistent with the knowledge and understanding of a POSITA without the use of hindsight. In this Reply Declaration, I respond to the areas of dispute raised by Dr. Levine and Dr. Bikson.

IV. LEGAL PRINCIPLES

9. In my First Declaration, I set forth the applicable principles of patent law that counsel provided to me, which I incorporate by reference here. Ex.1002-Decl., ¶¶15-30. I have continued to apply those principles in providing my opinions in this Reply Declaration.

V. OVERVIEW OF THE TECHNOLOGY AND THE '675 PATENT

10. In my First Declaration, I included a detailed overview of the technology background, the '675 patent, and the prosecution history of the '675 patent, which I incorporate by reference here. Ex.1002-Decl., ¶¶31-54.

11. Dr. Levine includes sections in his declaration titled "General Overview," "Nasal Anatomy and Physiology," and "Treatment of Mechanical Obstructions." Ex.2003-Levine, ¶¶23-30, 40-49. Dr. Bikson includes a section in his declaration titled "Overview of the '675 patent and the Challenged Claims." Ex.2005-Bikson, ¶¶43-49. I disagree with several aspects of Dr. Levine's and Dr. Bikson's characterizations of the state of the art, the '675 patent, and the'675 patent's prosecution history. I address those points relevant to the issues before the Board in response to Dr. Levine's and Dr. Bikson's substantive arguments below.

VI. LEVEL OF ORDINARY SKILL IN THE ART

12. As explained in my First Declaration, a person of ordinary skill in the art at all relevant times (2005-2019) (hereinafter, a "POSITA") would have had (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. Ex.1002-Decl., ¶29.

13. Dr. Levine proposes the following definition of a person of ordinary skill in the art:

> "(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*."

Ex.2003-Levine, ¶38 (emphasis in original).[4, 5]

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[4] Dr. Bikson does not offer any opinions on the level of ordinary skill in the art. *See* Ex.2005-Bikson, ¶¶36-42.

[5] I understand that Patent Owner's proposed definition of a person of ordinary skill in the art differs from Dr. Levine. I understand that Patent Owner argues that a person of ordinary skill in the art has "at least three years of experience in the design and development of nasal medical devices, ***including nasal medical devices that deliver energy to tissue***," whereas Dr. Levine argues "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***." Ex.2003-

14. Dr. Levine therefore agrees that a person of ordinary skill in the art would have had "a Doctor of Medicine (M.D.) or at least a bachelor of science degree in engineering or a related discipline." Ex.2003-Levine, ¶38. However, Dr. Levine disagrees with aspects of the second part of my definition of a person of ordinary skill in the art. Ex.2003-Levine, ¶38.

15. First, Dr. Levine opines that an individual that has three or more years of experience in the clinical use of medical devices that deliver energy or testing such medical devices is not a person of ordinary skill in the art. That is, according to Dr. Levine, a person of ordinary skill in the art is exclusively limited to someone that has designed or developed devices.

16. Second, Dr. Levine opines that an individual must have experience with nasal medical devices, including nasal medical devices that deliver energy to the nasopharyngeal passage to have ordinary skill in the art. That is, according to Dr. Levine, a person of ordinary skill in the art is limited to individuals that have specific experience with nasal medical devices, including nasal medical devices that deliver energy to the nasopharyngeal passage. These differences are highlighted in the

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Levine, ¶38. These differences do not change my opinions regarding the appropriate level of a person of ordinary skill in the art.

following chart (blue text relates to the first difference and green text relates to the second difference):

My Definition of a POSITA (Ex.1002-Decl., ¶29)	Dr. Levine's Definition of a POSITA (Ex.2003-Levine, ¶38)
(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.[6]	(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.

As detailed below, I disagree with Dr. Levine regarding the type of experience that a person of ordinary skill in the art would have had related to the patent at issue.

17. As explained in my First Declaration, I understand from Petitioners' counsel that several factors are to be considered in determining who would be a person of ordinary skill in the art. These factors include: (1) the types of problems encountered in the art; (2) the prior art solutions to those problems; (3) the rapidity

[6] Dr. Levine does not opine whether "[a] higher level of education may compensate for less work experience, and vice versa." Ex.2003-Levine, ¶¶32-39.

with which innovations are made; (4) the sophistication of the technology; and (5) the educational level of active workers in the field. *See* Ex.1002-Decl., ¶28. The facts in view of the above factors support my definition of the type of experience a person of ordinary skill in the art would have had at the time of the patent at issue.

A. Three Years' Experience Using and Testing Devices Would Have Provided a Person with Ordinary Skill in the Art

18. As noted above, Dr. Levine opines that in order to qualify as a person of ordinary skill in the art, a medical doctor would have needed prior experience designing or developing medical devices, and effectively, therefore, opines that clinical use and testing would not have provided a person with ordinary skill. Ex.2003-Levine, ¶38. I disagree.

19. As a preliminary matter, each of the opinions I offered in my First Declaration and in this Reply Declaration is based on my experience, which I have detailed at length. More specifically, I am a Board certified otolaryngologist, and have myself been performing ablation procedures in the airway for decades. I routinely used and use radiofrequency devices like the one described in the '675 patent claims as a part of my clinical practice. An otolaryngologist like myself is the type of clinician who would use the device claimed in the '675 patent and would be responsible for its safe and effective use. As the doctor responsible for the safety

of my patients, I was required to and did understand the operation of devices I was using, including the operation and function of radiofrequency electrodes. I gained this understanding in multiple ways, including my medical training in obtaining my M.D., and years of experience using and testing devices afterwards. I have routinely taught other physicians how to use radiofrequency ablation devices in the nasal cavity and nasopharynx throughout my career, including prior to 2006, during and before their first three years of practice. I consider myself to be an expert on the anatomy of the nasal cavity and nasopharynx, and Dr. Levine appears to agree. Ex.1089-Levine-Tr., 170:21-171:2. Based on my experience, including before 2006, I also consider myself to be an expert on radiofrequency ablation devices that are used to treat tissue in the nasal cavity and nasopharynx.

20. Dr. Levine has not presented in his declaration any disputed issue that is outside the realm of my expertise and experience (or that of a person with an M.D. or engineering degree and three years of clinical use or testing of medical devices for applying energy to tissue as of 2006).

21. I understand that patent owner addresses the level of ordinary skill in the context of the operability of Makower. I addressed the operability of Makower's Figure 5H in my initial declaration (*see, e.g.*, Ex.1002-Decl., ¶¶80, 151-152, 154-156, 160-162, 165-180), and provide further analysis in this Reply Declaration. As

I further discuss in Section IX, I understand Dr. Levine and Dr. Bikson's opinions regarding the operability of Makower to turn on the functionality of the types of electrodes Makower Figure 5H would use in view of what would be present at the site of a procedure in the nasal cavity/nasopharynx (i.e., whether blood or mucus would interfere with the procedure or cause it to be unsafe). That is, I understand the dispute to be about how the device Makower teaches would be affected by anatomy and clinical procedure. My experience performing ablation procedures as a practicing otolaryngologist and my decades of experience using medical devices (including for radiofrequency ablation and devices with ring electrodes and surface electrodes) have informed me about the conditions of the nasal cavity and nasopharynx and support my opinions on these issues, including my opinions that the conditions under which Dr. Levine and Dr. Bikson claim Makower's Figure 5H device would operate would not actually be present in typical clinical practice. In fact, Dr. Levine agrees with me that during nasal procedures like those at issue, "mucus isn't the issue" and that to the extent mucus or blood were at the site of a procedure, a clinician could simply use suction to remove blood, mucus, or other fluid in the nasal airway before or during treatment. *E.g.*, Ex.1089-Levine-Tr., 82:8-83:18.

22. A person in the relevant field with a relevant degree and three years' experience with the use or testing of medical devices for applying energy to tissue would likewise have had the requisite skill to consider these issues as of 2006.

23. I have also considered Dr. Levine's proposed definition of a person of ordinary skill in the art, which requires only device design or development and does not include clinical use or testing, in light of the factors identified above and in my First Declaration. Ex.1002-Decl., ¶28. For the reasons below, the level of ordinary skill in the art related to the patent and claims at issue would have included experience with clinical use or testing (and not just device design or development).

24. **First**, my review of the problem and alleged solution of the '675 patent and the challenged claims supports my determination that clinical use and testing would give a person of ordinary skill in the art to address the problems and solutions in the art and that particularized device or design experience alone would not have been required. The alleged problem identified by the '675 patent related to the delivery of toxin for therapy. The methods and devices of the claims of the '675 patent that reflect a purported solution are phrased at a very high level of generality, do not identify their purported solution with particularly complex, specialized, or non-generic design details, or tie any non-generic design features to a specific way of affecting treatment. As an example, the claims merely purport to solve problems

in the art by providing "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." Ex.1001-USP675, claim 1; *see also id.*, claim 17. The claims are then directed to treatment of rhinitis symptoms (e.g., reducing mucus secretion and congestion) using these generic devices, which treatment would be performed and accomplished by a clinician using or testing the device and who would have been qualified to consider the art based on experience using or testing devices.

25. For example, the Somnoplasty device was available to and used by clinicians in the prior art, including those with three years' post-education experience. That device, which included bipolar electrodes for performing ablation in the nose, is commensurate in scope with the generic devices recited in the '675 patent claims. Through my clinical use and testing of the Somnoplasty device, I understand that it has a distal portions, bipolar electrodes at the distal end, and a generator that supplies the electrodes. *See* Ex.1001-USP675, Claim 1 (reciting "positioning a distal portion of a treatment device;"); Claim 3 (reciting "wherein the energy comprises RF energy"); Claim 20 (reciting "wherein the energy delivery element comprises a monopolar or bipolar electrode"); Claim 21 (reciting "wherein the energy delivery element comprises a plurality of electrodes").

26. **Second**, clinicians like myself used and tested radiofrequency devices in clinical settings for many years before the '675 patent, including the Somnoplasty and other devices I described in my First Declaration and in this Reply Declaration. Those radiofrequency devices were used to deliver energy to tissue in the nasal cavity safely and effectively by clinicians like myself, and by those without device design or development experience. In this context, three years' of medical device use and testing would have provided clinicians ample time to obtain knowledge of ablation devices and their use. I note that Dr. Levine testified that he has experience performing similar radiofrequency ablation procedures as early as the 1990s, and that he had not designed or developed any devices having electrodes prior to doing so. Ex.1089-Levine-Tr., 54:3-10, 157:12-159:5. Dr. Levine agrees with me that experience using RF energy devices such as the Somnoplasty device is relevant to the qualifications of a POSITA. Ex.2003-Levine, ¶12 ("I note that Dr. Nicholas Bu-Saba and I have both used Somnoplasty™ devices in our clinical practices, which involves the application of RF energy for treating, for instance, sleep apnea and nasal obstruction. I have performed thousands of procedures using Somnoplasty™ devices (Sunnyvale, California)."). The Fang reference includes another example radiofrequency ablation device (the SHP-I) that was used in a clinical setting in the nose using factory settings (i.e., "Level 3 intensity") to produce a desired treatment

result. Ex.1006-Fang, 876-77. The ’675 patent itself includes many examples of known energy delivery devices:

- Ex.1001-USP675, 16:37-44 (“Referring to FIG. 5, electroporation catheter system 20 further comprises a pulse generator 24 such as those generators available from Cytopulse Sciences, Inc. (Columbia, Md.) or the Gene Pulser Xcell (Bio-Rad, Inc.), or IGEA (Carpi, Italy), electrically connected to a catheter having a proximal end and a distal end and adapted for minimally invasive insertion into the desired region of the body as described herein.”),
- Ex.1001-USP675, 17:67-18:5 (“Various catheters useful for delivering vibrational energy to tissue are described in U.S. Pat. Nos. 6,361,554 and 6,464,680 to Brisken, the contents of which are expressly incorporated herein by reference in their entirety, for various therapeutic effects, such as enhancing cellular absorption of a substance.”),
- Ex.1001-USP675, 18:20-33 (“Any of the catheter devices described herein, or described in the contemporaneously filed U.S. Patent Application 60/701,747, previously incorporated by reference in its entirety, may be adapted to include an energy delivery element such as those described herein for purposes of providing a membrane transport system for delivery of a fragment of neurotoxin. In addition, certain catheter devices and methods such

as those set forth in U.S. Pat. Nos. 5,964,223 and 6,526,976 to Baran may be adapted to include energy transmission elements capable of producing a porative effect at the cellular level, including electrodes, ultrasonic elements and the like, for treatment in the respiratory tract."),

- Ex.1001-USP675, 19:22-29 ("As detailed in U.S. Pat. Nos. 6,626,855 and 6,719,694 to Weng, the contents of which are expressly incorporated herein by reference in their entirety, an ultrasound beam can be controlled from outside the patient to focus the ultrasound beam in the desired location and intensity. For use in the present invention, it may be desirable to pulse or otherwise attenuate the ultrasound beam to achieve reversible cellular poration at the targeted site.").

27. Those with a relevant medical or university degree and three years' of clinical use or testing experience would have the skill necessary, based on that experience, to consider such devices and particularly to understand their operation and clinical effects in the relevant anatomical locations.

28. **Third**, rather than relying solely on design or development experience, clinicians like myself have been able to learn safe and effective use of many medical energy delivery devices and to consider problems and solutions in the art—including those that involve radiofrequency electrodes—by using and testing devices in a

clinical setting, reading instructions for use, through educational programs and seminars, and reviewing the scientific literature available on such devices. By 2006, radiofrequency ablation—including in the nose—had been performed for many years and was the subject of many educational programs and lectures. The Fang reference is just one example of using a radiofrequency ablation device safely and effectively in the nose prior to 2006. I catalogued many other examples in my First declaration. Ex.1002-Decl., ¶¶36-42, 46.

29. Dr. Levine agrees with me that physicians learned about radiofrequency ablation devices—including the Somnoplasty device—safely and effectively by reading instructions for use and using the device. Ex.1089-Levine-Tr., 62:7-63:11 ("Q: Did you receive any instructions for use for the somnoplasty device? A: Yes. Q: Did that help you learn how the device worked? A: Yes. Q: So you were able to understand from your use of the device and the instructions for use how the device worked? A: Yes. Q: And from the instructions for use and your use of the device you were able to understand how to safely and effectively use the somnoplasty device? A: Yes. Q: And again, from the instructions for use and your use of the device you were able to understand the effects of the use of the somnoplasty device on the patient? A: Yes. "); *see also* Ex.1091-Bikson-Tr, 89:2-94:8. Dr. Levine also agrees with me that physicians learned about how to operate devices, including

which parameters to select and how tissue is impacted, by reading available literature without any development experience. Ex.1089-Levine-Tr., 74:9-75:11 ("Q: As a clinician did you understand how the Somnus device achieved that greater control over the outcome that you were looking for? A: I'm glad you say as a clinician, clinician meaning I'm someone treating versus someone developing. In this instance, well, I've developed many, many instruments and we can talk about that if you so wish, this was developed by electrical engineers. It's what I've already said the data, the histological data, where work was done on animals, which showed with different energy and time parameters the kind of creation of zone of injury that then would permit me as a clinician to be instructed as to how long, and what energy this would be used. The histologic images that I saw, I believed and believed them to be transferable as a clinician that it then could apply to my patients. What was so beautiful about it, there are many slides in the literature, it's really sort of oblong, three-dimensional oblong zone around the tip of the needle.").

30. Thus, the fact that experience of those with three years' clinical use and testing would have provided them with an understanding of the functionality of use of medical devices for applying energy to tissue (including, e.g., with radiofrequency electrodes) confirms they would have had the requisite ordinary skill to consider alleged problems and solutions in the art as of 2006.

31. **Fourth**, in 2006, the devices used for ablation were simple and easy to understand. For example, for radiofrequency devices, an ordinary physician would understand how energy would be dispersed by understanding the particular arrangement of electrodes and type of energy (e.g., bipolar or monopolar) they would apply, and use that information (along with instructions for use and other education) to determine the appropriate dosage (i.e., power and amount of time) for treating a patient. It was, and remains common for physicians to determine that a medical device used for one indication can be safely and effectively used for another indication, irrespective of whether they have design or development experience. This is frequently referred to as off-label use. I note that the Kong, Liang, Fang, and Chen references already of record in this proceeding appeared in medical journals and address the problem of treating rhinitis symptoms by selecting settings for various off-the-shelf RF ablation devices in a clinical setting—and there is no indication that any of the authors had prior device design or development experience. Ex.1043-Kong, 214 (selecting "grade 6" and treatment time); Ex.1045-Liang, 341 (selecting "Level 3" and treatment time); Ex.1006-Fang, 876 (similar); Ex.1044-Chen, 240 (similar). Dr. Levine agrees with me that clinicians evaluated and performed off-label use based on their clinical experience without any need for design or development experience. Ex.1089-Levine-Tr., 13:10-16 ("Q: Understood.

So in the instances where you've performed off-label use of medical devices, you decided to perform that off-label use based on your experience as a clinician?…A: Yes."); *see also id.*, 124:19-125:13 ("Clincian[s]" would not have needed to develop a device to "see another place that it could be used different from its early use…."). In a similar vein, clinicians frequently provided feedback to medical device manufacturers on problems they encountered or ways to improve the device. Moreover, when determining how to treat a patient, clinicians would also select among different devices and treatment modalities based on their clinical expertise and understanding of how those devices operate, and select appropriate dosage and parameters in doing so. Dr. Levine agrees with me on these points as well. Ex.1089-Levine-Tr., 72:16-75:11, 122:19-124:3.

32. The fact that devices were relatively unsophisticated and accessible to those with relevant education and clinical experience confirms a person with three years' use or testing experience would have had ordinary skill to evaluate the problems and solutions in the prior art relevant to the '675 patent.

33. **Fifth**, Dr. Levine agrees with me regarding the level of familiarity clinicians had with the devices that they use. In an article describing a laser ablation handpiece that he says he helped design, Dr. Levine noted that "the surgeon…must be familiar with the laser" and that they should understand "[i]ssues such as safety,

energy dosage, fiber management, and instrumentation." Ex.1107-Levine-Article, 451. For example, Dr. Levine provided a simple calculation clinicians would have been able to use to calculate dosage based on concepts clinicians that had experience with devices applying energy to tissue would have been familiar with—spot size, wattage, and exposure time. Ex.1107-Levine-Article, 452. Based on these quantities, he recognized that a clinician could determine how to cut or coagulate tissue. Ex.1107-Levine-Article, 452. This is consistent with my experience described above. Moreover, this is precisely why, as I mentioned above, clinicians were able to identify new uses for devices based on their prior use. On this point, Dr. Levine also agrees with me. Ex.1089-Levine-Tr, 124:19-125:13 ("Q: Understood. You were talking a little bit earlier about the inception for this laser device that you help develop; is that right? A: I didn't develop the laser. I didn't develop the laser device. Rodney Perkins developed the laser device. What I did was to try to see another place that it could be used different from its early use and see if the there was an indication. By indication I mean, did I, as a clinician, see value and then was there safety, was there durability, and then would a regulatory body agree if I could meet those criteria. What I created wasn't the laser or the energy, it was a tool used to deliver it into a place that was difficult to get to.").

34. Accordingly, it is my opinion that a person with the relevant degree and three years' experience using or testing medical devices for the application of energy to tissue would have had ordinary skill for considering the problems and solutions relevant to the '675 patent. In view of what I discussed above, including the experience that clinicians had, the problems and solutions in the art, and the lack of sophistication of the technology, I disagree with Dr. Levine that only device design or development experience would provide a person with ordinary skill.

B. A Person of Ordinary Skill in the Art Need Not Have Specific Nasal Experience

35. Dr. Levine also opines that in order to qualify as a person of ordinary skill in the art, an engineer would have needed prior experience with nasal medical devices, including those that deliver energy to the nasopharyngeal passage as opposed to medical device experience with delivering energy to tissue. I have also considered Dr. Levine's proffered definition of a person of ordinary skill in the art, which requires specific experience with nasal medical devices (Ex.2003-Levine, ¶¶32-39), in light of the factors identified above and in my First Declaration. Ex.1002-Decl., ¶28. For the reasons below, I disagree that nasal medical device experience would have been required to qualify an engineer as a person of ordinary skill in the art with respect to the '675 patent. I note, in any event, that I had more

than three years' experience with nasal medical devices that applied energy to tissue as of 2006.

36. **First**, contrary to Dr. Levine's declaration, Ex.2003-Levine, ¶35, I did not testify (and do not agree) that the level of ordinary skill for purposes of the '675 patent must be limited to those that had prior knowledge of the nasopharyngeal passageway. Ex.2003-Levine, ¶35; Ex-2002-Bu-Saba-Tr., 125:15-127:11 ("Q: So all claims of the '675 Patent recite a requirement that relates to the nasopharyngeal passage, correct? A: That's correct. Q: So my question is, since the claims of the '675 Patent all relate, at lease in part, to the nasopharyngeal passage, wouldn't it be better if somebody with experience with the nasopharyngeal passage or the nasal cavity, in general?…A: I've answered. I mean, when I say -- when I define a POSITA, these are the requirements of a POSITA and it all depends on what that POSITA is asked to opine about, which part of this claim, which specific area of that claim that POSITA is opining on. Q: But your definition leaves open the fact that somebody with no nasal experience could be opining on Claim 1, correct? … A: It depends on what that POSITA is asked to opine on. Which word of the claim. Which phrase of that claim. Which sentence of that claim that the POSITA is asked to opine on. There are many words listed in this claim. There is 'device,' there is 'target tissue,' there is 'therapy,' there are 'administering.' I mean, there are many words

listed here. So it depends on what that POSITA is asked to opine on. Q: So as it relates to the nasopharyngeal passage, should that person have nasal/nose experience? … A: So you're saying they're opining about nasopharyngeal passage? Q: That's right. A: So that POSITA should be a person with -- person of ordinary skill in the art about the nasopharyngeal passage. Q: Okay. That's what I was asking.").

37. Taken in context, I explained that someone asked to opine ***about*** the nasopharyngeal passage should be someone with knowledge of the nasopharyngeal passage. I did not say, and do not agree, that a person of ordinary skill considering the '675 patent would require prior experience with the nasopharyngeal passage. Rather, a person of ordinary skill in the art could have obtained knowledge regarding a particular location in the body (to the extent necessary) from scientific literature or conversations with those knowledgeable about the nasopharyngeal passage. Further, I note that nothing in the '675 patent claims requires an opinion ***about*** the nasopharyngeal passage. The claims merely require "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." The claim is directed to doing so with an unspecific

energy delivery without tying any of these features to any particular anatomical feature in the nasopharyngeal passage. Ex.1001-USP675, Claim 1; *see also id.*, Claim 17. As I explained throughout my First Declaration and in this Reply Declaration, as of 2006, nasal anatomy was well understood, methods of treating rhinitis symptoms in the nasal cavity—including with radiofrequency ablation—were well known, and the particular treatment locations for treating rhinitis symptoms had also been identified in the relevant literature. *See, e.g.*, Ex.1002-Decl., ¶¶31-46. A medical doctor or engineer with medical device experience applying energy to tissue without prior experience with devices in the nasal cavity specifically could draw upon the wealth of knowledge about treating that portion of the body to apply their ordinary skill to the issues presented by the ’675 patent.

38. **Second**, the ’675 patent specification supports my opinion that specific nasal experience would not have been part of the necessary level of ordinary skill. For example, the ’675 patent discusses applying neurotoxins to *any* area of the body—not just the nose. Ex.1001-USP675, 2:17-51 (discussing “use of neurotoxin for control of … conditions” throughout the body), 4:63-5:10 (“In addition to the methods described thus far, the present invention further provides systems for delivering toxins to target cells in a mammalian host. The target cells may be in **any of the target regions** described above or in **any other target region which may**

benefit from the specific and enhanced delivery of a neurotoxin to cells within the region."), 4:59-63 (describing "methods and apparatus for treating or inhibiting **a variety of diseases or syndromes** that have an underlying neurogenic component"), 17:7-11 ("Such steering ability enables the operator to introduce the device into tight or tortuous spaces (such as the **bronchial passages or cardiovascular vessels**) so that optimal placement of the device at the target location may be achieved."), 20:17-25 ("It may further be advantageous to position catheters of the present invention through **vessels in the body** to direct them to various regions to affect neurotransmitters in the **cardiovascular system**. Intraluminal catheters such as those shown in United States Patent Applications 2001/0044596 to Jaafar and 2002/0198512 to Seward, hereby incorporated by reference in their entirety, may be used in this application of the present invention."), 21:12-32 (discussing "target site in the **bronchus** … **of a lung**"). Neither the claims nor the '675 patent's specification identify any particular challenges with delivering treatment to particular parts of the nasal anatomy. Claim 1 simply recites "a nasopharyngeal passage," and elsewhere the patent states that treatment can be applied to "any portion of the nasal cavity." Ex.1001-USP675, claims 1, 17, 8:4-29. The patent identifies no purportedly challenging nasal anatomy, but rather "the entire nasal cavity." Ex.1001-USP675, claims 1, 17, 8:4-29.

39. The general application of the patent to multiple types of tissue and lack of specialized or unique issues with the nasopharyngeal passage identified in the patent support that a person with medical device experience applying energy to tissue would not need specialized experience with nasal devices applied in the nasopharyngeal passage to have ordinary skill in the art.

40. **Third**, the problems and solutions presented in the prior art support my opinion that a person of ordinary skill in the art would not need specific nasal experience, at least because they all emphasized devices could be used in multiple parts of the body. As one example, the Makower reference explains that its disclosed devices can be used throughout in the ear, nose, and throat. Ex.1005-Makower, [0043]. As another example, the Stern reference, which discusses uterine ablation, emphasizes that its teachings are applicable elsewhere in the body. Ex.1009-Stern, 1:15-23. Similarly, the Fang reference uses a generic radiofrequency device using its existing settings (Level 3 intensity). Ex.1006-Fang, 876-77. I note Dr. Levine does not dispute that these references are analogous art to the challenged claims of the ’675 patent. I also note that Dr. Levine agreed that “safety concerns that would be relevant to using [the laser the device he says he helped design was based on] in other parts of the body were also relevant to using the laser in the nose[.]” Ex.1089-Levine-Tr, 126:3-9; Ex.1107-Levine-Article, 451.

41. The fact that prior art devices could be and were used in multiple parts of the body confirms that a person of ordinary skill in the art with general medical device experience would have ordinary skill in the art.

42. **Fourth**, I have reviewed some of the prior art references (Ex.1110 and Ex.1111) that I understand Patent Owner provided to the United States Patent and Trademark Office during prosecution of the '675 patent. I understand that such references were submitted because the applicant believed them to be material to the patentability of the '675 patent. Ex.1110 is a patent that relates to "systems and methods for mapping or ablating heart tissue for treating cardiac conditions." Ex.1110, 1:12-14. Ex.1111 is a patent that "relates to methods for selectively ablating target sites in the lung while protecting adjacent lung and tissue structures." Ex.1111, 1:15-17. Though each relates to ablation, neither relates to ablation in the nasopharyngeal passage specifically. This again supports that medical device experience need not have been specific to the nasopharyngeal passage to provide one with ordinary skill in the art.

43. **Fifth**, as I mentioned above, the education level of the inventors can be relevant. Dr. Levine did not discuss the inventors' backgrounds in his declaration. Based on my review of publicly available information, the named inventors of the '675 patent appear to be engineers. *See* Ex.1108-Deem; Ex.1109-Gifford. I have

not, however, seen any evidence that the named inventors had prior experience with nasal medical devices, which confirms that no such experience would have been required.[7] While the '675 patent does discuss some portions of the nasal anatomy, it does so by citing other literature that would have been available to those of ordinary skill in the art. Ex.1001-USP675, 3:25-49. Moreover, these discussions do not involve particular complexity. For example, while the '675 patent discusses the use of neurotoxin, it does not identify any particular nerves or locations where nerves can be found. Rather, it is consistent with generally known and readily accessible principles in the art relating to nasal anatomy. *See* Ex.1002-Decl., ¶¶31-33; Ex.1064-Lane; Ex.1065-Gray.

44. Dr. Levine states that "Nasal anatomy and physiology are complex with many interrelated anatomical features" and that "one cannot properly treat a properly diagnosed nasal issue without fundamentally understanding the complete nasal

[7] I have also reviewed Dr. Bikson's declaration (Ex.2005-Bikson), CV (Ex.2006), and his deposition transcript (Ex.1091-Bikson-Tr.). His experience appears to be focused on generic neuromodulation devices and others that are not specifically designed for the nose. *See, e.g.*, Ex.1091-Bikson-Tr, 63:17-64:9, 80:13-81:1; Ex.2002; Ex.2001, ¶¶12, 15.

anatomy and physiology of that issue" (Ex.2003-Levine, ¶40), but the patent does not appear to recognize any such complexity or understanding of the nasal anatomy, or identify problems or solutions that suggest that an understanding of that complexity is required to understand and implement the disclosed embodiments. This supports my conclusion that a person with medical device experience but not specific nasopharyngeal medical device experience could learn about the relevant anatomy and apply their ordinary skill to problems or solutions for that area by reviewing the relevant literature.

45. **Sixth**, as I explained above in Section VI.A, the claims of the '675 patent only mention generic components like "a distal portion," an "energy delivery element," and a "bipolar electrode" without tying any of these features to any particular anatomical feature in the nasopharyngeal passage. Ex.1001-USP675, Claims 1, 2, 17, 20. Not only is the technology itself unsophisticated, but it is also not tied to any particular treatment site. In my review of the '675 patent, I did not find any device design details that are specifically tied to a particular feature of the nasal anatomy. Rather, as I explained above, much of the '675 patent disclosure emphasizes how the disclosed embodiments can be used in multiple, various portions of the body. I note that the patent also does not describe any studies

performed to determine the effectiveness of any particular device design in a particular portion of the body or any results from such studies.

46. Accordingly, I disagree that nasal medical device experience is required to qualify an engineer as a person of ordinary skill in the art to the ’675 patent. Instead, as detailed above, a medical doctor or at least a bachelor of science degree in engineering or a related discipline that has 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***, qualifies as a person of ordinary skill in the art.

VII. CLAIM CONSTRUCTION

47. As explained in my First Declaration, I applied the plain and ordinary meaning of the claim terms in my analysis. Ex.1002-Decl., ¶¶55-58. Dr. Levine and Dr. Bikson appear to agree that the plain and ordinary meaning of the claim terms should be applied in this IPR. Ex.2003-Levine, ¶31; Ex.2005-Bikson, ¶56.

VIII. PRIORITY DATE

48. As explained in my First Declaration, in my opinion, the Challenged Claims of the ’675 patent do not have written description support in any application

dated prior to October 22, 2019. Ex.1002-Decl., ¶59.[8] As also explained in my First Declaration, I have been informed and understand that this means the '675 patent is not entitled to a priority date prior to October 22, 2019. Ex.1002-Decl., ¶59.

49. Dr. Levine opines that the '675 patent specification "supports the use of energy alone to reduce mucus secretion and/or congestion." Ex.2003-Levine, ¶¶50-60. I disagree.

50. In my First Declaration, I explained that the subject matter of the '771 Provisional did not provide written description support of the Challenged Claims of the '675 patent. Ex.1002-Decl., ¶¶70-76. In particular, I explained that a person of ordinary skill in the art would not have understood that the '771 Provisional (and corresponding disclosure in the '675 patent, '011 patent, and '077 patent) described a "method of treating a nasal condition of a patient" or "administering therapy" by delivering energy to the target tissue "to disrupt neural activity [or alter

[8] As noted in my First Declaration, I have been informed and understand that to satisfy the written description requirement, the patent's specification must describe the claimed invention in sufficient detail that a person of ordinary skill in the art could reasonably conclude that the named inventor had possession of the claimed invention at the time of filing. Ex.1002-Decl., ¶23.

nasopharyngeal cells] such that mucus secretion [or congestion] is reduced in the nasopharyngeal passage" as claimed. .[9] Ex.1001-USP675, claims 1, 17.

51. Dr. Levine opines that "the '675 patent reasonably conveys to a POSITA the use of energy alone to "administer[] therapy" to "disrupt or alter tissue: 'such that mucus secretion is reduced in the nasopharyngeal passageway' (claim 1); OR 'such that congestion in the nasopharyngeal passageway is reduced' (claim 17)." Ex.2003-Levine, ¶60. Dr. Levine's declaration does not directly address the '771 Provisional and instead focuses on the '675 patent. *See* Ex.2003-Levine, ¶¶50-60. In any event, and as detailed below, I disagree with Dr. Levine's opinions.

52. As a preliminary matter, Dr. Levine's declaration does not adequately account for the fact that the '675 patent[10] is directed to the therapeutic administration

[9] I refer collectively to mucus secretion and congestion as rhinitis symptoms below.

[10] I understand that the Board's Institution Decision cited to and referenced the '675 patent when discussing whether the '675 patent, '771 Provisional, and priority applications provide written description support for the Challenged Claims. *See* Institution Decision, 23-26. For the purposes of this Reply Declaration, I primarily

of toxins. The title of the ’675 patent is “Systems and Methods for Delivery of a Therapeutic Agent,” Ex.1001-USP675, Cover, and the title of the ’771 Provisional is “Methods and Systems for Toxin Delivery to the Nasal Cavity,” Ex.1011-FH771, 26. The Abstract of the ’675 patent states that “[m]ethods and apparatus are provided for applying an fragment of a neurotoxin…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.” Ex.1001-USP675, Cover. Relatedly, the Abstract of the ’771 Provisional states that “[m]ethods and systems for delivering toxin and toxin fragments to a patient’s nasal cavity provide for both release of the toxin and delivery of energy which selectively porates target cells to enhance uptake of the toxin,” and “[t]he use of energy-mediated delivery is particularly advantageous with light chain fragment toxins which lack cell binding capacity.” Ex.1011-FH771, 56. Each of these conveys that the ’675 patent is directed to toxin delivery.

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cite to the ’675 patent. However, my opinions apply equally to the ’771 Provisional, ’011 patent, ’077 patent, and the other priority applications.

53. The ’675 patent also discusses energy delivery, but in the context of this toxin delivery, not as a treatment/therapy in and of itself. The background of the ’675 patent specifically states that “[t]he ***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***…to cause a clinical benefit in various regions within the body,” and “[m]ore 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.” Ex.1001-USP675, 1:33-42. Thus, the’675 patent emphasizes that energy is used to facilitate toxin delivery, it does not discuss using energy in isolation for any purpose other than poration. *E.g.*, Ex.1001-USP675, 1:33-42, 8:4-21, 8:61-65 (“***Any type of energy which is capable of reversibly permeablizing or porating the cell wall to allow passage of the toxin*** molecule, either whole toxin or preferably light chain fragment, into the cell cytoplasm may be applied to the cell membrane.”), 21:35-37 (“[T]he ***present invention*** is directed to ***methods and systems for delivering toxins*** to target cells within a patient’s nasal cavity.”).

54. The ’675 patent does not purport to have invented toxins or energy delivery or discovered that neurotoxins could be used to treat rhinitis symptoms. For

example, the ’675 patent admits that toxins were known, and it cites a number of references discussing disorders that could be treated with neurotoxins. Ex.1001-USP675, 1:43-2:51. It also acknowledges that energy devices were known. *E.g.*, Ex.1001-USP675, 13:58-63, 16:15-28, 16:37-44. It further acknowledges that another individual—Dr. Sanders—purportedly determined that toxins could be used to treat rhinitis symptoms. Ex.1001-USP675, 3:25-49, 3:66-4:15; *see also* Ex.1089-Levine-Tr., 199:5-8 (“Q And so Dr. Sanders had already used neurotoxin in the nose to reduce mucus secretion before the Foundry patents? A Yes.”), 199:12-15 (“Q So Dr. Sanders had already used neurotoxin in the nose to treat rhinitis before The Foundry patents? A Yes.”). Thus, because using toxins to “block[] mucus production by mucus-producing cells in the nasal membrane” was known, the ’675 patent’s purported invention was to “provide improved methods and systems for delivering toxins…to the nasal membrane of a patient, particularly a patient suffering from rhinitis or other conditions associated with nasal inflammation and conditions[.]” Ex.1001-USP675, 3:50-65; *see also id.* 3:50-65 (“The systems and methods should provide for the safe and effective delivery of the toxins, and in particular should reduce or eliminate the risk of toxin being delivered to non-targeted tissues outside of the nasal cavity.”), 21:35-22:3. That is, the ’675 patent is directed to “applying energy to the target cells under condition [sic] which cause poration of

the cell membranes to enhance delivery of the toxins and/or their active fragments." Ex.1001-USP675, 5:13-16.

55. As my First Declaration explained, the '675 patent does not describe that the named inventors possessed the Challenged Claims because it discusses the use of energy (e.g., RF energy) to porate cells to enhance the delivery of toxins (as described above), and not the use of energy alone for treatment/therapy as recited in the Challenged Claims. Ex.1002-Decl., ¶¶71-72.

56. Dr. Levine relies on a small number of sentences in the '675 patent to suggest otherwise, and I disagree that a person of ordinary skill in the art would have understood from those sentences that the named inventors possessed the claims directed to energy treatment/therapy. Ex.2003-Levine, ¶¶50-60. As detailed below, none of the sentences cited by Dr. Levine provide written description support for the Challenged Claims.[11]

[11] Dr. Levine suggests that non-challenged dependent claims 12-13 and 28-30 are supported by the specification. Ex.2003-Levine, ¶30. I have not considered and do not offer any opinions on whether claims 12-13 and 28-30 have written description because those claims are not at issue in this proceeding.

57. **First**, Dr. Levine's declaration cites one sentence of the '675 patent that recites "non-reversible" poration. The totality of this sentence is the following:

> 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***.

Ex.1001-USP675, 8:4-21.[12] I also reviewed this sentence and the surrounding parts of the specification and disagree that it recites or discloses treatment/therapy with non-reversible poration energy alone. The sentence does not state that non-reversible poration alone results in treatment/therapy. Rather, as made clear by the end of this sentence, toxins "are delivered to a patient's nasal membrane while applying energy" and the energy is applied to "cause a reversible (or in some instances non-reversible) poration of the cell membranes ***to enhance delivery of the toxin into the cells***." Ex.1001-USP675, 8:4-21. That is, this sentence specifically teaches to those of ordinary skill in the art that the named inventors are describing

[12] This sentence is also present in the '771 Provisional. Ex.1011-FH771, 29 ([0031]).

that energy is to be used ***with*** a neurotoxin for the purpose of causing "poration of the cell membranes to ***enhance delivery of the toxin into the cells***." Ex.1001-USP675, 8:4-21. This single sentence never states or suggests using energy without a neurotoxin to treat any condition. This sentence is also consistent with the '675 patent's statements that toxins treat rhinitis symptoms (not that energy alone does so), as the '675 specifically states that the introduction of toxins results in the therapeutic effect even if energy is not used to facilitate toxin delivery. *E.g.*, Ex.1001-USP675, 3:25-34, 8:38-60, 21:43-22:3 ("***Botulinum toxin blocks acetylcholine release*** from cells [to prevent mucus production] and ***can thus be effective even without energy-mediated delivery*** in accordance with the principles of the present invention.").

58. Moreover, the '675 patent's single reference to "non-reversible" poration does not teach or suggest that non-reversible poration alone (i.e., non-reversible poration without neurotoxins) treats rhinitis symptoms.[13] As noted above,

[13] The '675 patent specifically defines "poration" as "various forms of electroporation…[that] create temporary pores in a targeted cell membrane." Ex.1001-USP675, 13:27-34. Thus, the '675 patent defines "poration" as reversible poration. Dr. Levine does not address this definition or teaching is his analysis.

the text surrounding the single reference to "non-reversible" poration specifically refers to the "present invention" as "deliver[ing] [toxins] to a patient's nasal membrane while applying energy to target cells within the membrane under conditions which cause… poration of the cell membranes to enhance delivery of the toxin into the cells." Ex.1001-USP675, 8:4-21. The immediately follow portion of the specification (which is not discussed by Dr. Levine) confirms that the focus of energy delivery is "where the ***toxin is introduced***," as the specification states that the "region where the toxin is introduced may comprise any portion of the nasal cavity" or the "nasopharynx" which is a region that has cells "which are responsible for mucus secretion and which are susceptible to the disabling mechanism of the botulinum toxin and other neurotoxins." Ex.1001-USP675, 8:11-37. Therefore, in my opinion, this first sentence cited by Dr. Levine that references "non-reversible" does not provide written description support for an apparatus that uses energy alone without neurotoxins to treat rhinitis symptoms as recited by the Challenged Claims.

59. **Second**, Dr. Levine's assertion that his opinions are confirmed by my testimony is also misplaced and mispresents my testimony.[14] Ex.2003-Levine, ¶58. I never stated in my First Declaration or at my deposition that irreversible poration and ablation are identical. Rather, consistent with the knowledge of those skilled in the art, I testified that poration and ablation are distinctly different techniques and cited references to support my statements. *See, e.g.*, Ex.1002-Decl., ¶41 ("[I]t was well-known that the energy used for RF ablation was 'distinctly different from the pulses which produce electroporation.'") (quoting Ex.1059-Rubisnky, [0005]). Nor, in describing the known effects of ablation used ***for therapy*** did I testify that the

[14] Dr. Levine's assertion that I "failed to address the 'non-reversible' energy teachings of the '675 patent" is also misplaced and mispresents my testimony. Ex.2003-Levine, ¶59. My First Declaration explained that the '675 patent (and the '771 Provisional) did not disclose using energy without neurotoxins to treat rhinitis. It does not. My First Declaration explains irreversible (i.e., non-reversible) electroporation is a form of energy, and does not identify an instance in which non-reversible electroporation is described in the '675 patent for treatment, because there is none. Therefore, my declaration addressed the totality of the '675 patent's (and the '771 Provisional's) disclosure.

'675 patent described use of non-reversible poration ***for therapy***. As discussed above, it does not. Consistent with the passages of my First Declaration cited by Dr. Levine, the goal of "enhanc[ing] delivery" of neurotoxin taught in the '675 patent can be achieved with reversible poration, ***not*** non-reversible poration, and one of ordinary skill in the art reading the '675 patent specification would have understood that irreversible poration would have at most been an undesirable side effect of reversible poration. *See* Ex.1002-Decl., ¶71. Dr. Levine's suggestion that my testimony confirms his opinions regarding description of therapy in the '675 patent is incorrect and misrepresents my testimony.

60. I note also that Dr. Bikson testified that whether irreversible poration will occur for a given cell will depend on a variety of factors. Ex.1091-Bikson-Tr., 55:9-21 ("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."), 55:22-57:9, 59:1-60:2, 65:10-67:8.[15] There is no description in the '675 patent

[15] Dr. Bikson also testified that his work related to non-reversible poration was "over the past few years." Ex.1091-Bikson-Tr., 60:7-13.

specification regarding what effect irreversible poration would have on the cells targeted for neurotoxin delivery by the ’675 patent (or any other). There is no data, report of any clinical study, or even discussion of the potential effects of irreversible poration in the ’675 patent at all.

61. Additionally, a person of ordinary skill in the art would have understood that the ’675 patent’s single reference to “non-reversible” poration was an acknowledgement that when applying energy for reversible poration, a minority of cells may be incidentally destroyed. That is, the ’675 patent’s single reference to “non-reversible” poration simply acknowledges that some cells will be incidentally destroyed when reversible poration energy is applied. Indeed, Dr. Bikson agrees that there is a risk that if a device is intended to produce reversible poration, there is nonetheless a risk of irreversible poration. Ex.1091-Bikson-Tr., 57:10-19 (“[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.”). This is notably different from treatment such as ablation which is specifically intended to destroy a large number of target cells to cause a therapeutic effect. Dr. Levine does not address these mechanics of ablation in his declaration.

62. **Third**, Dr. Levine suggests that the '675 patent teaches 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." Ex.2003-Levine, ¶56. I disagree. The '675 patent describes certain cells that are involved in mucus production. *E.g.*, Ex.1001-USP675, 3:25-49; 8:4-26, 8:38-40, 9:41-46, 21:43-53, 23:66-6. However, as described in my First Declaration and this Reply Declaration, the '675 patent never describes that destroying the cells involved in mucus production with non-reversible poration alone (i.e., non-reversible poration without toxins) for treatment or therapy of rhinitis symptoms. Rather, the specification routinely acknowledges that the ***toxins*** result in the treatment of rhinitis symptoms, consistent with what was previously known and as acknowledged by the '675 patent. *E.g.*, Ex.1001-USP675, 1:48-2:46, 3:25-49 ("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."). The '675 patent never discloses that the named inventors were in possession of applying energy without neurotoxins to destroy cells to treat rhinitis symptoms as claimed by the '675 patent.

63. **Fourth**, contrary to Dr. Levine's suggestion (Ex.2003-Levine, ¶¶52-54), while the '675 patent states that areas of toxin delivery and energy delivery may

not necessarily overlap, the '675 patent does not describe that the named inventors made any discovery regarding the effects of energy delivered to areas that do not overlap with the toxin, let alone that it would result in the treatment of rhinitis symptoms. In particular, Dr. Levine's declaration cites two portions of the '675 patent that describe where energy is applied with respect to neurotoxins. Ex.2003-Levine, ¶¶52-53. The first portion Dr. Levine cites is from the section of the patent titled "Brief Summary of the Invention and is reproduced below:

> 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.

Ex.1001-USP675, 9:58-10:3;[16] Ex.2003-Levine, ¶52.

[16] This sentence is also present in the '771 Provisional. Ex.1011-FH771, 32 ([0020]).

64. In the preceding paragraphs, the ’675 patent states that “the toxin may be introduced to the target region through a catheter,” and “[w]hile the energy may be applied from a separate external source, as generally described above, the energy will most often be applied from the same catheter or other apparatus used to deliver the toxin.” Ex.1001-USP675, 9:11-40. That is, the ’675 patent states that toxin and energy will be delivered together or contemporaneously, either via the same catheter or separate catheters. The ’675 patent also states that “the present invention further provides systems for delivering toxins to goblet and other target cells as defined above in a nasal membrane” and that “[a]n 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***.” Ex.1001-USP675, 9:41-57. That is, the ’675 patent states (again) that energy is used to enhance delivery of the toxin, not as a stand-alone treatment. Dr. Levine never addresses the preceding paragraph in his declaration.

65. The second portion Dr. Levine cites is an excerpt of a paragraph that is also in a section of the patent titled “Brief Summary of the Invention.” The full paragraph containing the sentences cited by Dr. Levine is below, and Dr. Levine’s declaration only cites the first two sentences (i.e., the sentences that are not in bold below):

> 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 permeabilized or porated to receive the toxin within the cytoplasm of the cell.**

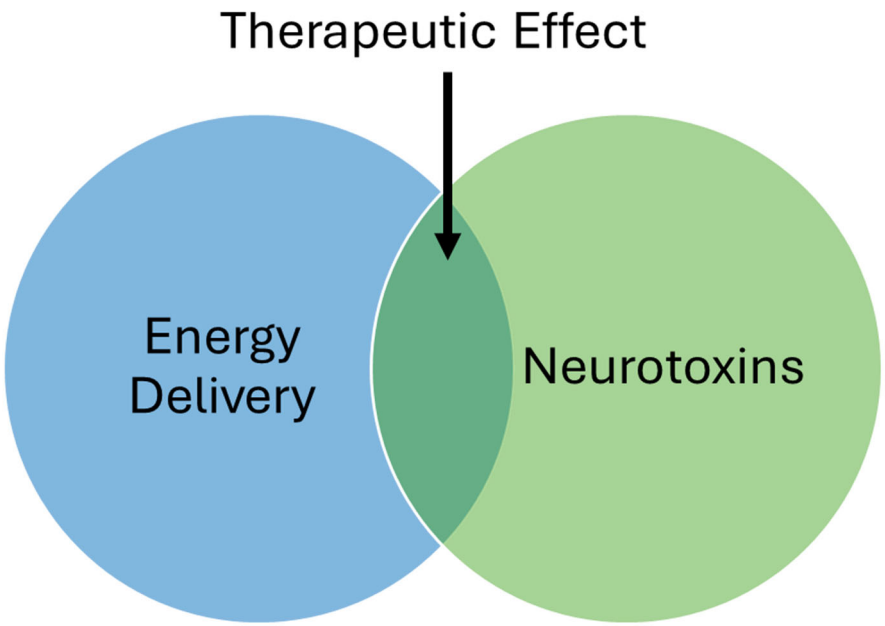
Ex.1001-USP675, 8:22-37;[17] Ex.2003-Levine, ¶53. The second half of the above paragraph (omitted and not addressed by Dr. Levine specifically) again explains why energy is applied—to facilitate the delivery of neurotoxins to specific locations in the nasal membrane, not alone for therapy.

66. Based on these two passages, Dr. Levine contends that "a POSITA with the proper knowledge of nasal anatomy and physiology would have recognized that

[17] This sentence is also present in the '771 Provisional. Ex.1011-FH771, 30 ([0014]).

the ’675 patent specification discloses applying energy in regions that may or may not overlap with the region of neurotoxin delivery and that those regions may relate to, for instance, goblet cells.” Ex.2003-Levine, ¶54. He also contends that based on these two passages, the ’675 patent discloses three “energy delivery options in relation to neurotoxin delivery:” (1) “Reversible energy applied; region of energy delivery co-extensive with region of neurotoxin delivery;” (2) “Reversible energy applied; region of energy delivery partially overlapping with region of neurotoxin delivery;” and (3) “Irreversible energy applied; region of energy delivery partially overlapping with region of neurotoxin delivery.” Ex.2003-Levine, ¶55. I disagree that these contentions support that ’675 patent provides description that the named inventors were in possession of treatment of rhinitis symptoms with energy alone.

67. As explained in my First Declaration and this Reply Declaration, the ’675 patent does not state, teach, or suggest using energy without a toxin to treat rhinitis symptoms. Indeed, each portion of the specification cited by Dr. Levine teaches using energy ***with*** neurotoxins to facilitate the delivery of the toxins to tissue. In particular, the passages cited by Dr. Levine indicate that the therapeutic effect is directed to the specific portions of tissue that have overlapping regions of energy delivery (e.g., electroporation) and neurotoxin, as shown in the Venn diagram below.



This is made clear by specification sections that Dr. Levine omits from his analysis (as I described above). *E.g.*, Ex.1001-USP675, 8:22-37 ("By controlling the delivery area of both the toxin delivery and the energy delivery, the…present invention can more specifically target the…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 permeabilized or porated to receive the toxin within the cytoplasm of the cell.").

68. Moreover, the ’675 patent specifically states that toxins treat rhinitis symptoms, not energy alone (i.e., energy without toxins).[18] For example, the ’675 patent states that “toxin blocks acetylcholine release from cells [to prevent mucus production] and can thus be effective even without energy-mediated delivery in accordance with the principles of the present invention.” Ex.1001-USP675, 21:43-22:3. The ’675 patent also states that “even if the toxin fragments are accidentally dispersed beyond the desired target regions, the fragments will not generally enter cells without the additional application of cell permeablizing or porating energy.” Ex.1001-USP675, 21:63-66; *see also id.*, 21:67-22:3. The ’675 patent does not describe the effects of energy in the areas that receive energy but not toxins and is

[18] Dr. Levine does not point to a single portion of the specification that describes using energy, including non-reversible poration, without neurotoxins to treat rhinitis because the ’675 patent never makes such a disclosure. Instead he relies only on what he opines a person of ordinary skill allegedly “would have recognized” or “would know.” Ex.2003-Levine, ¶¶54-57, 60. As discussed, in my opinion a person of ordinary skill in the art would not have understood from the ’675 patent specification, including considering what was known in the art, that the named inventors had ***described*** that they possessed an energy-only treatment method.

silent on this point. Dr. Levine also does not point to a single portion of the specification that describes the effects of energy in the areas that receive energy but not toxins because such a passage does not exist. Instead, the ’675 patent explains that toxins—not energy alone—treat rhinitis symptoms. The fact that the specification states that energy can be delivered to non-overlapping portions of toxin delivery simply shows that precision of energy delivery and toxin delivery is not required for treatment. It would not have conveyed to a person of ordinary skill in the art reading the specification that the named inventors were in possession of a treatment/therapy method or apparatus for the non-overlapping areas.

69. Accordingly, as explained in my First Declaration and above, it is my opinion that the priority applications do not provide written description for the Challenged Claims. As a result, I understand that the Challenged Claims are therefore, at best, only entitled to claim priority to no earlier than the date in which the ’675 patent was filed, which was October 22, 2019.

IX. GROUND IV: CHALLENGED CLAIMS 1-3, 7, 9-10, AND 17-25 ARE OBVIOUS OVER MAKOWER AND FANG

70. In my First Declaration, I explained that independent claims 1 and 17 of the ’675 patent would have been obvious over the combination of Makower, Fang, and Edwards-535. Dr. Levine and Dr. Bikson do not contest that Makower and Fang

teach each limitation of claims 1 and 17 of the '675 patent. Dr. Levine and Dr. Bikson instead collectively opine that a person of ordinary skill in the art would not have been motivated to combine Makower and Fang with a reasonable expectation of success. As detailed below, I disagree with Dr. Levine and Dr. Bikson.

71. The only dependent claim for Ground V that Dr. Levine and Dr. Bikson address is claim 22. As detailed below, I also disagree with Dr. Levine's and Dr. Bikson's opinions regarding claim 22.

A. A Person of Ordinary Skill in the Art Would Have Had a Reasonable Expectation of Success at Combining Makower and Fang

72. I understand that Patent Owner argued in its Patent Owner Response that a person of ordinary skill in the art would not have had a reasonable expectation of success at combining Makower and Fang and cites Dr. Levine and Dr. Bikson's declarations in support of this argument. *See* POR, 32-45. For the reasons detailed below, I disagree.

73. **First**, Dr. Levine opines that Makower "is directed to flexible catheters and other instrumentation for use in ear, nose, and throat procedures" (Ex.2003-Levine, ¶¶77-85), and the POR cites Dr. Levine's opinion in support of the contention that "Makower is not directed to RF energy delivery devices." POR, 34. I disagree.

74. As I explained in my First Declaration (e.g., Ex.1002-Decl., ¶¶80, 151-152, 156, 162), Makower teaches "medical devices and methods and more particularly…minimally invasive, catheter based devices, systems and methods for treating sinusitis and other ear, nose & throat disorders." Ex.1005-Makower, [0001]; *see also id.* [0043], [0161], [0187].[19] Makower specifically teaches a radiofrequency device (e.g., Figure 5H) that delivers ablation energy to tissue and treats "nose…disorders." Ex.1005-Makower, [0001], [0161], [0187]. Makower teaches that Figure 5H multiple electrodes that can be operated in a bipolar mode and can ablate tissue in the nasal cavity and/or nasopharynx. Ex.1005-Makower, [0001], [0043], [0161], [0187]. Makower also specially teaches that the radiofrequency device shown in Figure 5H utilizes "w[e]ll known] "designs and constructions," including "radiofrequency electrodes." Ex.1005-Makower, [0164].[20]

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[19] Although I am not aware of a commercial embodiment of Makower's Figure 5H device, my opinion about what Makower teaches and what a person of ordinary skill in the art would have expected regarding its teachings, remains unchanged.

[20] Dr. Bikson's opinion that "Makower is extraordinarily light on details" (Ex.2005-Bikson, ¶66), which is also cited by the POR (POR, 34), is misleading and wrong.

75. While Makower describes "flexible catheters," Makower does not limit its focus to flexible catheters, but states that its "present invention provides a variety of apparatus[es]" (i.e., working device) that "may be delivered through or incorporated into flexible catheters or flexible rod-like shafts." Ex.1005-Makower, [0161]-[0162]. That is, Makower describes the working devices—such as Figure 5H—as part of its "present invention" and separate from "the catheters used to deliver them." Ex.1005-Makower, [0161]-[0162]. Makower also specifically claims "working devices" that do not recite flexible catheters. For example, claim 1 of Makower, which I discussed in my First Declaration (Ex.1002-Decl., ¶162) and Dr. Levine does not address in his declaration, specifically recites a "working device" and does not recite a flexible catheter (i.e., claim 1 does not recite that the working device is a flexible catheter). Ex.1005-Makower, claim 1.

As described in my First Declaration and in this Reply Declaration, Makower teaches a radiofrequency device that delivers ablation energy to tissue in the nasal cavity and nasopharynx. *E.g.*, Ex.1005-Makower, [0001], [0043], [0161], [0164], [0187], FIG.5H, claim 1. Makower also discloses as many, if not more, details than the'675 Patent, particularly with respect to treatment using RF energy.

76. Regardless, a person of ordinary skill in the art would have understood that flexible catheters and radiofrequency devices such as Figure 5H of Makower can be used together. Indeed, the '675 patent specifically teaches that its described catheter "may be used to refer to an elongate element, hollow or solid, flexible or rigid and capable of percutaneous introduction to a body (either by itself, or through a separately created incision or puncture), such as a sheath, a trocar, a needle, a lead." Ex.1001-USP675, 16:20-25. The '675 patent thus explains that its described catheter, which includes electrodes, can be a flexible catheter, Ex.1001-USP675, 16:20-25, 16:29-53, and Dr. Levine agrees that the '675 patent "disclose[s] using flexible catheters, Ex.1089-Levine-Tr., 171:17-19 Thus, a person of ordinary skill in the art would have understood that Makower teaches a radiofrequency device to deliver energy to tissue as described in the context of Figure 5H.

77. **Second**, Dr. Bikson contends that "Makower is unsuited to treat tissue in the nasopharyngeal passage." Ex.2005-Bikson, ¶¶57-72. Dr. Levine similarly opines that "Makower's FIG. 5H device would result in ineffective and/or undesirable energy delivery to the targeted and surrounding tissue, raising safety and efficacy issues." Ex.2003-Levine, ¶¶91-97, 99-101. I disagree.

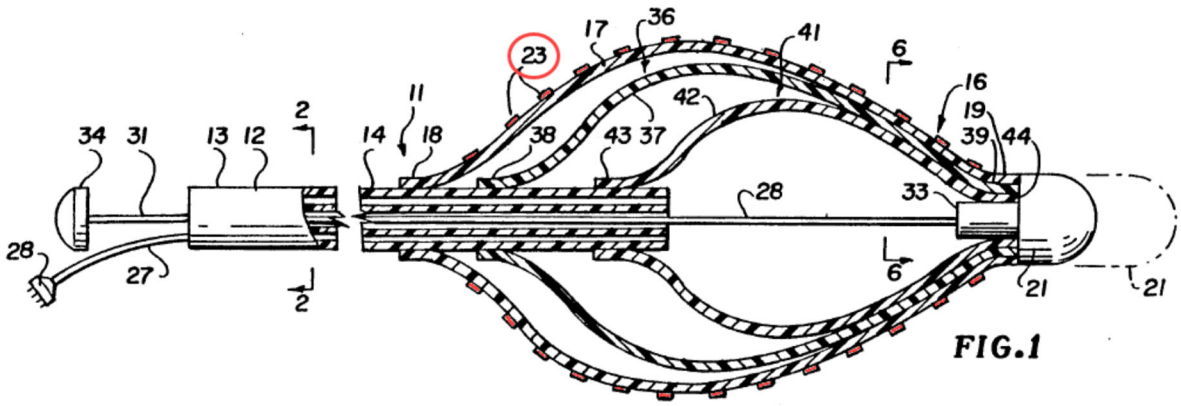
78. As a preliminary matter, Dr. Bikson and Dr. Levine improperly assume that Makower's Figure 5H radiofrequency device is limited to ring electrodes.

Contrary to their suggestion, Makower's disclosure never mentions or uses the words "ring electrodes." Instead, Makower teaches that Figure 5H is an "electrosurgical device" that includes "electrodes 216," and Makower explains that "[t]he electrodes 216 may be bipolar, monopolar or [use] any other suitable form of energy…." Ex.1005-Makower, [0187].[21] Makower further teaches that the electrosurgical device described in Figure 5H utilizes "w[e]ll known] "designs and constructions." Ex.1005-Makower, [0164]. One reference that Makower specifically incorporates as describing well-known designs and constructions in Imran. Ex.1005-Makower, [0164] ("Non-limiting examples of some such designs and constructions are set forth in… U.S. Pat. No. 5,255,679 (Imran)….").[22] Figure

[21] Dr. Levine and Dr. Bikson rely on Figure 5H itself for their argument that Makower discloses ring electrodes. Ex.2003-Levine, ¶¶93-94; Ex.2005-Bikson, ¶¶63-65. I understand from counsel that patent drawings do not necessarily define the precise proportions of the elements depicted and must be considered in the context of the specification.

[22] Dr. Levine suggests that "it is unclear why a POSITA would have looked to Imran…." Ex.2003-Levine, ¶106. I disagree that it is unclear—Makower specially

1 of Imran, reproduced below, teaches electrodes 23 (shown in red) that are disposed on the side of a strut. Ex.1068-Imran, claim 1, 62-66, 2:57-64, 3:2-7.



Ex.1068-Imran, FIG.1. That is, Imran teaches electrodes that are on the side of, instead of wrapping around, a strut, or surface electrodes.

79. A person of ordinary skill in the art would have understood that because Makower teaches that Figure 5H incorporates well-known designs and constructions and specifically cites Imran as an example of well-known designs and constructions, Makower teaches that the electrodes in its Figure 5H electrosurgical device include surface electrodes such as Imran's. Ex.1005-Makower, [0164], [0187], FIG.5H. A

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teaches that Figure 5H incorporates well-known components and assemblies, and cites Imran as one example of a radiofrequency device that depicts such well-known components and assemblies. Ex.1005-Makower, [0164]. Makower Figure 5H is the only electrode device specifically depicted in Makower.

person of ordinary skill in the art would have also understood that Makower teaches that its electrodes, which includes surface electrodes such as Imran's, would be suitable for the purpose of applying current to tissue via the electrodes 216 such that "tissue adjacent to the struts 214 [would] be cauterized or heated." Ex.1005-Makower, [0187]; *see also id.* [0043], [0164]. As a result, Dr. Levine's and Dr. Bikson's assertion that Makower is not suitable for ablating tissue in the nasal cavity or nasopharynx is misplaced.

80. I note that Dr. Levine testified that he knows Dr. Joshua Makower, the named inventor of the Makower reference, and he "respect[s] [Dr. Makower's] work as an engineer as high or beyond anyone that [he] know[s]." Ex.1089-Levine-Tr., 47:1-10. Dr. Levine has also relied on a different Makower reference when offering testimony in a separate IPR proceeding that another patent was invalid. *See* Ex.1104, ¶¶1, 15, 59-67. Therefore, Dr. Levine's opinions that this Makower reference includes an unsafe and inoperable embodiment appear inconsistent with his prior reliance on a Dr. Makower patent and his opinion of Dr. Makower's engineering ability.

81. Regardless, even (incorrectly) assuming that Figure 5H of Makower was limited to ring electrodes, a person of ordinary skill in the art would have understood that Figure 5H of Makower was operable to successfully ablate tissue.

In particular, Dr. Levine's and Dr. Bikson's opinions do not account for how physicians treat patients with radiofrequency ablation devices. Typical steps for treating a patient with radiofrequency ablation before 2006 (and even today) include the following:[23]

- First, when the patient is being treated at a physician's office, the patient is typically positioned in a seated position (i.e., their head would be above their chest) or reclined slightly from a seated position (e.g., like a dentist's office). Dr. Levine agrees that the patient could be in such a seated position or reclined slightly from a seated position. Ex.1089-Levine-Tr., 86:1-9 ("If I'm working in my office, which I would on some of these patients, patient would be sitting

[23] Some radiofrequency ablation procedures were also performed in an operating room. The procedures are nonetheless similar, with the primary difference being that the patient would be under general anesthesia instead of receiving local anesthesia (if necessary). I have taught numerous physicians and medical students how to perform radiofrequency ablation procedures in a physician's office or operating room, and the procedures I describe herein conform to standard medical practices that are taught throughout the United States in medical school and residencies.

in an examination chair."), 86:10-87:2 ("There are times, again, doing an office procedure, much like a dentist office, the patient would be reclined slightly.").[24] 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.

[24] If the patient is under general anesthesia, the patient is typically lying flat on their back with their head slightly elevated. Ex.1089-Levine-Tr., 86:10-87:2 ("If I were working under general anesthesia, I would say every single one of those patients is laying almost flat, perhaps the head evaluated a little tiny bit to maintain their airway, to help with congestion and swelling.").

- Second, decongestants were applied to the treatment area (e.g., the nasal cavity or nasopharynx). For example, Afrin was a topical decongestant that was commonly used to decongest tissue in the treatment area, and other decongestants were frequently used by physicians. The decongestant would serve several purposes: (1) it would shrink or constrict the size of the relevant tissue, making it easier to see and to manipulate and use an instrument in the relevant passage; and (2) it would reduce mucus production in the area of treatment for the same reasons. Dr. Levine agrees that decongestants are used during treatment. Ex.1089-Levine-Tr., 76:10-80:19 ("[The decongestant] would be either the generic name is oxymetazoline, which could be bought today over-the-counter at any pharmacy, one of brand names Afrin it is a topical, valuable, powerful decongestant."), 81:18-20. Dr. Levine also agrees that decongesting the patient was important, including for being able to visualize the treatment area. Ex.1089-Levine-Tr., 82:8-22.[25]

[25] When performing a nasal procedure under general anesthesia, physicians may also administer an anticholinergic drug (one of a class of drugs that would block the parasympathetic nerves in the patient's nasal cavity or nasopharynx) to reduce

- Third, topical anesthesia was applied to the treatment area. This would numb the treatment area and make the patient more comfortable during the procedure. This is similar to dental procedures that use topical anesthesia to numb the treatment areas during an in-office procedure. Dr. Levine also agrees that topical anesthesia is used. Ex.1089-Levine-Tr., 76:10-80:19, 81:13-20 (agreeing that "[o]ne of [the pretreatment] goals was to apply some form of anesthetic in order to make the patient more comfortable[.]").

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mucus production. One common anticholinergic agent was atropine. Anesthesiologists have administered atropine (as well as other anticholinergics) to block the parasympathetic stimulation in a patient's nasal cavity or nasopharynx to reduce mucus production during general anesthesia since at least the 1980s when I was in my residency, and I have used this drug and class of drugs throughout my career during procedures for the same purpose. This further demonstrates that it was known that blocking parasympathetic nerves in the nasal cavity and nasopharynx reduced mucus production and congestion. Administration of such anticholinergics also was part of what practicing physicians used to prevent mucus from interfering with the site of procedures in the nasal cavity/nasopharynx where necessary.

82. Once these preparatory steps were performed, the patient would be ready for treatment. In some circumstances, there would still be mucus in the treatment area. When this occurred, and to the extent it would present an issue for administering treatment, a physician would suction the mucus out of the treatment area to optimize visualization of the surgical site. Dr. Levine also agrees that a physician would suction mucus out of the treatment area if it remained present. Ex.1089-Levine-Tr., 83:3-16 ("If [mucus] was obstructing my view. If it was this thick, tenacious secretion, I might have to mechanically remove it with forceps, I might have to suction it….").

83. Additionally, if there was blood in the treatment area, this would also typically be removed prior to treatment. Otherwise, the presence of blood could impact the ability of the physician to see the treatment area or, potentially interfere with treatment.

84. In rare circumstances, such as in an emergency, mucus or blood may be present during a procedure. Generally, however, as discussed above mucus or blood would either be removed or not be present in the treatment area.

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.

87. For these reasons, Dr. Levine's and Dr. Bikson's suggestion that the nasal cavity or nasopharynx would be completely filled with blood or mucus (Ex.2003-Levine, ¶¶95-96; Ex.2005-Bikson, ¶70) is incorrect and inconsistent with how procedures are performed by physicians.[26] Accordingly, a person of ordinary

[26] Dr. Bikson testified that he lacks familiarity with the specific steps that are taken by physicians before performing nasal procedures. Ex.1091-Bikson-Tr., 56:2-9 ("Q Do you know what steps are taken by a physician before they perform a procedure where they deliver energy inside -- into the nasal cavity for ablating tissue? A Since

skill in the art would have understood that Makower's hollow Figure 5H device would not be completely filled with fluid when used during a procedure.

88. Moreover, because mucus and blood would be removed prior to a radiofrequency procedure in the nasal cavity or nasopharynx, air would be present in the nasal cavity or nasopharynx. The nasal cavity or nasopharynx is an airway, and it is fundamental human knowledge that one can breathe through their nose (i.e., nasal cavity and nasopharynx) if there are no blockages. It is also known that air is an insulator that insulates against the transmission of current, and Dr. Bikson agrees that current cannot travel through air. Ex.1091-Bikson-Tr., 218:9-11 ("Q Well, current really can't travel through air, correct? A That's correct."), 221:18-222:7. The '675 patent similarly acknowledges that air is an insulator. Ex.1001-USP675, 18:6-9 ("air is a very effective insulator"), 23:60-65. As described in my First Declaration, "RF current travel[s] from one bipolar electrode to another bipolar electrode." Ex.1002-Decl., ¶135 (citing Ex.1009-Stern, 5:54-55, 13:11-20, FIG.17). As a result, a person of ordinary skill in the art would have reasonably expected that

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I'm not a doctor, I don't think I would have the same level of -- or the complete level of familiarity that a physician would have. I would understand some of those steps.").

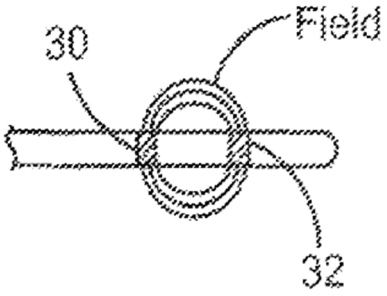
when Makower's bipolar electrodes (even if they are ring electrodes) contact tissue in the nasal cavity or nasopharynx to apply ablation energy (as Makower teaches), current would travel from one electrode to the other through the tissue, and would not travel through the surrounding air (which is an insulator). *E.g.*, Ex.1005-Makower, [0001], [0043], [0161], [0164], [0187], FIG.1, claims 1-2. This would allow for safe and effective delivery of energy to tissue without significant or unsafe transmission to other areas.[27]

89. Dr. Levine's and Dr. Bikson's suggestion that ring electrodes are unable to successfully apply energy to tissue (e.g., Ex.2003-Levine, ¶96; Ex.2005-Bikson, ¶70) is also incorrect. Devices with ring electrodes to ablate tissue, where portions of the ring electrodes contact the target tissue and the remaining portions of the electrodes do not, were well-known in the prior art before 2006. For example, prior to 2006, I personally used cautery devices with ring electrodes to treat tissue in the nasal cavity. In such circumstances, the fact that portions of the ring electrode were not in contact with tissue did not render the device inoperable in the nasal

[27] I note that in some instances, physicians performing RF ablation procedures could have used a gel on the surface of the target tissue to facilitate delivery of the energy into that tissue. Such gel further acts to conduct the energy to the desired location.

cavity/nasopharynx. Instead, such devices could safely and effectively treat tissue at the point of electrode-to-tissue contact given non-contact portions were surrounded by air, or to the extent fluid was present, only non-significant amounts of fluid.

90. Additionally, the ’675 patent itself discloses ring electrodes. For example, Dr. Levine agrees that Figure 5B of the ’675 patent (below) depicts ring electrodes, is within the scope of the claims, and is operable to deliver energy to tissue. Ex.1089-Levine-Tr, 195:4-6 (“Q Is Figure 5B operable to deliver energy to tissue? A According to this description, yes. Q. Do you have any reason to doubt that description? A No. Q. And Figure 5B shows ring electrodes; is that correct? A Yes.”), 195:20-196:6 (“Q Is Figure 5B within the scope of the ’011 Patent claims? A Yes. Q Okay. Is Figure 5B within the scope of the ’077 Patent claims? A Yes. Q Okay. Is Figure 5B within the scope of the ’675 Patent claims? A Yes.”); Ex.1001-USP675, claim 1.



Ex.1001-USP675, FIG.5B.

91. Therefore, at least based on this prior-art experience with operable ring-electrode devices and the patent's acknowledgment, a person of ordinary skill in the art would have understood that even if Makower's Figure 5H radiofrequency device utilized ring electrodes, Makower's Figure 5H device would successfully ablate tissue in the nasal cavity or nasopharynx as Makower teachers. *E.g.*, Ex.1005-Makower, [0001], [0043], [0161], [0164], [0187], FIG.1, claims 1-2.

92. **Third**, I understand that Patent Owner argues that (i) I never "address[ed] the threshold issue of whether Makower's hypothetical device is even suited to ablate tissue in the nose" and (ii) I never "considered Makower as a whole." POR, 41. This is incorrect and misstates my testimony. My First Declaration makes clear that Makower teaches that it ablates tissue in the nasal cavity to treat nasal conditions. For example, as I explained in my First Declaration, Makower teaches "medical devices and methods…for treating sinusitis and other ear, nose & throat disorders." Ex.1005-Makower, [0001]; [0043], [0043], [0161], [0187], FIG.5H, claim 1; *see also*, *e.g.,* Ex.1002-Decl., ¶152. And I extensively discussed and considered Figure 5H of Makower, which specifically teaches an electrosurgical device that includes bipolar electrodes for delivering ablation energy to tissue. Ex.1005-Makower, [0001]; [0043], [0043], [0161], [0187], FIG.5H, claim 1; *see*

also, *e.g.,* Ex.1002-Decl., ¶¶151-152, 156. Thus, I considered Makower's teachings that explain Figure 5H ablates tissue in the nasal cavity and nasopharynx, which Dr. Levine's and Dr. Bikson's declarations do not account for.

93. I also never testified that I did not consider Makower as a whole. I agree that Makower contains numerous teachings. However, as explained extensively in my First Declaration, Makower plainly teaches a radiofrequency ablation device that ablates tissue in the nasal cavity. *E.g.,* Ex.1002-Decl., ¶¶150-214. The fact that Makower teaches additional embodiments or devices to Figure 5H does not detract from what Makower taught a person of ordinary skill in the art with respect to Figure 5H. As a result, the fact that my declaration and testimony focused on Figure 5H of Makower and the teachings of Makower with respect to Figure 5H does not mean that I did not consider the entire reference when forming my opinions. I did.[28]

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[28] For example, when asked whether any of Makower's other devices besides Figure 5H contained electrodes, I testified that "I haven't considered other aspects of Makower in the declaration, so I cannot sit here and give you a complete and accurate answer, when I have not considered all the other factors or all the other

94. Additionally, PO's citation of my testimony to suggest that "there are numerous unknowns regarding Makower's device" that somehow undermine a person of ordinary skill in the art's expectations regarding Figure 5H misstates my testimony and Makower's teachings.

- With respect to the "tip" of Makower's device, I testified that I did not know what Makower himself "intend[ed]," but based on the disclosure, the "tip" is part of the shaft. Ex.2002-Bu-Saba-Tr., 279:16-280:4.
- With respect to the strut configuration, I testified that the electrodes are on struts, which is what Makower teaches in paragraph 187—I did not testify that

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issues that are out there." Ex.2002-Bu-Saba-Tr., 272:20-273:10. My answer was an acknowledgment that Makower discloses a number of devices, and I would need to review the disclosure about the other devices to provide a complete and accurate answer, which is made clear by the following question and answer omitted by PO in the POR. *See* Ex.2002-Bu-Saba-Tr., 273:11-18 ("Q Sitting here today, can you recall any figure in Makower besides Figure 5H that has electrodes that -- for a device that is inserted into a body cavity?...A Well, I have to go back and look at every figure now. Because I cannot recall every figure listed in the Makower.").

Makower's strut configuration is unknown. Ex.2002-Bu-Saba-Tr., 281:6-282:8.

- With respect to the tissue that Figure 5H can treat, I testified that from Figure 5H alone, the anatomical location is not specified. Ex.2002-Bu-Saba-Tr., 285:20-286:6. But as explained in detail in my First Declaration and this Reply Declaration, this is consistent with the fact that Makower specifically teaches that Figure 5H ablates tissue in the nasal cavity and nasopharynx. *E.g.*, Ex.1005-Makower, [0043], [0161], claims 1-2. That is, the drawing of unspecified tissue in Figure 5H is consistent with the disclosure of Makower that its devices could apply to multiple tissue locations.
- With respect to whether Figure 5H can treat tissue in the sinus, I explained that there are multiple sinuses, and Makower does not state which sinus may be treated. Ex.2002-Bu-Saba-Tr., 288:3-289:7. But independent of the sinus, Makower specifically teaches that its device can ablate tissue in the nasal cavity and nasopharynx as recited by the Challenged Claims. *E.g.*, Ex.1005-Makower, [0043], [0161], [0187], claims 1-2.
- With respect to how Makower's electrodes are energized, I testified that Makower does not discuss how the electrodes are energized, but Makower teaches that the devices use well-known components and a person of ordinary

skill in the art would understand that the electrodes are connected to a generator. Ex.2002-Bu-Saba-Tr., 290:2-291:9. Makower's teachings in this regard are consistent with the '675 patent. The '675 patent admits that generators that created energy for electroporation were well-known and commercially available. Ex.1001-USP675, 16:37-53. The '675 patent also assumes that a person of ordinary skill in the art would have understood how electrodes are energized, as it does not provide any implementation details regarding applying energy to electrodes, which is consistent with the fact that a person of ordinary skill in the art would have understood how to apply energy to electrodes.

- With respect to whether Figure 5H can apply energy to tissue via gas or plasma, I explained that these are topics outside my immediate area of expertise and these were not areas on which I conducted a further review of what would have been available to a person of ordinary skill in the art. Ex.2002-Bu-Saba-Tr., 297:11-298:12. But whether and how Figure 5H applies energy to tissue via gas or plasma is irrelevant, as Makower specifically teaches that ablation energy is applied to tissue adjacent to struts via electrodes, and the device is placed in the nasal cavity or nasopharynx to treat tissue. *E.g.*, Ex.1005-Makower, [0043], [0161], [0164], [0187], FIG.5H,

claims 1-2. Moreover, as detailed in my First Declaration, I have extensive experience with radiofrequency ablation devices (*e.g.*, Ex.1002-Decl., ¶7), and Makower's teachings with respect to electrodes are consistent with my expertise and experience.

The fact that Makower's inventors did not cite every detail does not detract from what Makower does clearly teach with respect to Figure 5H—Figure 5H is a radiofrequency device that applies ablation energy to tissue in the nasal cavity and nasopharynx. *E.g.*, Ex.1005-Makower, [0043], [0161], [0164], [0187], FIG.5H, claims 1-2. I do not understand Dr. Levine or Dr. Bikson to have identified any one of the details that is not included in Makower or that was addressed in my cited testimony to be relevant to the issues in this case. I have fully analyzed Makower in performing my analysis and while my declarations, analysis, and testimony have focused on Makower's teachings with respect to Figure 5H, none of the purportedly missing details identified by PO, Dr. Levine, or Dr. Bikson change or affect my opinions.

95. **Fourth**, in my First Declaration, I explained that "[a] person of ordinary skill in the art would have understood that Makower's electrosurgical device with electrodes to deliver RF energy would operate in a similar manner as Fang's generic catheter, particularly since Makower expressly states that the design of RF devices

was well-known to those skilled in the art." Ex.1002-Decl., ¶178. I disagree with Dr. Levine's contention (Ex.2003-Levine, ¶¶69-70) that those skilled in the art would not know how to operate Fang's SHP-I device, for the reasons below and in Section IX.B.

96. As explained in my First Declaration, a person of ordinary skill in the art would have found the Challenged Claims obvious based on (i) Makower's teachings regarding a radiofrequency ablation device that delivers ablation energy to tissue in the nasal cavity or nasopharynx via bipolar electrodes and (ii) Fang's teachings—which were consistent with multiple references and what was known in the art—that ablating nerves in the nasal cavity or nasopharynx reduced the symptoms of rhinitis (e.g., mucus production and congestion). *E.g.*, Ex.1002-Decl., ¶¶170-171, 177-179. For reasonable expectation of success, I explained that Fang taught the relevant details regarding the generic ablation device that was used to perform the disclosed ablation procedures. Ex.1006-Fang, 876-877; Ex.1002-Decl., ¶178. In particular, Fang explains that the ablation procedures were performed

"[u]nder nasal endoscopy"[29] using a "SHP-I five-organ radiofrequency therapy instrument (manufactured by Guangzhou Medical Instrument Factory)" "with the Level 3 intensity selected."[30] Ex.1006-Fang, 876. Fang explains that the "firing head [was] aligned with the sphenopalatine foramen on both sides, to carry out radiofrequency," and, given Fang's teaching of the application of radiofrequency energy, a person of ordinary skill in the art would have understood that the firing

[29] Nasal endoscopy is a common procedure where a physician performs a procedure using an endoscope to visualize the nasal cavity, the nasopharynx, and potentially the paranasal sinuses. I have performed thousands of nasal endoscopy procedures throughout my career, including before 2006.

[30] Although I have not personally used Fang's SHP-I five-organ radiofrequency therapy instrument (manufactured by Guangzhou Medical Instrument Factory), because Fang teaches those of ordinary skill in the art regarding the effect of radiofrequency ablation generally, not as specific to the particular radiofrequency device being used, my opinion about what Fang teaches and what a person of ordinary skill in the art would have expected regarding its teachings, remains unchanged.

head included electrodes to deliver the radiofrequency energy. Ex.1006-Fang, 876; Ex.1002-Decl., ¶¶163, 178.

97. As I explained in my First Declaration, Makower's Figure 5H electrosurgical device has the same relevant features—it is a radiofrequency ablation device that includes electrodes that deliver radiofrequency energy to tissue in the nasal cavity or nasopharynx. Ex.1005-Makower, [0043], [0161], [0164], [0187], FIG.5H. As a result, because Makower's device has the same relevant features as Fang's generic device, a person of ordinary skill in the art would have reasonably expected that Makower's device would achieve Fang's results when applying ablation energy to tissue in the nasal cavity or nasopharynx.

98. Indeed, Fang's teachings are consistent with numerous references that I included in my First Declaration that teach that ablating parasympathetic nerves, even with various forms of ablation such as radiofrequency ablation or cryotherapy, treats rhinitis symptoms. *See* Ex.1044-Chen, 240 ("The use of radiofrequency thermocoagulation of the posterior inferior nasal nerve, anterior ethmoidal nerves, and inferior turbinate…can widely block the source of the parasympathetic nerves in the nasal cavity and reduce the excitability of the parasympathetic nerves [to eliminate symptoms such as nasal congestion and runny nose]."); Ex.1043-Kong, 214-215 (using "radiofrequency ablation" to treat "perennial allergic rhinitis");

Ex.1045-Liang,4 341-342 ("The increased activity of the parasympathetic nervous system in the nasal cavity is an important factor in the onset of allergic rhinitis. From October 1996 to September 1997, we used radiofrequency hyperthermia devices under nasal endoscopy to treat 88 cases of ethmoidal nerve with allergic rhinitis by thermocoagulation. After 1 year of follow-up, the therapeutic effect was significant."); Ex.1054-Arora, 80 ("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.1002-Decl., ¶46 (discussing Fang, Chen, Kong, Liang, and Arora). Dr. Levine does not address Chen, Kong, Liang, or Arora in his declaration, and he agrees—consistent with my opinions—that the role of nerves for mucus production was known before the '675 patent. Ex.1089-Levine-Tr., 197:7-12 ("Q You would agree with me that the role of nerve cells in mucus production causing rhinitis symptoms was known before The Foundry patents?...A Yes."). Thus, Fang's teachings are consistent with what was known in the art, and as a result, a person of ordinary skill in the art would have reasonably expected that Makower's device would achieve Fang's results when applying ablation energy to tissue in the nasal cavity or nasopharynx.

99. **Last**, I understand that PO suggests that there is not evidence that Makower Figure 5H could be used in the locations Fang teaches. I disagree.

Makower specifically teaches that the "electrosurgical device 208 [shown in Figure 5H] compris[es] a flexible shaft 210 (e.g., a catheter or solid shaft) having arched strut members 214 attached thereto," and "the strut members may be of fixed configuration and in other cases the strut members 214 may be collapsible and expandable." Ex.1005-Makower, [0187]. A person of ordinary skill in the art would have understood, as a result and consistent with Makower's teaching that Figure 5H could be used throughout the nasal cavity and nasopharynx, that Makower's device could be used to treat tissue throughout the nasal cavity and nasopharynx. In this regard, I note that Dr. Levine and I agree, consistent with Fang's teaching, that administration of radiofrequency ablation was known to be possible in the nasal cavity and nasopharynx. *See* Ex.1089-Levine-Tr., 48:7-14, 54:3-10; Ex.1006-Fang, 876-877. Makower's flexible, collapsable device would reasonably be expected to be able to do the same.

100. In addition, and as discussed above, my testimony that Figure 5H does not depict a specific location in the nose, Ex-2002-Bu-Saba-Tr., 285:20-286:6, was in acknowledgement, as explained in detail in my First Declaration and this Reply Declaration, that Makower teaches that Figure 5H ablates tissue in multiple anatomical locations, including the "nasal cavity, meatus, ostium, interior of a sinus,

etc." or the "nasopharynx or middle ear to perform diagnostic or therapeutic procedures. *E.g.*, Ex.1005-Makower, [0043], [0161], [0187]. claims 1-2.

101. Therefore, Makower specifically teaches that its device can apply energy to tissue in the nasal cavity and nasopharynx, i.e., the same location taught by Fang. Ex.1006-Fang, 876-877; Ex.1002-Decl., ¶¶177-179.

102. In conclusion and as explained in my First Declaration and above, a person of ordinary skill in the art would have had a reasonable expectation Makower's Figure 5H device would successfully treat rhinitis as taught by Fang.

B. A Person of Ordinary Skill in the Art Would Have Been Motivated to Combine Makower and Fang

103. I understand that Dr. Levine[31] offers opinions that a person of ordinary skill in the art would not have been motivated to combine Makower and Fang. Ex.2003-Levine, ¶¶61-98. For the reasons detailed below, I disagree with Dr. Levine's opinions.

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[31] Dr. Bikson's declaration is relied on by Dr. Levine to opine that a person of ordinary skill in the art would not have been motivated to combine Makower and Fang. *E.g.*, Ex.2003-Levine, ¶94. I also address any of Dr. Bikson's arguments relevant to the motivation to combine Makower and Fang here.

1. A Person of Ordinary Skill in the Art Would Have Considered Fang

104. In my First Declaration, I explained that Fang teaches applying radiofrequency energy to tissue in the nasal cavity and that doing so alters the activity of parasympathetic nerves in such tissue to treat rhinitis. *E.g.*, Ex.1002-Decl., ¶¶153, 157-159, 163, 172-174. Dr. Levine contends that Fang's teachings are inconclusive.[32] Ex.2003-Levine, ¶¶65-76. I disagree.

105. Contrary to Dr. Levine's suggestion, Fang's taught those of ordinary skill in the art its conclusions. Fang compared one patient group that received radiofrequency ablation of the parasympathetic nerves in the nasal cavity to another group that did not receive radiofrequency ablation of the parasympathetic nerves in the nasal cavity. Ex.1006-Fang, 876-877. As discussed in Section IX.A, Fang explains that the ablation procedures were performed "[u]nder nasal endoscopy" using a "SHP-I five-organ radiofrequency therapy instrument (manufactured by Guangzhou Medical Instrument Factory)" "with the Level 3 intensity selected," and a person of ordinary skill in the art would have understood that the firing head

[32] Dr. Bikson does not offer any opinions on the substance of Fang's teachings. *See* Ex.2005-Bikson.

included electrodes to deliver the radiofrequency energy. Ex.1006-Fang, 876; Ex.1002-Decl., ¶¶157-159, 178. Fang also specifically explains where the radiofrequency energy was applied. Ex.1006-Fang, 876. It explains that the "firing head [was] aligned with the sphenopalatine foramen on both sides, to carry out radiofrequency…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…." Ex.1006-Fang, 876. Fang thus teaches that the locations where radiofrequency ablation energy was applied are locations where parasympathetic nerves that control mucus production are located (*see* Ex.1002-Decl., ¶¶32-33), and Dr. Levine does not contend otherwise. As discussed below, this anatomical teaching is consistent with multiple other references in the prior art and the '675 patent itself. *See* Ex.1044-Chen, 240; Ex.1043-Kong, 214-215; Ex.1045-Liang,4 341-342; Ex.1054-Arora, 80; Ex.1002-Decl., ¶46 (discussing Fang, Chen, Kong, Liang, and Arora); *see also* Ex.1051-Windsor, 284; Ex.1052-Fenton, 23; Ex.1107-Levine-Article, 451; Ex.1001-USP675, 1:60-2:46, 3:25-49.

106. Fang also teaches why the group that received radiofrequency ablation saw their rhinitis condition treated: "[t]he use of radiofrequency technique completely blocks the parasympathetic pathway of the nasal mucosa," which "reduces glandular secretion, and thus achieves the therapeutic purposes" of treating

"perennial allergic rhinitis." Ex.1006-Fang, 876-877. That is, Fang teaches that ablating parasympathetic nerves in the nasal cavity treats rhinitis because it blocks such nerves. *See, e.g.*, Ex.1002-Decl., ¶¶163, 170-176. Moreover, Fang specifically stated that the group that received radiofrequency ablation had a "statistically significant" improvement as compared to the control group that did not receive ablation, which further demonstrates that Fang teaches that radiofrequency ablation in the nasal cavity or nasopharynx treats rhinitis. Ex.1006-Fang, 876-877. A person of ordinary skill in the art would have understood these conclusions, which, as discussed in my First Declaration, would have contributed to their reasonable expectation of success. Ex.1002-Decl., ¶¶177-179.

107. Dr. Levine does not suggest that Fang's ultimate conclusion that ablating parasympathetic nerves in the nasal cavity or nasopharynx to treat rhinitis is inaccurate. *See generally* Ex.2003-Levine, ¶¶65-76. Any such suggestion would be incorrect—as noted above in Section IX.A, Fang's teachings are consistent with numerous references that I included in my First Declaration that teach that ablating parasympathetic nerves, even with various forms of ablation such as radiofrequency ablation or cryotherapy, treats rhinitis. *See* Ex.1044-Chen, 240; Ex.1043-Kong, 214-215; Ex.1045-Liang, 341-342; Ex.1054-Arora, 80; Ex.1002-Decl., ¶46 (discussing Fang, Chen, Kong, Liang, and Arora); *see also* Ex.1051-Windsor, 284 ("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…."); Ex.1052-Fenton, 23 ("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."). Dr. Levine does not address these references—Chen, Kong, Liang, Arora, Windsor, or Fenton—in his declaration. As also noted above, Dr. Levine agrees that the role of nerves for mucus production was known before the '675 patent. Ex.1089-Levine-Tr., 197:7-12 ("Q You would agree with me that the role of nerve cells in mucus production causing rhinitis symptoms was known before The Foundry patents?...A Yes."). Dr. Levine's own writings (described in more detail in Section IX.B.3) have also explained that applying energy via a laser to nasal tissue "decreases the number of goblet-secreting cells and the autonomic innervation of the turbinate" and "reduces secretion." Ex.1107-Levine-Article, 453.

108. Fang is also consistent with the '675 patent. The '675 patent indicates that it was known in the prior art that "neurotoxins (BoNTs) block the release of acetylcholine from peripheral cholinergic nerve endings thereby disabling the release of neurotransmitters from the cells." *See* Ex.1001-USP675, 1:60-2:46. With

respect to rhinitis, the '675 patent states that it was known that "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…." Ex.1001-USP675, 3:25-49. That is, the '675 patent indicates that it was known in the prior art that neurotoxins can block the relevant cells in the nasal cavity to treat rhinitis. Ex.1001-USP675, 1:60-2:46, 3:25-49. Dr. Levine agrees that it was known prior to the '675 patent that neurotoxins reduce the symptoms of rhinitis. Ex.1089-Levine-Tr., 199:5-8 ("Q And so Dr. Sanders had already used neurotoxin in the nose to reduce mucus secretion before the Foundry patents? A Yes."). 199:12-15 ("Q So Dr. Sanders had already used neurotoxin in the nose to treat rhinitis before The Foundry patents? A Yes."). There is nothing in Fang that is contrary to what was known in the art or any suggestion in Fang that radiofrequency ablation would not help treat rhinitis. *See generally*, Ex.1006-Fang. Thus, Fang's teachings are consistent with multiple references (which Dr. Levine does not dispute) and the '675 patent itself, and as explained in my First Declaration, a person of ordinary skill in the art would have been motivated to apply Fang's clear teaching regarding the known outcome of applying RF energy in the nasal cavity with Makower's electrosurgical device and methods.

109. Dr. Levine also contends that a person of ordinary skill in the art would not have been motivated to consider Fang because it does not provide "conclusive proof that RF energy alone was responsible for the improvement in perennial allergic rhinitis." Ex.2003-Levine, ¶71.[33] I disagree.

110. As an initial matter, Dr. Levine's opinions that the '675 patent provides written description for priority are inconsistent with his opinions that Fang's disclosure is somehow insufficient. Although Dr. Levine cites a single parenthetical regarding non-reversible poration as providing written description support for claims directed to treatment, the '675 patent does not include any data or discussion on the effects of non-reversible poration to any tissue (*see generally* Ex.1001-USP675), and Dr. Levine agrees that the '675 patent does not include any data on the effects of non-reversible poration to any tissue. Ex.1089-Levine-Tr., 185:22-186:7 ("Q Okay. Do the patents provide any data regarding the use of irreversible electroporation energy without the use of neurotoxins? A They do not."). The '675 patent also does not include any data or discussion on the effects of RF ablation

[33] I understand from counsel that a prior art reference must be viewed in the context of what was generally known in the art at the time of the invention and be considered for all that it teaches.

alone. *See generally* Ex.1001-USP675. In contrast, and unlike the '675 patent, Fang specifically explains that the application of radiofrequency energy to tissue in the nasal cavity treats rhinitis and how it does so—by completely blocking the "parasympathetic pathway of the nasal mucosa," which "reduces glandular secretion, and thus achieves the therapeutic purposes" of treating "perennial allergic rhinitis." Ex.1006-Fang, 876-877. Fang thus provides significantly more description than the '675 patent, and would have motivated a person of ordinary skill to apply its teachings.

111. Additionally, the challenged claims at issue do not require any efficacy measure or particular degree of efficacy, and the '675 patent does not describe any such efficacy measures or requirements for treating rhinitis. *See generally* Ex.1001-USP675. Dr. Levine agrees that the '675 patent does not describe any efficacy requirements. Ex.1089-Levine-Tr., 184:21-185:7 ("[The Foundry patents] don't define any efficacy requirements for the treatment of rhinitis? A Not any parameters or requirements but that it is treated."), 185:8-186:2. Nor do the claims of the '675 patent require achieving any particular degree of treatment. *See, e.g.*, Ex.1001-USP675, claims 1, 17. Dr. Levine's contention that a person of ordinary skill in the art would have only been motivated to consider Fang if it provided "conclusive proof" is inconsistent with the fact that the '675 does not describe or claim specific

degrees of efficacy and my understanding that for obviousness, a person of ordinary skill in the art need only have had a reasonable expectation of success with the challenged claims.

112. Dr. Levine further contends that Fang is "inconclusive" because "Fang does not disclose to a POSITA the "'diagnostic criteria for perennial rhinitis' that it used in its study." Ex.2003-Levine, ¶66. I disagree. A person of ordinary skill in the art would have been familiar with the diagnostic criteria for perennial rhinitis prior to 2006, which included evaluating the patient's symptoms, evaluating the patient's history, and performing allergy tests. Indeed, Dr. Levine testified at his deposition that the diagnostic criteria for rhinitis included evaluating the patient's symptoms, evaluating the patient's history, and performing allergy tests. Ex.1089-Levine-Tr., 96:13-101:8, 104:11-22.

113. The diagnostic criteria that were known in the art prior to 2006, and recognized by Dr. Levine, are consistent with the diagnostic criteria set forth in the document cited in Fang's footnote 1—Haikou.[34] *See* Ex.1006-Fang, 876-877 (citing "Otolaryngology Society of Chinese Medical Association, Editorial Committee of

[34] See Ex.1114 (translation declaration for Haikou).

Chinese Journal of Otolaryngology. Diagnostic Criteria and Efficacy Evaluation Criteria for Allergic Rhinitis (revised in 1997, Haikou) [J]. Chinese Journal of Otolaryngology, 1998, 33:134-135"); Ex.1113-Haikou. As shown in the below, Haikou teaches diagnostic criteria—evaluating the patient's symptoms, evaluating the patient's history, and performing allergy tests—that were fully consistent with what Dr. Levine and others used in the art prior to 2006.

Diagnostic Criteria Recognized by Dr. Levine	Haikou (Ex.1113)
"Q So what symptoms would you be looking for in the patient's history? A They would be things of **nasal obstruction, nasal congestion, secretions, various triggers, were there foods, were there environmental factors that were present, were there exposure to animals, industrial factors**. Where they're working, occupational, things of that kind. Or, if those were negative, I go further, because I mention there's these nonallergic rhinitis or what we call vasomotor rhinitis. There are -- we don't have itchy eyes, itchy nose, watery eyes, sneezing fits, sometimes asthma, wheezing, that is associated with the allergic." Ex.1089-Levine-Tr., 99:7-101:8. ""Q All right. So thinking about the Snot 20, I'm not familiar with those, so	"Scoring conditions: ① perennial onset, with three primary clinical manifestations: sneezing (more than 3 consecutive times), runny nose, and nasal mucosa swelling; the cumulative number of onset days in one year exceeds 6 months, and the cumulative onset time in one day exceeds 0.5 hours; ② the course of disease lasts at least one year." Ex.1113-Haikou, 134. "Scoring criteria: clear sign of inhaled allergens, personal and/or family history of allergic diseases, and typical signs and symptoms during onset[.]" Ex.1113-Haikou, 134.

Diagnostic Criteria Recognized by Dr. Levine	Haikou (Ex.1113)
can you walk me through what some of those are. A Yeah. And I can't give you all of them off the top of my head. But they would be things like **nasal obstruction, nasal drainage, breathing, sleep issues because of nasal obstruction, snoring**. There's a whole host of these things, easily found on -- you can easily find what that document is. I don't have that off the top of my head right now." Ex.1089-Levine-Tr., 104:11-22.	
"A If I suspected or was unsure of the cause, **I would typically send the patient to an allergist**. I am not an allergist. don't practice allergy. I do give medication to treat some patients for allergic rhinitis. **But I would send them to an allergist and some allergists would do skin testing. Some allergists would do a scratch testing on the back. I mean, a whole host of things**." Ex.1089-Levine-Tr., 97:8-16. "Q What's an **IGE** panel? A **It is a group of blood tests where they are looking at various immune factors within the blood to determine is there allergic rhinitis or not**. Q So that could be relevant for determining if there is rhinitis? A But I never ordered it. But other physicians that I sent patients to did.	"Scoring criteria: … positive specific IgE antibody test or positive nasal allergen challenge (NAC) test, and consistent with skin test and medical history[.]" Ex.1113-Haikou, 134.

Diagnostic Criteria Recognized by Dr. Levine	Haikou (Ex.1113)
Q **But the results of that IGE could be relevant to your rhinitis diagnosis**? A **The interpretation of those results by someone skilled who knows allergy would be something I would look at, their opinion**." Ex.1089-Levine-Tr., 97:22-98:15	

Haikou also references evaluation of "eosinophils on the nasal secretion smear and/or mast cells (basophils) on nasal mucosa smear." Ex.1113-Haikou, 134. Eosinophils are a type of white blood cells that may indicate a patient has rhinitis, and mast cells are another type of white blood cells that may indicate a patient has rhinitis. Analyzing the presence of these white blood cells when evaluating rhinitis was also known prior to 2006.

114. Haikou's efficacy criteria were consistent with other criteria used in the art prior to 2006. *See* Ex.1113-Haikou, 134. To evaluate the efficacy of treatment, those skilled in the art would evaluate whether a patient's symptoms improved by analyzing the same symptoms and physical examination (e.g., nasal endoscopy findings). Indeed, Dr. Levine agreed that to evaluate whether a treatment is effective, a physician would analyze a patient's symptoms and analyze the patient's nose, including evaluating whether there is "less swelling within the nasal cavity, swelling and obstruction from the tissue." Ex.1089-Levine-Tr., 101:17-102:10.

Haikou's teachings are consistent with what was known in the art—to evaluate the efficacy of the treatment, Haikou taught performing the same analysis and comparing the patient's score before treatment with the patient's score after treatment. *See* Ex.1113-Haikou, 134-135.

115. Therefore, I disagree with Dr. Levine's opinion that a person of ordinary skill in the art would have found Fang's results "inconclusive" based on its incorporation of criteria from Haikou. Haikou's criteria, which Fang's references in its note 1, are consistent with what was used in the art prior to 2006. They support that the conclusions Fang reached that ablating parasympathetic nerves in the nasal cavity and nasopharynx treated the symptoms of rhinitis (e.g., mucus secretion and congestion), were evaluated through appropriate efficacy criteria.

116. Dr. Levine additionally contends that Fang is "inconclusive" because Fang's study performed additional procedures besides radiofrequency ablation. Ex.2003-Levine, ¶72. I disagree with Dr. Levine's contention. A person of ordinary skill in the art would have understood that it was common to treat a patient for multiple conditions at the same time, and Fang's additional procedures were directed to additional pathologies, and would have read and considered (and not discounted) Fang's attribution of results in terms of treating rhinitis to radiofrequency ablation in considering a motivation to combine and a reasonable expectation of success.

117. Prior to 2006 (and through today), it was common for physicians to treat a patient for multiple nasal, sinus, or other conditions at the same time. For example, a patient may have a deviated septum (cartilage and bone that divides the nasal passages is shifted to one side) and polyps (non-cancerous growths in the nasal passage), and although each of these conditions are different, they could be treated during the same overall procedure via different techniques. Combining multiple treatments in one procedure is often more efficient, as it reduces the number of times that a patient is required to come to a physician's office or a hospital for treatment and be prepared for the procedures. Dr. Levine agrees that multiple procedures could be performed concurrently to treat different pathologies because doing so is more efficient. Ex.1089-Levine-Tr., 89:12-91:8, 91:19-92:7; *see also id.* 76:10-80:19.

118. With respect to Fang, the additional procedures referenced by Fang treat additional pathologies. Fang specifically states that "[f]urther 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." Ex.1006-Fang, 876. A person of ordinary skill in the art would have understood that these procedures were directed to treating conditions in different ways than treating

rhinitis. For example, a person of ordinary skill in the art would have understood that "submucosal resection of the nasal septum" is a procedure for treating a deviated septum. This is a procedure I have performed numerous times throughout my career, including before 2006. As another example, a person of ordinary skill in the art would have understood that "nasal polypectomy" is a procedure for removing nasal polyps (non-cancerous growths in the nasal passage). This is also a procedure I have performed numerous times throughout my career, including before 2006. As noted above, these are procedures that could be performed simultaneously, and separately from specifically treating rhinitis.

119. Fang's authors were the physicians and clinicians performing the procedures and observing the results of the procedures and, despite performing multiple procedures on individual patients as detailed, attributed specific results to radiofrequency ablation based on their observation. A person of ordinary skill in the art would have credited Fang's attribution, which would have contributed to their motivation and reasonable expectation that a similar radiofrequency electrode device from Makower would deliver similar results.

120. A person of ordinary skill in the art would have read Fang in the context of the prior art, and would have understood that Fang—consistent with the prior art—teaches that applying radiofrequency ablation to tissue in the nasal cavity treats

rhinitis. This would have motivated a person of ordinary skill in the art to consider Fang's teachings and apply them in implementing Makower with a reasonable expectation of success.

121. Moreover, I understand that Patent Owner identifies that Fang was only cited by Hytönen (Ex.1112). POR, 48. Even if that were accurate, that would not affect my opinions regarding Fang. I understand that Fang is available as prior art for all that it teaches, irrespective of how often it was cited by others. As discussed above, its teachings are consistent with multiple other references in the prior art and the '675 patent's admissions regarding the scope of the prior art.

122. Moreover, I have reviewed Hytönen (which Dr. Levine does not appear to have considered and I understand Patent Owner did not submit as an exhibit in this proceeding) and it confirms my opinions that a person of ordinary skill in the art would have been motivated to consider and combine Fang. Hytönen is a review article published in 2009 that reflects the state of the art prior to that point. Ex.1112-Hytönen, 1257. It cites Fang's study favorably, detailing that it—like multiple other studies—"showed a statistically significant effect on allergic rhinitis symptoms." Ex.1112- Hytönen, 1261. It also described that "[r]adiofrequency ablation…has gained increasing popularity in the treatment of...nasal obsruction secondary to non-allergic or allergic rhinitis" among other disorders and symptoms. Ex.1112-

Hytönen, 1257. It reports that radiofrequency ablation "may...decrease subjective symptoms and nasal blockage." Ex.1112- Hytönen, 1264. Hytönen then confirms, consistent with my opinions, that results from studies like Fang contributed to a motivation to perform even further testing in additional trials. Ex.1112- Hytönen, 1264-1265.

123. Accordingly, I disagree with Dr. Levine that a person of ordinary skill in the art would have found Fang "inconclusive," and particularly in a way that they would have meant that they would not have been motivated to considered Fang at all, particularly in view of Fang's plain teaching that applying radiofrequency ablation to tissue in the nasal cavity treats rhinitis, consistent with extensive other prior art and the '675 patent's description of the prior art. Ex.1006-Fang, 876-877.

2. A Person of Ordinary Skill in the Art Would Have Considered Makower

124. In my First Declaration (and in Section IX.A), I explained that Makower teaches a radiofrequency device for treating nasal conditions. Ex.1005-Makower, [0001], [0043], [0160]-[0161], [0187], FIG.5H; *see also e.g.*, Ex.1002-Decl., ¶¶152, 156, 162. I also explained that Makower teaches that its radiofrequency device includes multiple bipolar electrodes for delivering energy to tissue in the nasal cavity or nasopharynx. Ex.1005-Makower, [0001], [0043],

[0160]-[0161], [0164], [0187], FIG.5H, claims 1-2; *see also e.g.*, Ex.1002-Decl., ¶¶152, 156, 162. Dr. Levine contends that Makower is directed to "flexible catheters" and that, as a consequence, a person of ordinary skill in the art would not have considered Makower's working device with electrodes (Figure 5H). Ex.2003-Levine, ¶¶77-85. I disagree.

125. As I explained in Section IX.A, Makower describes the working devices for treating nasal disorders—such as Figure 5H—as part of its "present invention" and separate from "the catheters used to deliver them." Ex.1005-Makower, [0001], [0043], [0161]-[0162], [0164], [0187]. Makower also claims "working devices" that do not recite flexible catheters. Ex.1005-Makower, claims 1-2. Thus, as described in Section IX.A, Makower is not limited to, and a person of ordinary skill would not have only considered, its "flexible catheters" as Dr. Levine contends. A person of ordinary skill in the art would have considered Makower, which is in the same field as the claims of the '675 patent and is reasonably pertinent to solving the problems allegedly addressed by those claims, for its Figure 5H electrode device for ablating tissue in the nasal cavity/nasopharynx, even though Makower also teaches flexible catheters.

3. A Person of Ordinary Skill in the Art Would Have Been Motivated to Combine Makower and Fang

126. In my First Declaration, I also explained why person of ordinary skill in the art would have been motivated to apply Fang's teaching of disrupting neural activity using ablation with Makower's device and method (applying energy in the nasal cavity) to reduce the symptoms of rhinitis (e.g., mucus production and congestion). Ex.1002-Decl., ¶¶170-176. Dr. Levine opines that a person of ordinary skill in the art "would not have been motivated to combine Makower with Fang." Ex.2003-Levine, ¶¶86-98. I disagree.

127. **First**, I did not use "hindsight" in my obviousness analysis as Dr. Levine suggests. Ex.2003-Levine, ¶27 ("[I]t is only with hindsight that a POSITA would have considered Makower even tangentially pertinent to the '675 patent."). As an initial matter, as I reflected in the legal principles section of the First Declaration, I understood and understand that "in considering obviousness, it is important not to determine obviousness using the benefit of hindsight derived from the patent being considered," and so considered and offered my opinions in accordance with this principle. Ex.1002-Decl., ¶¶18, 24. To be clear, my opinions in my First Declaration and this Reply Declaration do not use hindsight.

128. As explained in my First Declaration, Makower and Fang "are in the same field as the claims of the '675 patent and are reasonably pertinent to solving the problems addressed by the claims of the '675 patent." Ex.1002-Decl., ¶169. Dr. Levine does not disagree with this opinion. It remains accurate, and confirms that a person of ordinary skill in the art would have considered both Makower and Fang.

129. My First Declaration also explained in detail why a person of ordinary skill in the art considering treatments for nasal disorders would look to Makower's Figure 5H device. For example, I explained that "Makower expressly teaches that its device treats a nasal disorder" and that "its device applies energy to the nasal cavity and nasopharynx using electrodes, the same mechanism as Fang." Ex.1002-Decl., ¶170. Makower also specifically teaches that its "present invention provides a comprehensive system of devices and associated methods for diagnosing and treating disorders of the ears, nose and throat in a ***less invasive fashion than current day approaches***." Ex.1005-Makower, [0132]. That is, Makower teaches that its disclosed devices and methods—including Figure 5H—are "less invasive" than previously known devices and methods. As a result, a person of ordinary skill in the art would have looked to Makower's less invasive Figure 5H device that treats nasal conditions and understood that Fang simply clarifies that Makower's device

achieves the same therapeutic effect in the same manner as claimed in the '675 patent.

130. My opinions are grounded in Makower and Fang's teachings and what a person of ordinary skill in the art would have understood as of 2006, not on hindsight. I confirmed this by, among other things, citing the prior art references that support my opinion throughout my declaration. I note that, in contrast, Dr. Levine and Dr. Bikson cite no additional references outside of the references in the Grounds and my deposition testimony in support of their opinions regarding motivation to combine and reasonable expectation of success, including no references that suggest that there would have been skepticism, failure, or teaching away in the prior art.

131. **Second**, Dr. Levine contends that "Makower's FIG. 5H device is described as a 'tissue shrinking device,' (Ex-1005-Makower at [0092]), which a POSITA would have understood is used to shrink mechanical obstructions in the nasal cavity using energy," and that "[t]here are significant and important differences between the treatment of mechanical obstructions and the treatment of excess mucus caused by the nerves." Ex.2003-Levine, ¶¶87, 45-49. Dr. Levine concludes based on this distinction that a person of ordinary skill therefore would not have been

motivated to combine the device Makower teaches with Fang's teachings. Ex.2003-Levine, ¶¶87, 45-49. I disagree.

132. Makower describes an RF ablation device and never states such device (or its other devices) are limited to removing nasal obstructions. Makower explains that Figure 5H is "a tissue shrinking electrode device being used in accordance with the ***present invention***," and includes multiple bipolar electrodes that deliver ablation energy to tissue. Ex.1005-Makower, [0092], [0161], [0164], [0187], FIG.5H. Makower specifically explains that the "designs and constructions" of Figure 5H's components and assemblies were "w[e]ll known in the art," and "[f]urther aspects, details and embodiments of the present invention will be understood by those of skill in the art…." Ex.1005-Makower, [0046], [0164]. Because Makower specifically states that the goal of its "***present invention***" "provides methods, devices and systems for diagnosing and/or treating sinusitis or other conditions of the ear, nose or throat," including in the "nasal cavity" and "nasopharynx" (Ex.1005-Makower, [0001], [0043], [0046], [0164]), a person of ordinary skill in the art would have been motivated to look to combine Makower's teachings with other teachings such as Fang's that explain the effect ablation would have in the nasal cavity and nasopharynx to achieve Makower's stated goal.

133. I also disagree with Dr. Levine that "the treatment of mechanical obstructions" is entirely unrelated to treating the symptoms of rhinitis. Ex.2003-Levine, ¶¶45-49. Prior to 2006, it was known that the symptoms of rhinitis not only include mucus production and congestion (rhinorrhea), but also include nasal blockages (i.e., obstructions). Indeed, when evaluating patients for rhinitis prior to 2006 (and through today), one of the symptoms that I evaluated for rhinitis (and taught others to evaluate for rhinitis) was whether there were any nasal blockages among other symptoms.

134. Dr. Levine's own writings confirm my opinion. Dr. Levine authored a paper that was published in the "Advances in Sinus and Nasal Surgery" in 2007 titled "Lasers in Endonasal Surgery." Ex.1107-Levine-Article, 451. I note that lasers are an alternative form of energy to radiofrequency ablation, as recognized by Makower. Ex.1005-Makower, [0039] ("the surgeon may elect to perform a laser or radiofrequency procedure designed to create a coagulative lesion"). In his paper, Dr. Levine discusses "turbinate dysfunction," i.e., enlarged and disformed turbinates. Ex.1107-Levine-Article, 453. In the "turbinate dysfunction" section, Dr. Levine explains that "laser photocoagulation" is a treatment option for ***rhinitis***, and the specific laser treatment that he evaluated involved applying laser treatment "at 12 watts and 0.1 second at weekly intervals for 5 weeks to reduce the turbinate."

Ex.1107-Levine-Article, 453. That is, Dr. Levine's writing confirms that reducing turbinates is relevant to treating rhinitis. With respect to addressing specific symptoms, Dr. Levine's writing also states the effect of the laser treatment—"[t]he laser probably decreases the number of goblet-secreting cells and the autonomic innervation of the turbinate" and "[t]he laser improves the airway and reduces secretions in most instances." Ex.1107-Levine-Article, 453. In other words, the laser ablation that Dr. Levine indicated treats rhinitis would have reasonably been understood to reduce secretions (e.g. mucus production). Dr. Levine's writing is therefore consistent with what was known in the art—applying energy to tissue in the nose decreases "the autonomic innervation of the turbinate" (i.e., blocks the parasympathetic nerves) and reduces mucus secretion. As a result, contrary to Dr. Levine's opinions in this case, but consistent with his own writing, reducing tissue is relevant to treating rhinitis, and a person of ordinary skill in the art would have looked to Fang to explain the effects of applying radiofrequency ablation energy in the nasal cavity and nasopharynx as taught by Makower.

135. **Third**, Dr. Levine contends that Makower's device "raise[s] serious safety and efficacy concerns if used according to Petitioner's proposed combination," and Dr. Levine and Dr. Bikson contend that Makower does not teach a device operable to treat tissue in the nasal cavity or nasopharynx. Ex.2003-Levine,

¶¶89-98; Ex.2005-Bikson, ¶¶57-72. As discussed above in Section IX.A, a person of ordinary skill in the art would have understood that Makower's device would successfully ablate tissue in the nasal cavity and would be able to be operated safely and effectively. Therefore, I disagree with Dr. Levine and Dr. Bikson that Makower is not operable and there are safety and efficacy concerns.

136. **Fourth**, Dr. Levine contends that "[a] POSITA also would not have looked to combine Makower with Fang because a POSITA would have understood that they have diametrically opposed objectives and treatment effects." Ex.2003-Levine, ¶87. More specifically, Dr. Levine contends that because Fang is directed to "treatment methods [that] always involves a destructive surgical procedure," it is inconsistent with Makower's ablation device. Ex.2003-Levine, ¶87. I disagree with Dr. Levine's analysis and conclusion. As explained in my First Declaration, Makower and Fang are each directed to treating tissue in the nasal cavity and nasopharynx by applying energy to tissue and teach devices for doing so. *E.g.*, Ex.1005-Makower, [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."), [0043], [0164], [0187]; Ex1006-Fang, 876-877 (using "radiofrequency" to treat tissue near the "sphenopalatine foramen"); Ex.1002-Decl.,

¶169. Thus, contrary to Dr. Levine's opinions, the two references have similar objectives.

137. Additionally, I disagree with Dr. Levine's suggestion that Makower teaches to not ever perform procedures that are destructive. Ex.2003-Levine, ¶¶87-88. Makower does teach that its device designs—including Figure 5H—have "flexible construction" that "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." Ex.1005-Makower, [0161]. But in that context, Makower is simply confirming, as a person of ordinary skill would readily understand, that trauma to non-targeted tissues is to be avoided if possible. Makower separately explains that procedures that can be destructive, including "cutting, ablating, debulking, cauterizing, heating, freezing, lasing, dilating or otherwise modifying tissue," Ex.1005-Makower, [0043], may be performed, including with the devices it teaches. Thus, Makower explains that ***undesired*** trauma is avoided by avoiding certain rigid instrumentation and instead using its disclosed devices (e.g., Figure 5H), not that a physician should never perform desired destructive procedures. Thus, I disagree with Dr. Levine's opinion

that Makower is limited to "flexible treatment devices that can be used in procedures 'with minimal trauma to other tissues.'" Ex.2003-Levine, ¶¶87-88.

138. I also disagree that Fang's teachings regarding additional procedures (beyond radiofrequency ablation) would somehow mean a person of ordinary skill in the art would not consider it for combination with Makower. Ex.2003-Levine, ¶¶87-88. While Fang indicates that patients in its study received "submucous resection of the nasal septum," a person of ordinary skill in the art would have understood that this treatment is directed to addressing a deviated septum. Ex.1006-Fang, 876. The procedure to correct a deviated septum is medically desirable treatment for treating a condition (deviated septum) that is fully consistent with and often performed with other procedures directed to improving rhinitis symptoms, such as RF ablation. As discussed above in Section IX.B.1, combining multiple procedures was (and remains) common, and Dr. Levine agrees that multiple procedures could be performed concurrently to treat different pathologies because doing so is more efficient. Ex.1089-Levine-Tr., 89:12-91:8, 91:19-92:7; *see also id.* 76:10-80:19. Thus, the fact that Fang explains that it treated patients for a deviated septum does not detract from its teaching that applying radiofrequency to the nasal cavity and nasopharynx that treated rhinitis or mean it has the opposite objective as Makower. *See* Section IX.B.1. Indeed, Makower does not teach away from

additional surgical procedures or surgical procedures that involve other modalities. Makower states that its devices will be used for surgical procedures that involve "cutting, ablating, debulking, cauterizing, heating, freezing, lasing, dilating or otherwise modifying tissue[.]" Ex.1005-Makower, [0043].

139. **Fifth**, although Dr. Levine and Dr. Bikson do not offer this opinion I understand that Patent Owner argues that Makower's Figure 5H device would result in "undesirable energy delivery to the targeted and surrounding tissue." POR, 56-59. I disagree that a person of ordinary skill in the art would read Makower's teachings in this way. As I explained in my First Declaration, Makower's Figure 5H electrosurgical device utilizes bipolar electrodes. Ex.1005-Makower, [0187]; Ex.1002-Decl., ¶162. As also explained in my First Declaration, bipolar electrodes concentrate energy between the electrodes, as the radiofrequency current travels from one electrode to another. Ex.1002-Decl., ¶205; Ex.1009-Stern, 5:54-55, 13:11-20, FIG.17. Thus, the ablation energy applied by Makower's device to tissue in the nasal cavity or nasopharynx would be concentrated between the bipolar electrodes and into the contacted target tissue. A person of ordinary skill in the art would not have understood that Figure 5H would in practice deliver energy throughout the entire nasal cavity or nasopharynx.

140. As a matter of routine operation, a person of ordinary skill in the art applying the teachings of Makower would have understood that Makower teaches a device that would be positioned or configured in the nasal cavity or nasopharynx to treat the targeted nerves, not undesirable tissue, and that it could be positioned or configured to do so. For example, as discussed above in Section IX.A, physicians clean the nasal cavity and nasopharynx prior to procedures to ensure that the physician can visually see the treatment tissue and position the device. *E.g.*, Ex.1089-Levine-Tr., 81:21-82:22 (Dr. Levine explaining steps that he would perform prior to treatment for "visualization"). As a result, a physician, when using the device Makower teaches, would be able to position the device to target the parasympathetic nerves, not tissue that should not be ablated for a given patient in a given procedure.

141. As another example, even assuming that Figure 5H must only be oriented exactly as in the drawing and assuming it is contacting the nasal wall and septum as Dr. Levine contends, a person of ordinary skill in the art, as a matter of routine operation, could and would still operate the device taught by Figure 5H for its intended purpose. In that circumstance, a person of ordinary skill in the art would adjust the parameters of energy delivery to ensure that only the electrodes that are in contact with the lateral nasal wall where they want to apply energy are active so that

the target nerves receive ablation energy while minimizing the risk of delivering energy to undesired tissue. Indeed, as Dr. Levine recognized at his deposition, physicians knew how to adjust the parameters of energy delivery. Ex.1089-Levine-Tr., 74:9-75:17 (explaining that prior data "showed with different energy and time parameters the kind of creation of zone of injury that then would permit me as a clinician to be instructed as to how long, and what energy this would be used"); 123:1-10 ("Q It was your understanding at that time that clinicians would be able to garner an understanding of the energy dosage that they would need for their clinical applications? A Yes."), 123:11-124:3 ("Q Would a surgeon know how to calculate energy dosage at that time? A The piece of equipment was very user friendly. And it wasn't like you had to dial in a whole bunch of things, the energy was a certain energy, it was more the wavelength, and it was more the interface between the end of the laser fiber and the tissue."). Thus, a person of ordinary skill in the art would have understood how to use Makower's Figure 5H device to deliver energy via Figure 5H's bipolar electrodes to target nerves while minimizing the delivery of ablation energy to undesirable tissue.

142. To the extent there is any suggestion that Makower Figure 5H must ***always*** be used or positioned in a way that would apply ablation to undesirable tissue, I therefore disagree. A person of ordinary skill in the art would, as a matter of routine

operation, not operate the device taught by Figure 5H that way and would have been capable of operating it for its stated intended purpose.

143. **Finally**, although Dr. Levine and Dr. Bikson do not offer this opinion, I understand that Patent Owner argues that use of Makower's FIG. 5H device to implement Fang's method would risk perforating the nasal septum and that a person of ordinary skill would instead choose a different device from Makower. I disagree. As explained above in this section, a person of ordinary skill in the art would have understood, as a matter of routine operation, (i) how to position Makower's Figure 5H device to target the parasympathetic nerves, not tissue that should not be ablated for a given patient in a given procedure, and (ii) how to adjust the parameters of energy delivery to ensure that only the electrodes that are in contact with the lateral nasal wall are active so that the target nerves receive ablation energy while minimizing the risk of delivering energy to undesired tissue. In addition, as explained in my First Declaration and in this Reply Declaration, Figure 5H of Makower teaches a radiofrequency ablation device that applies ablation energy to tissue in the nasal cavity or nasopharynx, and Fang simplify clarifies that doing so as taught by Makower achieves the therapeutic effect of treating rhinitis (i.e., reducing mucus production and congestion). The fact that Makower discloses other,

additional, devices does not detract from Makower's teachings with respect to Figure 5H.

144. In conclusion, it is my opinion that a person of ordinary skill in the art would have had a motivation to combine Makower and Fang.

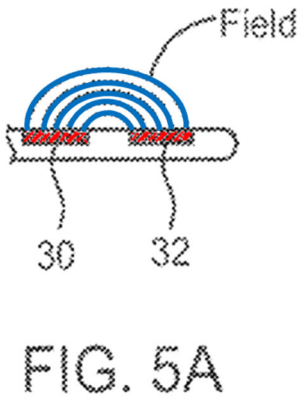
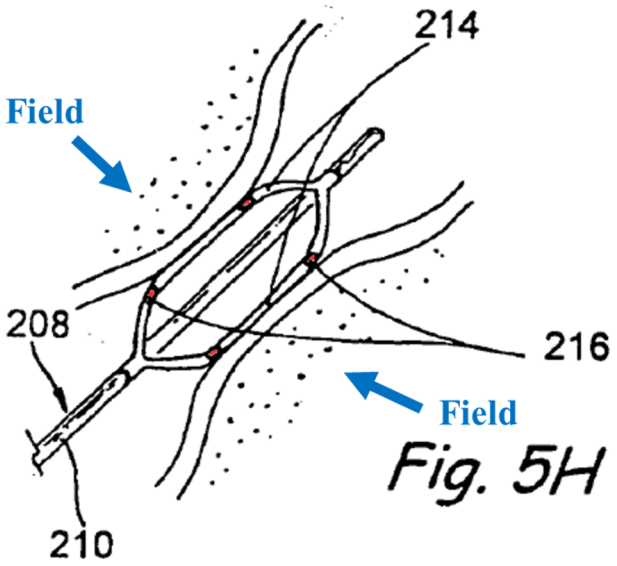
C. Claim 22: Makower Teaches Delivering Energy Laterally

145. The only dependent claim in Ground VI that Dr. Levine and Dr. Bikson contest is claim 22, which depends from independent claim 1 and recites that *the energy delivery element is configured to concentrate energy laterally relative to the distal portion of the treatment device*. Dr. Levine and Dr. Bikson contend that Makower does not disclose electrodes "configured to deliver energy laterally." Ex.2003-Levine, ¶¶102-111; Ex.2005-Bikson, ¶¶73-83. As detailed below, I disagree.

146. As explained in my First Declaration, Makower teaches that its electrosurgical device includes strut members 214 that include multiple "bipolar" radiofrequency electrodes 216 that deliver "current…causing tissue adjacent to the struts 214 to be cauterized or heated." Ex.1005-Makower, [0187]; Ex.1002-Decl., ¶205. It was well-known that bipolar electrodes are conductors and cause RF current to travel from one electrode to another. Ex.1009-Stern, 5:54-55, 13:11-20, FIG.17; Ex.1002-Decl., ¶205. Dr. Levine agrees that "bipolar" refers to energy that is

"transmitted between…two points." Ex.1089-Levine-Tr., 57:1-6 ("Q Can you tell me a little bit more about what a bipolar cautery device looks like? A It will be a device generating energy that will have two points. That's where the name bipolar comes from, where the energy will be transmitted between those two points."). Thus, as shown below and in my First Declaration, the concentration of current in Makower would be the same as the energy concentration depicted in the '675 patent in Figure 5A by similarly arranged electrodes (that is, it would create a field in the targeted tissue that is lateral to the body of the device). Ex.1001-USP675, 16:29-58 ("FIG. 5A depicts an arrangement of electrodes 30 and 32 that produces an electric field concentrated in a lateral direction from the catheter body…."), FIG.5A; Ex.1005-Makower, [0161], [0164], [0187], FIG.5H. [35]

[35] I cite Figure 5A (and Figures 5B and 6D) of the '675 patent as examples of the directions bipolar electrodes concentrate fields of energy, and specifically the fields they create lateral to the distal portion of the device and into tissue. Claim 22 is not limited to a specific configuration of electrodes, as it simply recites that *the energy delivery element is configured to concentrate energy laterally relative to the distal portion of the treatment device*. Ex.1001-USP675, claim 22. It is not my opinion

’675 Patent, FIG.5A	Makower, FIG.5H
	

147. Additionally, as I discuss in Section IX.A, contrary to Dr. Levine’s and Dr. Bikson’s opinions (*e.g.*, Ex.2003-Levine, ¶¶103-104; Ex.2005-Bikson, ¶76), Makower’s Figure 5H device is operable to ablate tissue in the nasal cavity and nasopharynx.

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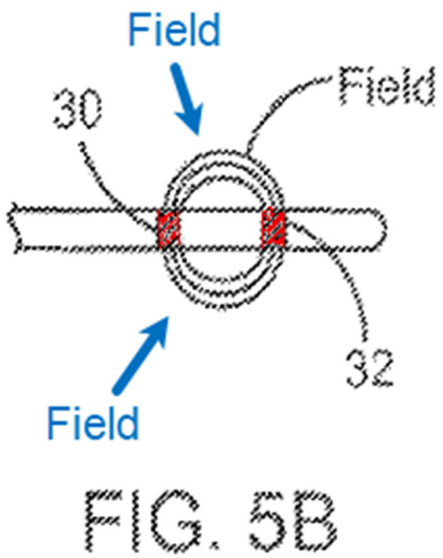
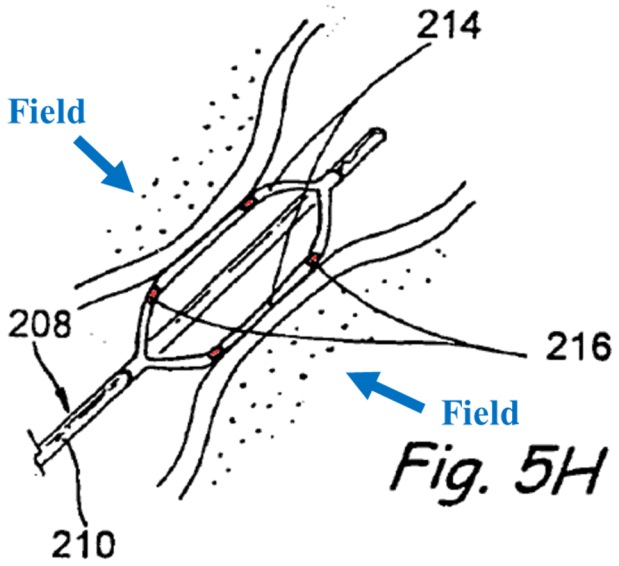
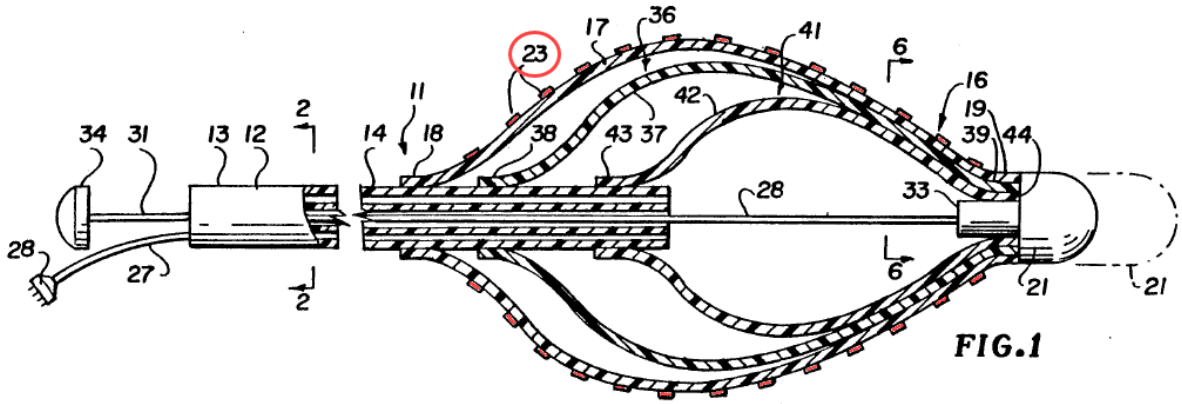
that Figure 5A (and Figures 5B and 6D) of the ’675 patent are the only arrangement of electrodes that could deliver energy laterally, and the ’675 patent does not teach otherwise.

148. Dr. Levine and Dr. Bikson appear to base their opinions on their assumption that Makower Figure 5H is limited to ring electrodes. As discussed in Section IX.A and below, I disagree that the teachings of Makower Figure 5H are so limited. Even if Makower's Figure 5H device is limited to ring electrodes, however, a person of ordinary skill in the art would have understood that Makower's electrodes would, at a minimum, deliver energy that is concentrated laterally into the target tissue in the nasal cavity or nasopharynx. Figure 5B of the '675 patent (below) shows an electrical field around the circumference of the device that is created by bipolar electrodes. Ex.1001-USP675, FIG.5B. Figure 5B also depicts energy that is, at a minimum, concentrated laterally into the target tissue in the nasal cavity or nasopharynx. Ex.1001-USP675, FIG.5B, 16:56-58. Dr. Levine testified that Figure 5B shows ring electrodes and agrees nonetheless that Figure 5B is "operable to deliver energy to tissue" and is within the scope of the '675 patent's claims. Ex.1089-Levine-Tr., 195:4-196:6. Dr. Levine also agrees that the "field lines shown in The Foundry patents are correct," "Figure 5B shows ring electrodes," and "Figure 5B delivers energy ***laterally*** and uniformly." Ex.1089-Levine-Tr., 190:6-9, 194:5-7, 195:10-12. Thus, Makower at a minimum is consistent with Figure 5B of the '675 patent, which depicts energy that is, at least concentrated laterally into the target tissue in the nasal cavity or nasopharynx.

’675 Patent, FIG.5B	Makower, FIG.5H
	

149. Makower also teaches Figure 5H utilizing surface bipolar electrodes. As discussed in my First Declaration and in Section IX.A, Makower teaches that Figure 5H incorporates well-known components and assemblies, including for example U.S. Patent No. 5,255,679 to Imran, which teaches surface electrodes (shown in red below).



Ex.1068-Imran, FIG.1, claim 1, 62-66, 2:57-64, 3:2-7. Ex.1005-Makower, [0164]. As explained in my First Declaration, a person of ordinary skill in the art would have understood that Imran's surface electrodes, which Makower teaches are incorporated into its disclosed devices (including Figure 5H), would create electrical fields that concentrate current lateral relative to the axis of the distal portion of the RF ablation probe, just like Figure 5A of the '675 patent.

150. Dr. Levine and Dr. Bikson contend that Imran's surface electrodes would not deliver energy laterally because they extend or protrude past the surface of the delivery device and "are not surrounded by an insulating material." Ex.2003-Levine, ¶¶108-110; Ex.2005-Bikson, ¶¶80-82. They appear to suggest that a person of ordinary skill in the art would have understood that these electrodes would not concentrate energy laterally, but would instead direct energy from side to side or in other directions. Ex.2003-Levine, ¶¶108-110; Ex.2005-Bikson, ¶¶80-82. I disagree.

151. As an initial matter, claim 22 of the ’675 patent does not recite that the electrodes must be surrounded by an insulating material. Ex.1001-USP675, claim 22.

152. In any event, a person of ordinary skill in the art would have understood that Makower teaches electrodes (either surface electrodes like Imran, ring-electrodes, or other configurations) that would deliver energy laterally into tissue. This is Makower’s central premise, which delivers radiofrequency energy to “tissue adjacent to” the electrodes to treat “nasal conditions.” Ex.1005-Makower, [0001], [0043], [0161], [0187], FIG.5H. As a matter of operation, electrodes of the device taught by Makower would contact target tissue and portions of the electrodes that are not contacting tissue would be insulated by air. As discussed in Section IX.A above, a person of ordinary skill in the art would have understood that mucus or blood would not affect treatment or would be removed from the nasal cavity and nasopharynx prior to ablation. Dr. Bikson agrees that air is an insulator, and the ’675 patent acknowledges that air is an insulator. Ex.1091-Bikson-Tr., 218:9-11 (“Q Well, current really can't travel through air, correct? A That’s correct.”), 221:18-222:7; Ex.1001-USP675, 18:6-9 (“air is a very effective insulator”), 23:60-65. Thus, in operation, a person of ordinary skill in the art would have understood that energy delivered from the electrodes of the device taught by Makower would be

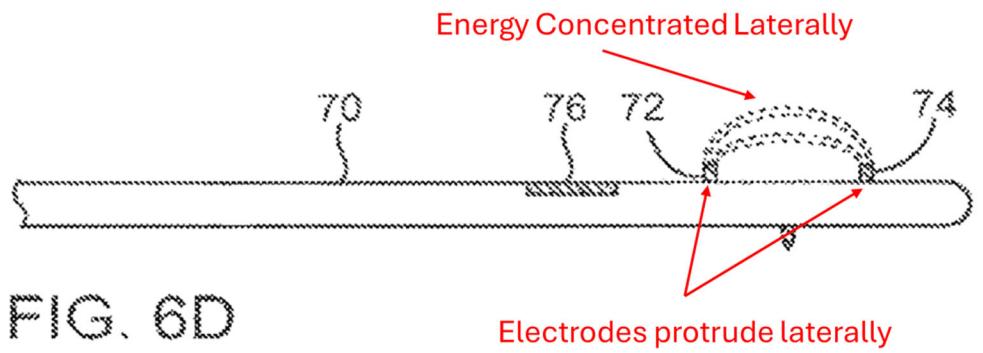
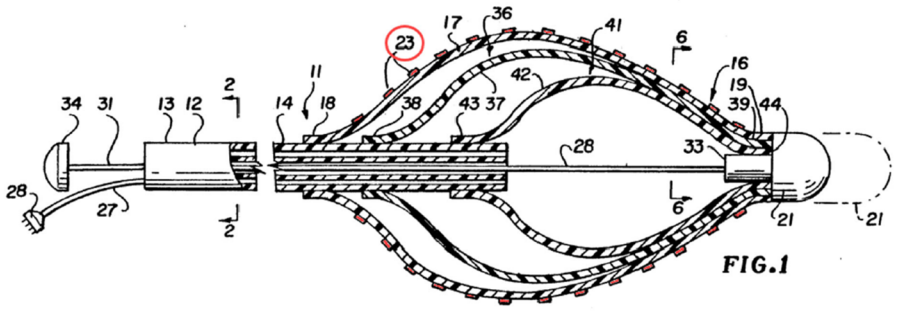
concentrated laterally through the tissue that the electrode is contacting and not travel through surrounding air.[36] To the extent implemented with ring electrodes, the electrodes of Makower Figure 5H would have air on parts of the electrode not in contact with tissue. *See* Section IX.A. To the extent implemented with Imran's electrodes, the electrodes would either fully contact tissue or, to the extent not contacting in full, would have air gaps between them.

153. With respect to Imran's electrodes specifically, my opinion that an electrode that extends laterally from the body (like those in Imran) would have been understood to concentrate energy laterally is supported by Figure 6D of the '675

[36] Dr. Levine and Dr. Bikson do not opine that Makower's electrodes do not contact tissue. *See* Ex.2003-Levine, ¶¶102-111; Ex.2005-Bikson, ¶¶73-83. I understand that Patent Owner has argued that because the Figure 5H drawing imprecisely shows an electrode that may not be fully contacting tissue, that Makower does not teach a device contacting tissue. I disagree. Makower teaches electrodes for contacting tissue, *e.g.*, Ex.1005-Makower, [0043], [0161], [0164], [0187], and a person of ordinary skill in the art would have understood that basic operation of the bipolar electrode device (i.e., that it creates a field between bipolar electrodes when in contact with tissue). Ex.1002-Decl., ¶205.

patent, which contradicts Dr. Levine's and Dr. Bikson's contention that Imran's surface electrodes would not deliver energy laterally because they "are not surrounded by an insulating material." Ex.2003-Levine, ¶¶108-110; Ex.2005-Bikson, ¶¶80-82. Figure 6D of the '675 patent (below) depicts electrodes that, like Imran's electrodes, "extend laterally from the main catheter body." Ex.1001-USP675, 17:27-35, FIG. 6D. Dr. Levine agrees that the "field lines shown in The Foundry patents are correct" (Ex.1089-Levine-Tr., 190:6-9), and as shown below, Figure 6D depicts field lines that create an energy field in a lateral direction, just like Figure 5A (Ex.1001-USP675, FIG.5A, FIG.6D, 16:54-56, 17:27-35. A person of ordinary skill in the art would have understood and expected that Imran's bipolar electrodes, when in contact with tissue, would, as in Figure 6D, create an electrical field that extended laterally from one electrode to another and concentrated energy laterally into that tissue.[37]

[37] Even if Dr. Levine and Dr. Bikson are correct that Imran's electrodes could or would transmit some energy in other directions, that would not dimmish the fact that a person of ordinary skill in the art would have understood it to at least also teach concentrating energy laterally into the tissue. *See also* Section IX.A.

Ex.1001-USP675, Fig. 6D	
Ex.1068-Imran, FIG.1 (annotated in Ex.2003)	

154. Finally, I understand that Patent Owner argues that Imran would deliver energy like Figure 5B and that Figure 5B does not practice the claims. As an initial matter, Dr. Levine and Dr. Bikson do not opine that Imran would deliver energy like Figure 5B. Ex.2003-Levine, ¶¶102-111; Ex.2005-Bikson, ¶¶73-83. And Dr. Levine testified that Figure 5B was within the scope of the claims. Ex.1089-Levine-Tr, 195:4-6 ("Q Is Figure 5B operable to deliver energy to tissue? A According to this description, yes. Q. Do you have any reason to doubt that description? A No. Q. And Figure 5B shows ring electrodes; is that correct? A Yes."), 195:20-196:6 ("Q Is Figure 5B within the scope of the '011 Patent claims? A Yes. Okay. Is Figure 5B

within the scope of the ’077 Patent claims? A Yes. Q Okay. Is Figure 5B within the scope of the ’675 Patent claims? A Yes.”). In any event, Imran would not deliver energy as in Figure 5B of the ’675 patent. Instead, because it has surface (as opposed to ring) electrodes, Imran would generate energy fields concentrating energy laterally into tissue consistent with, for example, Figures 5A and 6D of the ’675 patent, and as discussed above. My opinion that Makower teaches *the energy delivery element is configured to concentrate energy laterally relative to the distal portion of the treatment device* is thus consistent with the ’675 patent.

X. AVAILABILITY FOR CROSS-EXAMINATION

155. In signing this declaration, I recognize that the declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I also recognize that I may be subject to cross examination in the case and that cross examination will take place within the United States. If cross examination is required of me, I will appear for cross examination within the United States during the time allotted for cross examination.

XI. RIGHT TO SUPPLEMENT

156. I reserve the right to supplement my opinions in the future to respond to any arguments that the Patent Owner raises and to take into account new information as it becomes available to me.

XII. JURAT

157. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Dated: January 17, 2025

/s/ Nicolas Bu-Saba
Nicolas Bu-Saba, M.D.

APPENDIX D

Appendix D: Materials Considered

No.	Description
1001	U.S. Patent No. 10,610,675
1003	U.S. Patent No 10,307,200 to Saadat
1004	U.S. Patent Pub. No. 2008/0021369 to Deem
1005	U.S. Patent Pub. No. 2005/0240147 to Makower
1006	Fang Chao-xin and Zhen Shao-Shao, *Nasal endoscopy combined with multiple radiofrequency for perennial allergic rhinitis*, 25(07) J. First Mil. Medic Univ. 876 (July 20, 2005) (Translation) ("Fang")
1008	U.S. Patent No. 6,517,535 to Edwards
1009	U.S. Patent No. 5,562,720 to Stern
1010	U.S. Provisional Appl. No. 60/702,077
1011	U.S. Provisional Appl. No. 60/747,771
1012	U.S. Patent No. 7,608,275
1013	U.S. Patent No. 8,133,497
1014	U.S. Patent No. 8,338,164
1015	U.S. Patent No. 8,961,391
1016	U.S. Patent No. 9,498,283
1017	U.S. Patent No. 10,022,529
1019	U.S. Patent No. 10,729,897
1022	Prosecution History for U.S. Patent No. 10,610,675
1023	U.S. Patent No. 10,894,011
1024	Prosecution History for U.S. Patent No. 10,894,011
1026	U.S. Patent No. 7,655,243
1028	Prosecution History for U.S. Patent No. 8,636,684
1029	U.S. Patent No. 8,105,817
1030	U.S. Patent No. 8,636,684
1031	U.S. Patent Pub. No. 2014/0114233
1032	U.S. Patent No. 9,700,707
1033	U.S. Patent No. 10,052,465
1034	File History for U.S. Patent No. 10,335,221 assigned to Aerin
1040	U.S. Patent No. 8,939,970 to Stone
1041	Stedman's Medical Dictionary (27th ed. 2001)
1042	PDR Medical Dictionary (2nd ed. 2000)

No.	Description
1043	Kong Yonggang, *Low-temperature plasma ablation of inferior turbinate for the treatment of perennial allergic rhinitis*, 19(5) J Clin. Otorhinolaryngol 214 (Mar. 2005) (Translation) ("Kong")
1044	Chen Shi-qiang et al., *Preliminary study on radiofrequency thermocoagulation of the posterior inferior nerve, anterior ethmoidal nerve, and inferior turbinate under nasal endoscopy for the treatment of perennial allergic rhinitis*, 11(3) China Journal of Endoscopy 239 (Mar. 2005) (Translation) ("Chen")
1045	Liang Jianping, *Radiofrequency treatment of ethmoidal nerve with allergic rhinitis under nasal endoscopy*, 13(8) J Clin. Otorhinolaryngol 341 (Aug. 1999) (Translation) ("Liang")
1046	U.S. Patent No. 6,669,689 to Lehmann
1047	U.S. Patent No. 6,685,648 to Flaherty
1048	Stedman's Medical Dictionary (26th ed. 1995)
1049	Webster's Third New International Dictionary (2002)
1050	Seth Waxman, *Correlative Neuroanatomy* (23rd ed. 1996)
1051	Robert E. Windsor and Scott Jahnke, *Sphenopalatine Ganglion Blockage: A Review and Proposed Modification of the Transnasal Technique*, Pain Physician 7:283-286 (2004)
1052	Ralph Fenton, *Current Evaluation of Nasopharyngeal Defense Mechanisms* (1955)
1053	U.S. Patent No. 6,517,534 to McGovern
1054	M.M. L. Arora, *Cryodestruction of Vidian Nerve Branches*, 32:3 Indian J. Otolaryngology 80 (Sept. 1980)
1055	U.S. Patent Pub. No. 2014/0243793 to Morriss
1057	U.S. Patent No. 5,766,605 to Sanders
1058	U.S. Patent No. 874,178 to De Forest
1059	U.S. Patent Pub. No. 2005/0171574 to Rubinsky
1060	U.S. Patent No. 3,538,919 to Meyer
1061	U.S. Patent No. 3,117,571 to Fry
1062	International Pub. No. 2016/183337 to Townley
1063	U.S. Patent No. 4,411,266 to Cosman
1064	Andrew Lane, *Nasal anatomy and physiology*, Facial Plast. Surg. Clin. N. Am. 12:387-395 (2004)

No.	Description
1065	Gray's Anatomy (2003)
1068	U.S. Patent No. 5,255,679 to Imran
1071	Translator Declarations for Chen
1072	Translator Declarations for Liang
1073	Translator Declarations for Fang
1074	Translator Declarations for Kong
1079	Munford Appendices for Shanghai
1089	Deposition Transcript of Dr. Howard Levine
1091	Deposition Transcript of Dr. Marom Bikson
1100	Errata from the October 17, 2024 Deposition of Dr. Nicolas Bu-Saba
1104	Excerpts from the Declaration of Dr. Howard Levine filed in IPR2017-00498
1107	Howard L. Levine, Lasers in Endonasal Surgery, Ottolaryngologic Clinics of N. Am. 30:3, 451-455 (June 1997)
1108	Pitchbook Profile of Mark Deem
1109	Resume of Hanson Gifford
1110	U.S. Patent No. 6,658,279
1111	U.S. Patent No. 7,628,789
1112	Hytönen et al., Radiofrequency Thermal Ablation for Patients with Nasal Symptoms: A Systematic Review of Effectiveness and Complications, 266 EUR. ARCH. OTORHINOLARYNGOL. (2009) ("Hytönen")
1113	Haikou, Diagnostic Criteria and Efficacy Evaluation Criteria of Allergic Rhinitis, 33:3 Chin. J. Otorhinolaryngol 134 (June 1998)
1114	Translation Declaration for Haikou