

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AVATION MEDICAL, INC.,
Petitioner

v.

EMKINETICS, INC.,
Patent Owner

U.S. PATENT NO. 9,002,477
Case No. IPR2024-01378

EX. 1003 - DECLARATION OF DR. BRETT WINGEIER

Table of Contents

I.	INTRODUCTION	5
II.	QUALIFICATIONS	6
III.	MATERIALS REVIEWED AND CONSIDERED	10
IV.	SCOPE OF OPINION	10
V.	LEVEL OF ORDINARY SKILL IN THE ART	11
VI.	LEGAL PRINCIPLES.....	13
A.	Anticipation/Obviousness	13
B.	Priority Date	17
VII.	BACKGROUND OF THE TECHNOLOGY.....	17
A.	Overactive Bladder (“OAB”) and Incontinence	18
B.	Treatment of OAB and Incontinence	19
C.	Electrical Stimulation Feedback and Control	29
VIII.	U.S. PATENT NO. 9,002,477 (“’477 patent”).....	36
A.	Overview of the ’477 Patent.....	36
B.	Prosecution History of the ’477 Patent	40
IX.	CLAIM CONSTRUCTION	40
X.	SPECIFIC GROUNDS OF CHALLENGE.....	41
A.	Ground 1: Claim 1 Is Anticipated by Svihra (Ex.1004)	41
1.	Claim 1:.....	41
B.	Ground 2: Claim 1 Is Obvious Over Svihra (Ex.1004) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056).....	55
1.	Claim 1:.....	56
C.	Ground 3: Claims 2-10 Are Obvious Over Svihra (Ex.1004) Alone or in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), Further in View of the Knowledge of a POSA.....	81
1.	Claim 2: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat fecal incontinence.....	81

2.	Claim 3: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat restless leg syndrome.....	85
3.	Claim 4: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat premature ejaculation.	88
4.	Claim 5: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat chronic pain.	92
5.	Claim 6: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat osteoarthritis or arthritis.	95
6.	Claim 7: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof responsible for neuropathic pain to treat neuropathic pain.....	99
7.	Claim 8: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat neuralgia.	103
8.	Claim 9: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat atrophy.....	106
9.	Claim 10: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat paralysis.....	110
D.	Ground 4: Claim 1 Is Obvious Over Amarenco (Ex.1005) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056)	114
1.	Claim 1:.....	114
E.	Ground 5: Claims 2-10 Are Obvious Over Amarenco (Ex.1005) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), Further in View of the Knowledge of a POSA.....	137
1.	Claim 2: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat fecal incontinence.....	137
2.	Claim 3: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat restless leg syndrome.....	141

3.	Claim 4: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat premature ejaculation.	144
4.	Claim 5: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat chronic pain.	147
5.	Claim 6: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat osteoarthritis or arthritis.	150
6.	Claim 7: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof responsible for neuropathic pain to treat neuropathic pain.	153
7.	Claim 8: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat neuralgia.	157
8.	Claim 9: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat atrophy.	160
9.	Claim 10: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat paralysis.	165
XI.	CONCLUSION.....	168

I. INTRODUCTION

1. My name is Dr. Brett Wingeier, PhD, and I have been retained by counsel for Avation Medical, Inc. (“Avation”) as an expert witness in the above-captioned proceeding regarding U.S. Patent No. 9,002,477 (“the ’477 patent”) (Ex.1001).

2. My opinions are based on my years of education, research, and experience, as well as my investigation and study of relevant materials. The materials that I studied for this declaration include all the documents referenced in this declaration, Avation’s Petition for *Inter Partes* Review of U.S. Patent No. 9,002,477, and the cited exhibits.

3. I may rely upon these materials, my knowledge and experience, and/or additional materials to rebut arguments raised by the Patent Owner EMKinetics, Inc. (“EMK”). Further, I may also consider additional documents and information in forming any necessary opinions, including documents that may not yet have been provided to me.

4. This declaration represents only those opinions I have formed to date. I reserve the right to revise, supplement, and/or amend my opinions stated herein based on new information and on my continuing analysis of the materials produced in this proceeding.

5. I am being compensated on a per hour basis for my time spent working on issues in this case at the rate of \$500 per hour. My compensation does not depend on the outcome of this matter or the opinions I express.

II. QUALIFICATIONS

6. I am an expert in the field of neuromodulation. I have studied, researched, and practiced in the field of neuromodulation for over twenty years. I have summarized in this section my educational background, work experience, and other relevant qualifications. A true and accurate copy of my curriculum vitae is attached as **Appendix C** to this declaration.

7. I earned my Bachelor of Science in biomedical engineering from Tulane University in 1996. Having been awarded a National Science Foundation Graduate Research Fellowship to pursue further study, I earned my Doctor of Philosophy (“PhD”) in biomedical engineering from Tulane University in 2004, with additional research at Swinburne University’s Brain Sciences Institute (Melbourne, Australia) from 1998 to 2001. My dissertation focused on analysis of electric fields in the brain. After receiving my PhD, I completed additional professional development coursework in biodesign from Stanford University from 2005-06, focusing on regulatory, business, and intellectual property aspects of the medical device industry.

8. Following completion of my education, I joined the company NeuroPace, where I worked as a biomedical engineer to help create the first implantable and responsive neurostimulator for epilepsy. During this time, I wrote core firmware for the company's neurostimulator, served as product and program manager for new technologies, and additionally worked as a clinical scientist to lead analysis of incoming data. I also successfully worked to gain FDA approval for NeuroPace's neurostimulator, which remains on the market in the U.S. today.

9. As an additional part of my work at NeuroPace, I collaborated with the Movement Disorders Clinic at Stanford University on subthalamic nucleus stimulation for patients with Parkinson's disease. My involvement included collection of intraoperative data and analysis to study the mechanisms of deep brain stimulation and develop improved neurostimulation technology. To my knowledge I was the first to observe and publish the attenuation of beta-band rhythms after effective stimulation. Additionally, during this time I worked with the company Autonomic Technologies to develop an implant for use in stimulation of the sphenopalatine ganglion, a nerve cluster related to cluster headaches. I designed and developed the embedded software for the patient controller, assisted in architecture of the implantable system, and was also instrumental in planning the associated clinical trials and data analysis. Furthermore, during this time I also worked with the company Nevro to develop new technologies for assessment of

the position of leads implanted in the spinal cord, using analysis of impedance measured between the leads.

10. In 2013, I co-founded Halo Neuroscience, where we researched and developed noninvasive brain stimulation techniques using electrical currents, such as transcranial direct current stimulation (tDCS) and transcranial electrical stimulation (tES). While there, I helped bring to market two successful noninvasive electrical brain stimulation systems. In these projects, I led development of technology to safely and effectively deliver non-invasive stimulation in a wearable device; this technology included skin contact electrode design, usability features, and management of electrical output under error conditions, among other topics. I also led research in monitoring of brain signals and electromyographic (“EMG”) changes evoked by Halo’s neurostimulation.

11. In 2020, I co-founded Magnus Medical and helped develop and bring to market the SAINT treatment for major depression. The SAINT treatment uses functional MRI data to pinpoint individual, personalized targets for precise neurostimulation, and delivers this neurostimulation non-invasively with strong electromagnetic pulses. I led the SAINT treatment to FDA clearance and it was recently launched to the US market.

12. In 2024, I started performing consulting work through my company LT2 Labs. I have consulted with clients on various projects related to biomedical

engineering, neuromodulation, biosignal processing, and neurophysiology, as well as assisting bringing to market products focused on those same technologies.

Additionally, as of the date of this declaration, I am scheduled to return to NeuroPace and begin serving as Vice-President of Research and Development on August 30, 2024, where I will lead research and product development including mechanical, electrical, software, biomedical, and systems engineering for the company's implantable, responsive neurostimulation products for treatment of epilepsy.

13. I have authored and co-authored multiple scientific articles, reviews, and published abstracts. My research interest has primarily focused on neurostimulation, ranging from epilepsy to Parkinson's. I have researched, developed, and brought to market multiple noninvasive neuromodulation products, focusing primarily on electrical stimulation devices. I currently hold over seventy issued U.S. patents in the area of methods, systems, and devices for neuromodulation. I am also a registered patent agent with the United States Patent and Trademark Office ("USPTO").

14. I have not testified at trial, hearing, or by deposition within the preceding four years.

III. MATERIALS REVIEWED AND CONSIDERED

15. In connection with my work on this matter, I have reviewed and considered the documents listed in **Appendix B** and any other documents referenced in this declaration. I have also reviewed and considered Avation's Petition for *Inter Partes* Review of U.S. Patent No. 9,002,477 and the cited exhibits.

16. I also have relied on my academic and professional experience in reaching the opinions expressed in this declaration.

IV. SCOPE OF OPINION

17. I have been asked to provide my opinions regarding whether claims 1-10 of the '477 patent¹ are unpatentable based on the following grounds:

- **Ground 1:** claim 1 is anticipated under 35 U.S.C. § 102 by Svihra (Ex.1004);
- **Ground 2:** claim 1 is rendered obvious under 35 U.S.C. § 103 by Svihra (Ex.1004) in view of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056);
- **Ground 3:** claims 2-10 are rendered obvious under 35 U.S.C. § 103 by Svihra (Ex.1004) alone or in combination with Mann (Ex.1084), DiLorenzo

¹ Claims 1-10 are listed below in **Appendix A**.

(Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), further in view of the knowledge of a person of ordinary skill in the art (“POSA”);

- **Ground 4:** claim 1 is rendered obvious under 35 U.S.C. § 103 by Amarenco (Ex.1005) in view of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056);
- **Ground 5:** claims 2-10 are rendered obvious under 35 U.S.C. § 103 by Amarenco (Ex.1005) in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), further in view of the knowledge of a POSA.

18. This declaration, including the exhibits hereto, sets forth my opinion on these topics.

V. LEVEL OF ORDINARY SKILL IN THE ART

19. I have been told by counsel that a “person of ordinary skill in the art” (“POSA”) is a hypothetical person who is presumed to have known the relevant art at the time of the invention and to whom an expert in the relevant field could assign a routine task with reasonable confidence that the task would be successfully carried out. Such a person would necessarily have the capability of understanding any scientific and engineering principles applicable to the pertinent art. I understand that factors that may be considered in determining the level of ordinary skill in the art include, but are not limited to, the following: the

educational level of the inventor; the type of problems encountered in the art; prior art solutions to those problems; the rapidity with which innovations are made; the sophistication of the technology; and the educational level of active workers in the field. I understand that a person of ordinary skill in the art is not a real person, but rather is a hypothetical individual having the qualities reflected by the factors above. This hypothetical person has knowledge of all prior art in the relevant field and takes from each reference what it would teach to a person of ordinary skill in the art. I have also been informed that the level of skill in the art is evidenced by the prior art references.

20. The '477 patent acknowledges that the prior art teaches neuromodulation devices and methods to treat a variety of conditions, *see* Ex.1001 ('477 patent), 1:55-5:28, including stimulation for treating osteoarthritis, *id.*, 5:9-13, and stimulation for treating chronic pain, *id.*, 5:22-28. The claimed invention of the '477 patent relates to a method for performing electrical stimulation therapy targeting a patient's posterior tibial nerve, including using a sensor to detect electrical conduction or a muscular response and adjusting the current based on the sensor feedback. *Id.*, Cl.1. According to the '477 patent, stimulation targeting the tibial nerve "is particularly suited for the treatment of OAB [*i.e.*, overactive bladder] and VI [*i.e.*, urinary incontinence]." *Id.*, 9:52-54. The '477 patent also claims priority to applications, such as the '329 application, that acknowledge the

prior art teaches techniques for treating overactive bladder (“OAB”) and incontinence including neuromodulation procedures such as stimulation therapy and devices for performing procedures to treat OAB and incontinence. *E.g.*, Ex.1048 (‘329 application), [0003]-[0028].

21. Based on my education and experience, I believe that one of skill in the art would have had at least an undergraduate degree in the field of biomedical engineering or a related discipline, such as electrical engineering, and at least two years of experience in the design and/or analysis of biomedical devices. I believe, however, that additional work experience in the relevant field could serve as a substitute for a formal degree, and additional education could serve as a substitute for work experience.

VI. LEGAL PRINCIPLES

22. I am not an attorney and accordingly have not been retained as an expert in patent law. I have been informed, however, about several principles and standards of patent law, which I have used in developing my opinions expressed herein.

A. Anticipation/Obviousness

23. It is my understanding that prior art can be defined generally as evidence that an invention was already publicly known or available before the effective filing date of a patent or patent application, such as prior patents and/or

publications. It is my understanding that there are two ways in which prior art may render a patent claim unpatentable. First, the prior art can be shown to “anticipate” the claim. Second, the prior art can be shown to have made the claim “obvious” to a person of ordinary skill in the art.

24. It is my understanding that a patent claim is unpatentable as being anticipated if all the claim elements are found expressly or inherently within a prior art reference and arranged as in the claim.

25. I understand that if a prior art reference does not expressly set forth a particular claim element, the prior art may still disclose that element if it is “inherent” in its disclosure. To establish inherency, it is my understanding that evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference. It is my understanding that inherency may not be established by probabilities or possibilities. In other words, it is my understanding that the mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency.

26. I understand that under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform a claimed method, then the method will be considered to be anticipated by the prior art device. I also understand that when the prior art device is the same as a device

described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process.

27. It is my understanding that a patent claim is unpatentable as being obvious in view of prior art if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the alleged invention was made to a person of ordinary skill in the art to which said subject matter pertains. I further understand that an obviousness analysis takes into consideration factual inquiries such as the level of ordinary skill in the art, the scope and content of the prior art, and the differences between the prior art and the patent claim.

28. I understand that the U.S. Supreme Court has recognized several rationales for combining references and for modifying a reference as part of an obviousness analysis. These rationales include:

- combining prior art elements according to known methods to yield predictable results;
- simple substitution of a known element for another to obtain predictable results;
- a predictable use of prior art elements in accordance with their established functions;

- applying a known technique to improve a known device (or process) and yield predictable results;
- choosing from a finite number of known predictable solutions with a reasonable expectation of success (*i.e.*, “obvious to try”);
- known work in one field of endeavor that may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; and
- teaching, suggestion, or motivation in the prior art to combine teachings of multiple prior art references to arrive at the patent claim.

29. In addition to the above, I understand that a person of ordinary skill in the art may resort to logic, judgment, and common sense available to him or her at the time of the invention to find a claim feature obvious, even if the prior art relied on does not explicitly state or teach that feature. I understand that when common sense is relied on to find a feature obvious, the reasoning for that conclusion must be articulated with sufficient clarity.

30. Regarding “objective evidence” or “secondary considerations,” I understand that for such evidence to be relevant to the obviousness of a claim, there must be a causal relationship (called a “nexus”) between the claim and the evidence. I also understand that such objective evidence may include: commercial

success of products covered by the patent claims; long-felt need for the invention; failed attempts by others to solve the problem addressed by the invention; copying of the invention by others in the field; unexpected results achieved by the invention; praise of the invention; the taking of licenses under the patent by others; expressions of surprise by experts and those skilled in the art at the making or use of the invention; and that the patentee proceeded contrary to the accepted wisdom of the prior art.

B. Priority Date

31. I understand that the earliest claimed priority date for the ‘477 patent is October 2, 2006. I have for purposes of this proceeding therefore analyzed obviousness as of that date or somewhat before that date.

VII. BACKGROUND OF THE TECHNOLOGY

32. The ‘477 patent generally relates to a method of performing electrical stimulation therapy that includes delivering electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof. Ex.1001 (‘477 patent), cl.1. Although independent claim 1 does not specifically require a particular disease or condition to be treated with the electrical stimulation therapy, the ‘477 patent indicates that variations of the method that target the posterior tibial nerve are “particularly suited for the treatment of OAB and VI [urinary incontinence].” *Id.*, 9:52-54. Thus, the following background is focused on OAB and incontinence,

treatment of OAB and incontinence via electrical stimulation therapy, and feedback and control systems used in electrical stimulators.

A. Overactive Bladder (“OAB”) and Incontinence

33. Overactive bladder (“OAB”) is a “condition that encompasses a wide range of irritative bladder filling and storage symptoms,” which “includes the symptoms of urinary frequency, urgency, and urge incontinence, singly or in combination.” Ex.1008 (Davila), 173; *see also* Ex.1009 (Wein), 7 (OAB is a “symptom syndrome suggestive of lower urinary tract dysfunction”). A standardization committee in the early 2000’s specifically defined OAB as “urgency, with or without urge incontinence, usually with frequency and nocturia.” Ex.1009 (Wein), 7. According to Davila, “[u]rgency is a strong desire to void accompanied by a fear of leakage or fear of pain. Frequency represents the need to urinate on an abnormally frequent basis (more than eight times per day or more than two times per night [nocturia]). Urge incontinence refers to the symptom of urine loss preceded by a strong sense of urgency.” Ex.1008 (Davila), 173. Various terms were often used interchangeably with OAB in the art, including “overactive detrusor function,” “overactive detrusor,” “detrusor overactivity,” “detrusor instability,” and other related terms, all of which generally relate to abnormalities of detrusor (*i.e.*, a muscle in the bladder) function during filling of the bladder. *Id.*, 173-74; Ex.1009 (Wein), 7-8.

34. The symptoms associated with OAB can significantly affect the lives of individuals with the condition. According to Abrams, “[t]he symptoms are associated with significant social, psychological, occupational, domestic, and physical stigmas. Patients who suffer from OAB focus on and may be preoccupied with such concerns as locating the closest bathroom, looking for aisle seating, and estimating the amount of time until their next work break. Furthermore, OAB affects daily activities, such as travel, physical activity, relationships, sexual function, and nocturnal bladder control, which can affect sleep.” Ex.1010 (Abrams), 580. Various publications in the early 2000’s estimated that 17 to 33 million people in the United States suffered from OAB, although many believed the prevalence of the condition was likely much higher due to underreporting of OAB symptoms by patients. *Id.*; Ex.1011 (Kohli), 219.

B. Treatment of OAB and Incontinence

35. Various treatment options were used to treat OAB and incontinence, including pharmacotherapy, dietary and behavioral modifications, surgical interventions, and neuromodulation. Ex.1011 (Kohli), 219. Many of the available treatments had limitations that made them undesirable to patients. For example, behavioral modifications could include scheduled voiding and exercise, but required strict adherence to routines that many patients found inconvenient. *Id.* Pharmacotherapy, or drug therapy, was widely used but could be associated with

significant side effects and complications. *Id.* Surgical interventions, including permanent catheterization of the patient, were usually reserved for situations where all other treatment options had been tried or failed.

36. Given the limitations of available treatment options, including inconvenience, side effects, and other complications, neuromodulation emerged as an attractive alternative for the treatment of OAB and incontinence. *Id.*, 220 (“Due to unsatisfactory cure rates and significant associated adverse effects of conventional therapies, there has been growing interest in neuromodulation techniques for the treatment of these challenging conditions.”).

37. “Neuromodulation is defined as the physiological process in which the influence of the activity in one neural pathway modulates the pre-existing activity in another through synaptic interaction.” Ex.1012 (van der Pal), 261. In practice, neuromodulation involves altering nerve activity by delivering stimuli (*e.g.*, electrical stimulation, chemical stimulation, etc.) to specific neurological sites in the body. Although the precise mechanisms by which neuromodulation worked were not well understood in the early 2000’s, neuromodulation had already been used extensively to treat a wide variety of conditions. *E.g.*, Ex.1013 (Velasco), 232 (“The experimental effects of electrical and chemical stimulation of the nervous system on various behavioral and/or electrophysiological responses led to their use for therapeutic purposes. To date, both electrical (ES) and chemical

(CS) stimulation have been used to treat a number of neurological symptoms such as pain, movement disorders, spasticity, epilepsy, stupor and coma, psychiatric disorders, neurogenic bladder, peripheral vascular insufficiency, and diaphragmatic palsy.”). One of the most common applications of neuromodulation was for the treatment of pain, which typically involved electrically stimulating nerves for pain reduction.

38. There was also a long history of the use of neuromodulation for the treatment of other conditions, including OAB and incontinence. For example, “[n]euromodulation of the pelvic floor for the treatment of incontinence dates back to the 1960s when Caldwell reported the use of electrical stimulation by implanted electrodes to control stress urinary incontinence.” Ex.1011 (Kohli), 221. By 2006, numerous neuromodulation techniques had been developed and studied for the treatment of OAB and incontinence, including a variety of electrical stimulation methods. These techniques often targeted nerves that modulate the bladder and other muscles involved in normal voiding and storage. *Id.*, 220-21; Ex.1014 (Groen), 723.

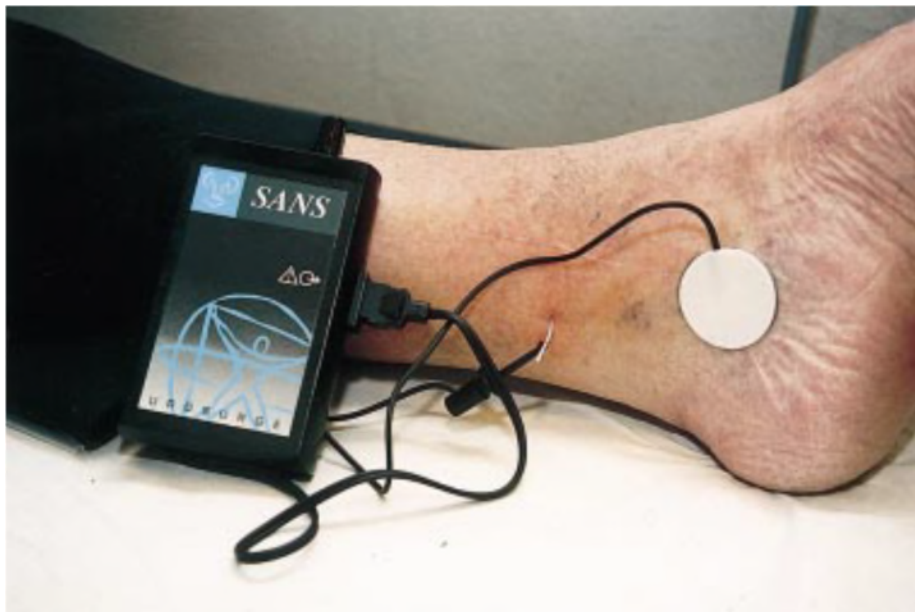
39. One widely known and studied electrical stimulation technique for treating OAB and incontinence was sacral nerve stimulation (“SNS”). According to Groen, “[a] characteristic feature is the implantation of a pulse generator and an electrode stimulating one of the sacral nerves S3. These nerves have a higher

representation in the bladder than the nerves S4 and cause less inconvenience to the legs than the nerves S2.” Ex.1014 (Groen), 726. Movement of specific muscles and flexion of the big toe was “used to verify correct positioning of the electrode and proper functioning of the nerve.” *Id.* Complications included needing to reposition the electrode after migration and electrode breakage and malfunction. *Id.*, 727 (“The need to reposition the electrode after migration is the most frequently reported complication, occurring in <20% of patients. Fracture of the electrode or the extension cable and technical problems with the pulse generator occasionally occur.”) (citations omitted). Numerous studies were published that showed successful treatment of patients with OAB; however, SNS was costly to patients and extremely invasive by nature given the need for implantation of the pulse generator and stimulating electrodes. *Id.*, 727.

40. Another commonly used electrostimulation neuromodulation technique was percutaneous posterior tibial nerve stimulation (“PTNS”), often also referred to as “SANS” (which stands for “Stoller Afferent Nerve Stimulation”). Ex.1014 (Groen), 727-28; Ex.1011 (Kohli), 221-23. According to Groen, “[i]ntuitively, the pelvic region is the most logical place to seek a site for neuromodulation, but physiological mechanisms permit suppression of bladder overactivity from a more distant location,” *i.e.*, the posterior tibial nerve. Ex.1014 (Groen), 727. PTNS targets the posterior tibial nerve—according to Kohli, “[t]he

technique uses a monopolar generator to deliver a pulse signal to the posterior tibial nerve via an acupuncture needle placed slightly above the ankle. This area, long recognized as the ‘bladder center’ (Spleen 6) by ancient Chinese acupuncturists, has projections to the S3 sacral segment, creating a feedback loop that neuromodulates bladder innervation.” Ex.1011 (Kohli), 221.

41. As shown in Figure 4 from Groen, in PTNS a needle connected to an electrical stimulator is inserted near the medial malleolus to stimulate the posterior tibial nerve. Ex.1014 (Groen), 727.



Ex.1014 (Groen), 728 Fig. 4

Groen states that “[t]reatment usually takes place weekly for 10-12 weeks over 20-30 min.” *Id.*, 727. An abundance of published peer-reviewed clinical trials demonstrated the safety and efficacy of the SANS therapy. *See, e.g.*, Ex.1014 (Groen), 727-28. Indeed, “Stoller [52] described an 81% clinical success rate in 90

patients.” *Id.*, 728; Ex.1015 (Stoller), 256. Although the overall results of PTNS were promising, the method still involved penetrating the skin of the patient with a needle electrode and was thus invasive in nature.

42. Noninvasive methods for electrostimulation were also known and used for the treatment of OAB and incontinence. Transcutaneous electrical nerve stimulation (“TENS”) was, for instance, another well-known stimulation technique that used noninvasive surface electrodes that did not penetrate the skin and instead supplied stimulation across the skin tissue to muscles and nerves underlying the skin surface. TENS was used to treat a wide variety of conditions, most commonly pain. Ex.1014 (Groen), 725. Well before 2006, however, TENS was investigated for the treatment of OAB and incontinence. *Id.* According to Groen, “[i]n treating the overactive bladder, the electrodes are usually attached over the S2 and S3 dermatomes (peri-anal region) or over the sacral foramina S2 and S3 (Fig. 2). Stimulation takes place for 20 min to several hours daily during one or more weeks.” *Id.* However, “[b]eneficial results of TENS at various sites” had been reported by the early 2000’s, including the posterior tibial nerve. *Id.*, 726. Many studies involving the use TENS for the treatment of OAB and/or incontinence showed positive results. *Id.*, 724-25.

43. Given the evidence that stimulation of the posterior tibial nerve effectively treated OAB and/or incontinence using PTNS and the beneficial results

using TENS to target the posterior tibial nerve to treat these conditions, many reports on similar noninvasive methods for electrically stimulating the posterior tibial nerve were published well before 2006. In fact, a study on noninvasive electrical stimulation of the posterior tibial nerve was published at least as early as 1983 by McGuire. McGuire reported “[a] new application of electrical stimulation to inhibit detrusor activity [] in 15 patients.” Ex.1041 (McGuire), 78. According to McGuire, current was “applied via a positive electrode transcutaneously to the common peroneal or posterior tibial nerve, with a ground electrode placed over the contralateral common peroneal or posterior tibial nerve with similar results.” *Id.* The electrode was a “electrocardiograph-type electrode with a foam backing.” *Id.*, 79. McGuire reported that “[t]he results were astonishingly good and the device was well tolerated. In patients treated successfully for detrusor instability an absence of urgency occurred as a by-product of electrical stimulation. Therefore, stimulation was used to treat uncomfortable bladder urgency without detrusor instability and was successful in the majority of patients.” *Id.*, 78. According to McGuire, “[t]his electrode placement, coupled with a commercially available transcutaneous electrical nerve stimulator used for the control of pain, provides a reasonable method to inhibit detrusor activity. The stimulator should have a variable output in voltage, frequency and pulse width so that the lowest effective intensity can be selected by the patient.” *Id.*, 79.

44. Other research groups published studies that relied on similar noninvasive techniques targeting the posterior tibial nerve in the early 2000's. For example, Svihra published a study aimed at "us[ing] non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation." Ex.1004 (Svihra), 480. Svihra's goal was to develop a modified version of the SANS treatment discussed above—indeed, according to Svihra, "Stoller's stimulation belongs to minimally invasive therapeutic methods because the stimulatory electrode is placed close to the tibial nerve in the region of medial ankle. The aim of this research was to produce non-invasive stimulation and achieve comparable effect by superficial electrode without iatrogenic damage to the tibial nerve. In 2001, it was for the first time . . . that the superficial stimulation of tibial nerve was used, which tested the effectiveness of modified superficial Stoller's afferent nerve stimulation (SANS)." *Id.*, 480-81. The patients in Svihra's study "suffered from overactive bladder (OAB)." *Id.*, 480. Svihra described the procedure as follows:

The original invasive SANS uses the region of medial ankle for percutaneous tibial nerve stimulation using a needle electrode inserted in the vicinity of the nerve. The intensity of stimulation reaches 10mA, the frequency from 1 to 10 Hz and application time is 30 minutes. It uses standard square impulses. When using the modified non-invasive stimulation SANS it is necessary to use surface electrodes for the area of medial ankle and stimulation of tibial nerve with different values, which cannot be set by the original SANS stimulator. We have used an electromyographic device Nicolet Viking

II E. The patient stayed in a horizontal position on her back and ***the electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation we had proceeded on with a therapeutic stimulation of tibial nerve. Intensity of the surface SANS was equal to 70% of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (stimulation by a constant voltage and regulated intensity of direct current).*** Frequency of stimulation was 1 Hz and duration of square impulse was 0.1ms. ***Surface stimulation of 30 minutes duration was repeated once a week*** for a period of 5 weeks.

Id., 481 (emphasis added). According to Svihra, “[n]oninvasive stimulation had improved subjective symptom related to overactive bladder, had no adverse events and was well tolerated.” *Id.*, 480. Svihra concluded that the technique “is acceptable and safe conservative treatment in case of [OAB].” *Id.*, 482.

45. In 2003, Amarenco published a similar study that tested noninvasive electrical stimulation targeting patients’ posterior tibial nerve. According to Amarenco, “[o]f the various treatments proposed for urge incontinence, frequency and urgency electrostimulation has been widely tested. Different techniques have been used with the necessity of surgical implantation (S3 neuromodulation or sacral root stimulation) or without requiring surgery (perineal transcutaneous electrostimulation). Recently peripheral electrical stimulation of the posterior tibial nerve was proposed for irritative symptoms in first intention or for intractable incontinence. Clinical studies have demonstrated good results and urodynamic parameters were improved after chronic treatment.” Ex.1005 (Amarenco), 2210.

Patients in Amarenco's study had "urge incontinence, frequency and urgency secondary to overactive bladder." *Id.* The study involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." *Id.* In particular, Amarenco's procedure was described as follows:

Stimulation was done using a self-adhesive surface stimulation electrode without an implanted needle electrode. Contact electrodes were placed with electrode gel on the ankle skin with the negative electrode behind the internal malleolus and the positive electrode 10 cm. above the negative electrode. The correct position of the negative electrode was determined by visualization of rhythmic flexion of the toes secondary to plantar muscle contraction during stimulation delivered at 1 hz. The intensity level was then chosen as the intensity immediately under the threshold determining motor contraction. In addition, no pain was to be noted during the stimulation procedure, which necessarily had to be comfortable for the patient. Stimulation frequency during cystometry was then applied at 10 Hz. and a pulse width of 200 milliseconds in continuous mode.

Id., 2211. According to Amarenco, the results of the study "suggest an objective acute effect of posterior tibial nerve stimulation on urodynamic parameters.

Improved bladder overactivity is an encouraging argument to propose posterior tibial nerve stimulation as a noninvasive treatment modality in clinical practice."

Id., 2210. Amarenco concluded that "[p]osterior tibial nerve stimulation is a minimally invasive technique that can suppress detrusor instability or

hyperreflexia. Improved bladder capacity is an encouraging finding that further supports its use as a noninvasive treatment modality in clinical practice.” *Id.*, 2214.

46. Various similar studies were also performed in the early 2000’s that used noninvasive electrical stimulation to target the posterior tibial nerve of patients with OAB and/or incontinence. *See, e.g.*, Ex.1016 (Queralto), 670 (“PTN neuromodulation without surgically implanted electrode could represent a safe and low-cost alternative to permanent sacral neuromodulation for idiopathic anal incontinence); Ex.1017 (Monti), 243 (“The use of surface electrode [PTN neuromodulation] seems to be a non-invasive and successful treatment option for [OAB].”). Thus, it is clear from the prior art that long before 2006, noninvasive electrical stimulation of the posterior tibial nerve was a known, common, and conventional technique for treating patients with OAB and/or incontinence.

C. Electrical Stimulation Feedback and Control

47. Given the decades-long, widespread use of electrical stimulation therapy for treating overactive bladder, incontinence, and a variety of other conditions, many devices and techniques were developed to improve stimulation treatment efficacy and patient convenience long before 2006. For example, it was well known prior to 2006 to use sensors to detect patient response to treatment and to use feedback from the sensors to adjust treatment parameters such as electrical stimulation current and/or voltage.

48. Mann (Ex.1084), for example, discloses a method and system for treatment of incontinence, urgency, frequency, and/or pelvic pain via electrostimulation of various nerves and branches emanating from the sacral nerve roots. Ex.1084 (Mann), Abstract, 10:65-11:19, 11:43-12:7. A preferred stimulation location is the tibial nerve (*i.e.*, the posterior tibial nerve). *Id.*, 12:42-54, 16:28-41. Mann's system includes a microstimulator "where current pulses delivered from its electrodes . . . stimulate nerve fibers," as well as electronic circuitry that dictates, among other things, the amplitude of the electrical current pulse. *Id.*, 14:53-15:24. According to Mann, "[i]n order to help determine the strength . . . of electrical stimulation and/or the amount and/or type(s) of stimulating drug(s) required to produce the desired therapeutic effect, in one preferred embodiment, a patient's response to and/or need for treatment is sensed. For instance, the muscle activity produced in response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG). Thus, when electrodes and/or catheters of a stimulator are implanted, for example, near the dorsal nerve of the clitoris (a branch of the pudendal nerve), the signals from an EMG sensor built into the stimulator may be used to adjust stimulation parameters." *Id.*, 23:4-15.

49. Mann further indicates that in some embodiments, "a stimulator, or a group of two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an

additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, the sensed information is transmitted to the stimulating stimulator(s). Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information. Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:9.

50. DiLorenzo (Ex.1054), which issued in 2002, discloses a system that uses sensors to monitor patient signals resulting from electrical stimulation therapy and adjusts treatment parameters based on sensor feedback. In particular, DiLorenzo discloses electrical stimulation systems that include a neurological control system for modulating nervous system components (*i.e.*, any component or structure of the nervous system, such as a nerve) of a patient. Ex.1054(DiLorenzo), 3:35-48. The system generates neural modulation signals (*e.g.*, electrical stimulation) delivered to a nervous system component through stimulating electrodes in accordance with treatment parameters derived from a neural response to previously delivered neural modulation signals sensed by one or more sensors. *Id.* According to DiLorenzo, the system “considers neural response, in the form of the sensory feedback, as an indication of neurological disease state and/or

responsiveness to therapy, in the determination of treatment parameters.” *Id.*, 3:49-53.

51. DiLorenzo’s system includes at least one stimulating electrode to deliver neural modulation signals to nervous system components of the patient, at least one sensor “to sense at least one parameter, including but not limited to physiologic values and neural signals, which is indicative of at least one of disease state, magnitude of symptoms, and response to therapy,” and a stimulating and recording unit to generate the neural modulation signal “based upon a neural response sensed by” the sensors. *Id.*, 4:4-18. According to DiLorenzo, the stimulating electrodes can be “implanted within” or be “adjacent to” (*i.e.*, noninvasive) various stimulation sites, including “a peripheral nerve” in the “lower extremities.” *Id.*, 6:38-43, 10:24-42, 28:54. The posterior tibial nerve is a peripheral nerve in the lower extremities, *i.e.*, leg. The sensor may include EMG electrodes that detect electrical conduction through a nerve or muscular response caused by electrical conduction through the nerve. *Id.*, 6:58-67, 9:1-14, 9:34-46, 9:54-65, 23:31-24:23, 29:27-44. Based on feedback from the sensors, the system automatically adjusts control parameters such as electrical stimulation treatment parameters in real-time “to provide optimal control of disease state.” *Id.*, 11:8-42, 13:35-53. Control parameters that can be adjusted may include pulse amplitude, which more specifically can include adjustment of either pulse voltage or pulse

current. *Id.*, 12:18-25, 16:14-26, 19:29-67. Advantages of the system include, among other things, “incorporating quantitative and qualitative measures of patient symptomatology and neuromotor circuitry function in the regulation of treatment magnitude,” performance of “automated determination of the optimum magnitude of treatment” in order to “expedite[] achievement of satisfactory treatment of the patient, reducing the time and number of interactions, typically in physician visits, endured by the patient,” and “optimiz[ing] the efficiency of energy used in the treatment given to the patient.” *Id.*, 4:38-5:38.

52. Similarly, Bourget (Ex.1056), which was filed April 28, 2006, discloses a system that delivers closed-loop therapy (*e.g.*, electrical stimulation) based on patient parameters sensed by a sensor. Ex.1056(Bourget), 3:52-4:14. More specifically, Bourget discloses “techniques for detecting a value of a sensed patient parameter, and automatically delivering therapy to a patient according to therapy information previously associated with the detected value.” *Id.*, Abstract, 1:38-41. Bourget’s system includes “a medical device that delivers a therapy to a patient, a sensor that senses a parameter of the patient, a user interface, and a processor. The processor receives a therapy adjustment from the patient via the user interface, determines therapy information based on the therapy adjustment, automatically associates a value of the sensed parameter detected via the sensor with the therapy information in response to receiving the therapy adjustment,

subsequently detects the value via the sensor, and automatically controls the medical device to deliver therapy to the patient according to the therapy information associated with the value in response to the detection.” *Id.*, 2:45-57.

53. According to Bourget, the system is “applicable to any type of stimulation therapy” for treating a variety of conditions, including incontinence. *Id.*, 4:23-25, 4:47-51. The system includes a medical device for delivering neurostimulation therapy such as electrical stimulation, which can be “[a]ny implantable or external medical device.” *Id.*, 4:28-35, 4:52-60. The medical device provides therapy according to a program for delivery of stimulation, which may define a voltage or current pulse amplitude. *Id.*, 4:61-5:1, 8:32-41. The amplitude adjustment may involve adjustment of voltage or current. *Id.*, 13:19-25. Sensed patient parameters may include, among other things, physiological parameters of a patient, including EMG signals. *Id.*, 7:32-44. Advantages of the system include that the system “may be able to more quickly and easily provide a patient with efficacious therapy through automatically ‘learned’ associations of sensed patient parameter values with therapy information. For example, a medical device according to the invention may automatically learn to automatically adjust therapy in the manner desired by the patient based on such associations. After a sufficient period of therapy, the patient may no longer need to manually adjust the therapy because the medical device has learned to use values of one or more sensed patient

parameters to anticipate any adjustments.” *Id.*, 2:23-34; *see also id.*, 3:5-14, 3:65-4:14, 7:54-65.

54. Another system directed to the treatment of incontinence is taught by Gerber (Ex.1055), which was filed April 28, 2005. Ex.1055 (Gerber), 1:16-18. Gerber discloses “an implantable neurostimulator and system capable of providing adaptive neurostimulation therapy to alleviate fecal or urinary incontinence. The neurostimulator operates according to a set of stimulation parameters stored in memory. During operation, information is obtained from the patient, the implanted neurostimulator, one or more implanted sensors, or some combination thereof. A processor analyzes the information to automatically generate proposed adjustments to the stimulation parameters applied by the neurostimulator.” *Id.*, 2:1-16.

55. Gerber’s system includes a neurostimulator that provides electrical stimulation to the patient, sensors, and an external monitor/programmer that transmits information such as adjustments to stimulation parameters to the neurostimulator. *Id.*, 3:35-4:18. The sensors “may provide a variety of information indicative of the level of efficacy achieved by the neurostimulation therapy delivered by neurostimulator,” including a physiological state of the patient such as electromyographic activity (*i.e.*, EMG). *Id.*, 5:39-6:7. Stimulation parameters that can be adjusted based on sensor feedback include the amplitude of stimulation. *Id.*, 5:19-38. It would have been readily apparent to a POSA that the “amplitude” of

electrical stimulation refers to the voltage and/or current of stimulation, which is a primary determinant of the magnitude of the effect of the stimulation on neural tissue. Adjusting stimulation voltage necessarily and inherently adjusts the stimulation current, and vice-versa. *E.g.*, Ex.1071 (De Lima), 499, Fig.4. Gerber's system may "without further input, or authorization from any other source, input and utilize the new stimulation parameters," or can send proposed new stimulation parameters to a clinician or the patient for approval. Ex.1055 (Gerber), 8:47-67. According to Gerber, adjustments to stimulation parameters by the system "provide an adaptive neurostimulation therapy that supports or enhances therapeutic efficacy based on the information obtained." *Id.*, 2:14-16.

VIII. U.S. PATENT NO. 9,002,477 ("’477 patent")

A. Overview of the ’477 Patent

56. The ’477 patent relates to devices and methods for providing stimulation therapy to a patient. Ex.1001 (’477 patent), Abstract. The patent states "systems for electromagnetic induction therapy may include one or more conductive coils disposed within or along an applicator. The coils may be configured to generate a magnetic field focused on a target nerve, muscle or other body tissues in proximity to the coil. One or more sensors may be utilized to detect electrical conduction in the target nerve, to detect a muscular response caused by an electrical conduction in the target nerve, or to detect stimulation of a nerve,

muscle or other body tissues and to provide feedback about the efficacy of the applied electromagnetic induction therapy. A controller in communication with the sensor may be adjustable to vary a current through the at least one coil so as to adjust the magnetic field focused upon the target nerve, muscle or other body tissues.” *Id.*, 5:32-48.

57. The ‘477 patent explains that the prior art teaches neuromodulation devices and methods to treat a variety of conditions, *see* Ex.1001 (‘477 patent), 1:55-5:28, including electric stimulation for treating chronic pain, *id.*, 5:22-28. The claimed invention of the ‘477 patent relates to a method for performing electrical stimulation therapy targeting a patient’s posterior tibial nerve, including using a sensor to detect electrical conduction or a muscular response and adjusting the current based on the sensor feedback. *Id.*, Cl.1. According to the ‘477 patent, stimulation targeting the tibial nerve “is particularly suited for the treatment of OAB [*i.e.*, overactive bladder] and VI [*i.e.*, urinary incontinence].” *Id.*, 9:52-54.

58. The ‘477 patent explains that various electromagnetic and electric stimulation devices and treatments were known in the art. *Id.*, 1:55-5:28. The ‘477 patent also claims priority to applications, such as the ‘329 application, that acknowledge the prior art teaches techniques for treating OAB and incontinence including neuromodulation procedures such as stimulation therapy and devices for performing procedures to treat OAB and incontinence. *Id.*, 1:8-51; Ex.1048 (‘329

application), [0003]-[0028]. The '329 application indicates that stimulation of the posterior tibial nerve was a known treatment that showed efficacy for patients with OAB and incontinence: “[r]ecent data on invasive, needle-based [pulsed electromagnetic stimulation] of the posterior tibial nerve in individuals with OAB and UI indicates that PES can modulate bladder dysfunction through its action on the pudendal and sacral plexus, which provide the major excitatory input to the bladder.” Ex.1048 ('329 application), [0024]. The '329 application further describes several known types of electrostimulation techniques used for treating OAB and incontinence. According to the application, “peripheral tibial nerve stimulation ("PTNS") had been found effective in treating OAB. The disclosed procedure involved the use of electrode and generator components, including a small 34-gauge needle electrode, lead wires and a hand-held electrical generator. However, the procedure requires the permanent implantation of an electrical stimulation device in the patient.” *Id.*, [0025]. Additionally, the application explains that “a neuromodulation alternative is a posterior tibial nerve stimulator, often referred to as SANS, but as is the case with other forms of neuromodulation, this procedure is invasive in nature and requires the insertion of a needle five centimeters into the patient's ankle region to stimulate the posterior tibial nerve. This procedure also requires a minimum of twelve sessions for initial treatment, possibly with additional sessions required for maintenance.” *Id.*, [0028].

Accordingly, the '477 patent and applications to which it claims priority acknowledge that electrical stimulation techniques targeting the posterior tibial nerve for the treatment of OAB and incontinence were known and effective prior to 2006.

59. Although prior stimulation techniques were known to be effective, the '477 patent is directed to devices and methods for providing magnetic induction therapy or electrical stimulation therapy. Ex.1001 ('477 patent), 8:3-16. Notably, a great deal of the patent relates to electromagnetic therapies and stimulation therapy applied via microneedles. The patent, however, discusses electrical stimulation therapy "variations":

In these variations, the source of energy for nerve stimulation is electrical energy that is dispensed through a percutaneous stimulator, such as a percutaneous needle 124, or a transcutaneous stimulator, such as an electrode 126. As shown in FIG. 10, an electrical pulse controller 128 is electrically connected both to percutaneous needle 124 and to sensor 134, to provide the desired feedback and modulate the power to percutaneous needle 134. In the variation of FIG. 11, electrical pulse controller 130 is connected both to electrode 126 and to sensor 136, and performs a function similar to that of electrical pulse controller 128.

Id., 16:25-46, Figs. 10-11 (below).

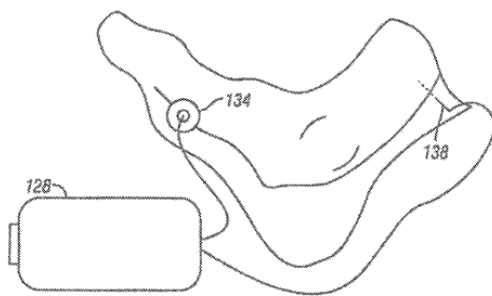


FIG. 10

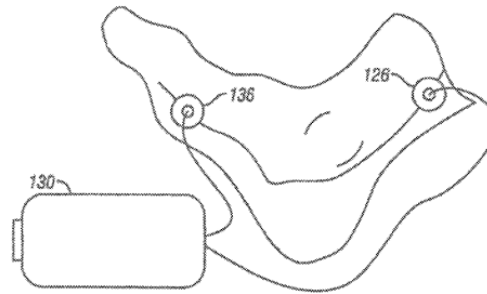


FIG. 11

B. Prosecution History of the '477 Patent

60. I have reviewed the prosecution history of the '477 patent. I understand the '477 patent issued on April 7, 2015 from U.S. Application No. 14/085,639 (“the ‘639 application”), which was filed on November 20, 2013. I understand the original claim was directed to a system for electromagnetic induction therapy, but that the claims were amended to generally relate to performing electrical stimulation therapy. Ex.1002 (‘477 patent file history), 258, 157-59. I further understand that the examiner rejected the claims as anticipated and/or obvious over various prior art references. *Id.*, 49-61. The applicant then amended the claims again to, for example, recite “**non-invasively** positioning . . .” and to change “target nerve” to a “posterior tibial nerve or branch thereof.” *Id.*, 30-31. The application then received a notice of allowance. *Id.*, 7-14.

IX. CLAIM CONSTRUCTION

61. I understand that the claims of the '477 patent are, in this proceeding, “construed using the same claim construction standard that would be used to

construe the claim in a civil action under 35 U.S.C. 282(b), including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.” 37 C.F.R. §42.100(b). Unless noted otherwise below, no terms require construction for purposes of this proceeding.

X. SPECIFIC GROUNDS OF CHALLENGE

A. Ground 1: Claim 1 Is Anticipated by Svihra (Ex.1004)

62. Based on my review and analysis of Svihra and with reasonable scientific certainty, it is my opinion that Svihra discloses all the elements of claim 1 of the ‘477 patent. Thus, it is my opinion that Svihra anticipates this claim of the ‘477 patent. My analysis supporting this opinion is detailed below.

1. Claim 1:

a. *[1.p] A method of performing electrical stimulation therapy, comprising:*

63. Svihra published a study aimed at “us[ing] non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation.” Ex.1004 (Svihra), 480. The patients in Svihra’s study “suffered from overactive bladder (OAB).” *Id.* According to Svihra, “[n]oninvasive stimulation had improved subjective symptom related to overactive bladder, had no adverse events and was well tolerated.” *Id.*, 480. Svihra concluded that the technique “is acceptable and safe conservative

treatment in case of [OAB].” *Id.*, 482. Svihra therefore discloses a method of performing electrical stimulation therapy, *i.e.*, noninvasive electrostimulation for therapy in patients with OAB.

- b. ***[1.a] non-invasively positioning a first portion of a patient's body relative to an electrical stimulator such that a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the electrical stimulator;***

64. Svihra’s study aimed at “us[ing] non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation.” *Id.*, 480. Svihra’s goal was to develop a modified, noninvasive version of the SANS treatment. According to Svihra, “Stoller’s stimulation belongs to minimally invasive therapeutic methods because the stimulatory electrode is placed close to the tibial nerve in the region of medial ankle. ***The aim of this research was to produce non-invasive stimulation and achieve comparable effect by superficial electrode without iatrogenic damage to the tibial nerve.*** In 2001, it was for the first time . . . that the superficial stimulation of tibial nerve was used, which tested the effectiveness of modified superficial Stoller’s afferent nerve stimulation (SANS).” *Id.*, 480-81 (emphasis added). Svihra described the procedure as follows:

The original invasive SANS uses the region of medial ankle for percutaneous tibial nerve stimulation using a needle electrode inserted in the vicinity of the nerve. The intensity of stimulation reaches 10mA, the frequency from 1 to 10 Hz and application time is 30

minutes. It uses standard square impulses. When using the modified non-invasive stimulation SANS it is necessary to use surface electrodes for the area of medial ankle and stimulation of tibial nerve with different values, which cannot be set by the original SANS stimulator. We have used an electromyographic device Nicolet Viking II E. The patient stayed in a horizontal position on her back and ***the electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation we had proceeded on with a therapeutic stimulation of tibial nerve. Intensity of the surface SANS was equal to 70% of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (stimulation by a constant voltage and regulated intensity of direct current).*** Frequency of stimulation was 1 Hz and duration of square impulse was 0.1ms. ***Surface stimulation of 30 minutes duration was repeated once a week*** for a period of 5 weeks.

Id., 481 (emphasis added).

65. In my opinion, Svihra's procedure involved "***non-invasively positioning a first portion of a patient's body relative to an electrical stimulator.***"

Svihra explicitly states the procedure was "non-invasive" in various portions of the publication. See *id.*, 480, 481, 482. Setting that aside, Svihra's explicit goal of the study was to develop a modified version of the SANS procedure, which was a minimally-invasive, percutaneous procedure that required penetrating a patient's skin with a needle electrode. *Id.*, 481. Svihra sought to develop a modified version of the SANS procedure using "superficial" "surface electrodes" in order to not damage the nerve. *Id.* In my opinion, "surface electrodes" in this context would be understood to be electrodes that are placed on the surface of a patient's skin and do

not break the patient's skin. Thus, in my opinion, Svihra's procedure was clearly non-invasive.

66. In my opinion, Svihra's "surface electrodes" and/or an electric stimulator source that would necessarily have been connected to the "surface electrodes" are an "electrical stimulator," as claimed. According to Svihra, the electrodes provided "stimulation by a constant voltage and regulated intensity of direct current." *Id.* If the electrodes were not connected to an electrical stimulator source, the electrodes could not provide electrical stimulation "by a constant voltage" and "regulated intensity of direct current" to the patient because the electrodes would have no source of electricity. Thus, in my opinion, the "surface electrodes" and/or the electrical stimulator source are an "electrical stimulator."

67. Svihra explicitly stated that the "surface electrodes" were "placed behind the medial ankle of the left lower extremity." *Id.*, 480, 481. The area of a patient's body "behind the medial ankle of the left lower extremity" is in close proximity to the ankle of the patients' left leg. Given that, as discussed above, the "surface electrodes" and/or the electrical stimulator source are an "electrical stimulator," in my opinion a portion of the patients' bodies were therefore positioned relative to an electrical stimulator.

68. Further, in my opinion, Svihra also discloses "***a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the***

electrical stimulator.” Svihra explicitly states “[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve.**” *Id.*, 480 (emphasis added). Svihra further explicitly states that “electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve.**” *Id.*, 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The “tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia.

69. In my opinion, the electrical stimulator used in Svihra’s procedure was positioned “in proximity” to the patients’ posterior tibial nerve. Based on my review of the ‘477 patent, the patent does not describe what “in proximity to” means in the context of noninvasive electrical stimulation. Rather, the patent simply discloses providing stimulation by placing a wide variety of devices – invasive and noninvasive, electrical and magnetic – over or in areas of the body that are intended to be stimulated. For example, Figure 11 of the ‘477 patent is the only embodiment shown in the patent that arguably shows noninvasive electrical stimulation of the posterior tibial nerve. Ex.1001 (‘477 patent), Fig.11. Svihra’s electrical stimulator was positioned “in proximity to” the patients’ posterior tibial nerve in the same way, by placing “surface electrodes” “behind the medial ankle of

the left lower extremity” and “proceed[ing] on with a therapeutic stimulation of tibial nerve.” Ex.1004 (Svihra), 481. Given that, as discussed above, the “surface electrodes” and/or the electrical stimulator source are an “electrical stimulator,” in my opinion Svihra’s electrical stimulator was positioned “in proximity to” the patients’ posterior tibial nerve, as claimed.

c. [1.b] passing a current through the electrical stimulator;

70. As discussed above, Svihra applied stimulation via “surface electrodes,” *id.*, which necessarily would have been connected to an electrical stimulator source. The “surface electrodes” and/or the electrical stimulator source are an “electrical stimulator,” as claimed. Svihra explicitly states that the electrodes provided “stimulation by a constant voltage and regulated intensity of direct current.” *Id.*, 481. In order for electrical stimulation to be applied through the electrodes “by constant voltage” and “regulated intensity of direct current,” current would necessarily have had to have been passed through the electrical stimulator source and electrodes. Accordingly, in my opinion and based on Svihra’s explicit disclosures, current was necessarily passed through the electrical stimulator in Svihra’s method.

- d. ***[1.c] delivering an electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof;***

71. In my opinion, Svihra discloses “***delivering an electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof.***” Svihra explicitly states that “electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.*** Intensity of the surface SANS was equal to 70% of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (***stimulation by a constant voltage and regulated intensity of direct current.***” *Id.*, 481 (emphasis added). In other words, Svihra delivered an electrical stimulus from the “surface electrodes”/electrical stimulator source (*i.e.*, the electrical stimulator) in order to stimulate the posterior tibial nerve. The posterior tibial nerve necessarily received the electrical stimulation, particularly given Svihra’s conclusion that “[n]oninvasive stimulation had improved subjective symptoms related to overactive bladder, had no adverse events, and was well tolerated.” *Id.*, 480. Therefore, in my opinion, Svihra delivered an electrical stimulus from the electrical stimulator to the posterior tibial nerve, as claimed.

- e. ***[1.d] detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a***

muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body;

72. In my opinion, Svihra discloses “***detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body.***” In my opinion a POSA would understand the claimed “at least one sensor” that “detect[s] electrical conduction through the posterior tibial nerve or branch thereof” or “detect[s] a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof” includes EMG electrodes/sensors.

73. EMG measures muscle response and electrical activity (*i.e.*, muscle action potentials) in response to a nerve’s stimulation of muscle. *E.g.*, Ex.1042 (Hof), 120-21 (“The EMG is the signal that can be recorded by electrodes from an active muscle. Branches of a nerve fibre each activate the motor endplate of a muscle fibre (fig. 1). This induces two depolarization waves which travel at a speed of 3-6 m/sec to either end of the muscle fibre. The tissue between and around the active fibre is electrically conductive. Electrical signals related to the fibre depolarization can therefore be recorded by electrodes at some distance from the fibre: the EMG.”); Ex.1084 (Mann), 23:8-11 (“the muscle activity produced in

response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG)"). When a nerve is stimulated, whether voluntarily or by electrical stimulation, an electrical impulse, or action potential, is conducted along the nerve which then activates muscles controlled by the nerve. Ex.1042 (Hof), 120-21; Ex.1043 (Noordhout), 174 ("In 1982, Marsden, Merton and Morton discovered that high voltage electrical stimulation over the cervical or lumbar spinal columns produced short latency EMG responses in relaxed muscles of the arm and leg respectively"). To activate the muscle, muscle cells perform biophysical processes that generate and conduct electric signals to cause the muscle to contract. Ex.1042 (Hof), 120-21. EMG detects and measures electric signals generated by and/or conducted by the muscle as a measure of muscle response and activity. *Id.* In other words, when a nerve is stimulated thereby activating a muscle, EMG of that muscle detects: (1) the presence or lack of presence of electrical conduction of the nerve impulse between the portion of the body at the point of stimulation and the portion of the body near the muscle; and (2) the muscular response caused by the electrical conduction. *See id.*

74. The claim language confirms that the claimed "sensor" encompasses EMG electrodes/sensors. Indeed, the claim recites "detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or

branch thereof” using a sensor “positioned along a second portion of the body.”

Detecting for electrical activity at a location on the body distant from the source of electrostimulation is common in EMG, as EMG electrodes (*i.e.*, sensor electrodes) are often placed at a location that is some distance away from the portion of the body being stimulated by stimulator electrodes to avoid interference, and/or to assess electrical conduction of nerve impulses between the stimulated portion of the body and the sensed portion of the body. *See, e.g.*, Ex.1028 (Hermens), 367 (EMG electrode placement “should always be chosen such that the two electrodes do not approach” “innervation or tendon zones”); Ex.1030 (Hasan), 10 (“electromyography was performed in patients undergoing [sacral nerve] neuromodulation. Using surface recording electrodes, evoked potentials were obtained from the small muscle of the foot and the great toe on the side of the implanted electrode”). Moreover, the claim also recites detecting “electrical conduction through” the nerve or “a muscular response caused by an electrical conduction through” the nerve, which in my opinion further supports the interpretation that this claim encompasses detection via EMG electrodes/sensors. As indicated above, nerves stimulate muscles, causing the muscles to generate and conduct electric signals causing muscle contraction. *E.g.*, Ex.1042 (Hof), 120-21; Ex.1084 (Mann), 23:8-11. EMG measurements that show electrical activity in the muscle necessarily means the muscle has been stimulated by a nerve. Thus, EMG

measurements showing electrical activity (or lack of electrical activity) in the muscle indicate there is electrical conduction (or lack of electrical conduction) in the muscle, and further necessarily indicate the presence (or lack of presence) of electrical conduction in the nerve that stimulates the muscle.

75. In addition to the claim language, the ‘477 patent specification also confirms this interpretation. The ‘477 patent clearly indicates that “electrical conduction through” a nerve or “a muscular response caused by an electrical conduction through” a nerve can be detected using sensors such as EMG electrodes/sensors. For example, the patent states “[v]arious sensors may be utilized, e.g., **a three lead EMG, other EMG electrode**, a microneedle electrode, or any sensor for detecting physiologic changes associated with nerve firing and/or muscle contraction.” Ex.1001 (‘477 patent), 36:32-37 (emphasis added); *see also id.*, 43:5-12. Notably, the ‘477 patent acknowledges that sensors used for detecting electrical conduction or muscular response could include any sensor known in the art, such as EMG electrodes/sensors. *See, e.g., id.*, 25:53-60 (“Optionally, other types of sensors may be used in place of a microneedle patch sensor, such as other sensors described herein and **sensors known to persons of ordinary skill in the art**. The sensor may be placed over a portion of the subject’s body suitable for detecting conduction of the target nerve (e.g., on the leg as shown) or over a muscle to detect muscle stimulation resulting from stimulating the target nerve.”)

(emphasis added). Thus, in my opinion, detecting “electrical conduction through” the nerve or “a muscular response caused by an electrical conduction through” the nerve via a sensor as claimed does not cover new or nonobvious features of the alleged invention. Setting that issue aside, based on the claim language, specification, and the knowledge of a POSA regarding detecting electrical conduction and muscular response in the body, a POSA would clearly understand the “detecting” via a “sensor” claim language to encompass EMG.

76. Svihra used “an electromyographic [EMG] device Nicolet Viking II E” and measured “the maximal amplitude of response [] registered from the abductor hallucis muscle” resulting from electrical stimulation of the posterior tibial nerve. Ex.1004 (Svihra), 481. Svihra did so in order to assess conduction of the electrical nerve impulse from the point of neurostimulation to the point of measurement (*i.e.*, electrical conduction through the posterior tibial nerve) and the muscular response caused by the electrical conduction (*i.e.*, the response of the abductor hallucis muscle resulting from electrical stimulation through the posterior tibial nerve). While Svihra does not explicitly describe the use of EMG electrodes or sensors, Svihra ***necessarily*** had to use EMG electrodes/sensors, or else the “electromyographic [EMG] device Nicolet Viking II E” could not have been used and the “maximal amplitude of response” of the muscle could not have been measured. Thus, in my opinion, Svihra necessarily discloses “detecting electrical

conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body,” as claimed.

- f. ***[1.e] receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy; and***

77. As explained above, Svihra describes using an “electromyographic [EMG] device Nicolet Viking II E,” which is a device used to measure electrical conduction through a nerve and muscular response resulting from electrical conduction through the nerve causing the nerve’s stimulation of a muscle. Ex.1004 (Svihra), 481; *see also supra*, §X.A.1.e. Further, according to Svihra, “[i]ntensity of the surface SANS was equal to 70% of intensity, ***at which the maximal amplitude of response*** was registered from the abductor hallucis muscle (stimulation by a constant voltage and regulated intensity of direct current).” Ex.1004 (Svihra), 481 (emphasis added). By “amplitude of response,” Svihra is referring to the electrical signal emanating from the muscle measured via EMG as a result of electrostimulation. The fact Svihra determined the “maximal amplitude of response” necessarily indicates the EMG results detected by the EMG device were received and displayed to Svihra. Given that “amplitude” of response is a

measure of electrical activity, there would be no way for Svihra to know what the “amplitude” of response was, let alone the “maximal amplitude,” unless it was both measured and displayed by the EMG to Svihra. Moreover, the fact Svihra determined the “**maximal** amplitude of response” registered from the muscle occurred at 70% intensity further indicates that Svihra was using the EMG sensor measurement as feedback about the efficacy of the electrical stimulation, because the EMG sensor measurement indicated to Svihra that the most effective intensity was 70% based on the response of the abductor hallucis muscle.

g. [1.f] adjusting the current via a controller in communication with the electrical stimulator based on the feedback.

78. As explained above, Svihra used an EMG device to measure electrical conduction through a nerve and muscular response resulting from electrical conduction through the nerve causing the nerve’s stimulation of a muscle. Ex.1004 (Svihra), 481; *see also supra*, §X.A.1.e. Svihra concluded that “[i]ntensity of the surface SANS was equal to **70% of intensity**, at which the maximal amplitude of response was registered from the abductor hallucis muscle (**stimulation by a constant voltage and regulated intensity of direct current**).” Ex.1004 (Svihra), 481 (emphasis added). A POSA would understand that “intensity” refers to the amount of current and/or voltage being delivered by an electrical stimulator. Adjusting stimulation voltage necessarily and inherently adjusts the stimulation

current, and vice-versa. Ex.1071 (De Lima), 499, Fig.4.. Here, Svihra explicitly states that the intensity of the current was “regulated” (*i.e.*, adjusted). By “70% intensity,” Svihra is referring to a certain level of current being delivered by the electrical stimulator. Svihra determined that the “maximal amplitude of response” of the muscle measured by EMG occurred at 70% intensity. Ex.1004 (Svihra), 481. To determine the “**maximal** amplitude of response,” Svihra **necessarily** must have adjusted the intensity (*i.e.*, current) of the electrostimulation via a controller to distinguish the “maximal amplitude of response” of the muscle from other, non-maximal responses from the muscle. As explained above, Svihra made these adjustments based on feedback from the EMG sensor indicative of the “amplitude of response” of the muscle. Accordingly, in my opinion, Svihra discloses “adjusting the current via a controller in communication with the electrical stimulator based on the feedback,” as claimed.

B. Ground 2: Claim 1 Is Obvious Over Svihra (Ex.1004) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056)

79. As explained above, in my opinion Svihra discloses all elements of claim 1 of the ‘477 patent. *See supra*, §X.A.1. To the extent it is determined Svihra does not disclose all elements of claim 1, based on my review and analysis of Svihra and with reasonable scientific certainty, it is my opinion that it would have been obvious to modify Svihra’s teachings based on Mann, DiLorenzo, Gerber, or

Bourget to achieve the method of claim 1 of the '477 patent. I am not aware of any evidence of secondary considerations of nonobviousness, but I reserve the right to respond to any such evidence that EMK may raise in this proceeding. My analysis supporting this opinion is detailed below.

1. Claim 1:

a. [1.p] A method of performing electrical stimulation therapy, comprising:

80. As explained above, in my opinion Svihra discloses this limitation. *See supra*, §X.A.1.a. In particular, Svihra published a study aimed at “us[ing] non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation.” Ex.1004 (Svihra), 480. The patients in Svihra’s study “suffered from overactive bladder (OAB).” *Id.* According to Svihra, “[n]oninvasive stimulation had improved subjective symptom related to overactive bladder, had no adverse events and was well tolerated.” *Id.*, 480. Svihra concluded that the technique “is acceptable and safe conservative treatment in case of [OAB].” *Id.*, 482. Svihra therefore discloses a method of performing electrical stimulation therapy, *i.e.*, noninvasive electrostimulation for therapy in patients with OAB.

b. [1.a] non-invasively positioning a first portion of a patient's body relative to an electrical stimulator such that a posterior tibial nerve or branch thereof within the

first portion of the body is in proximity to the electrical stimulator;

81. As explained above, in my opinion Svihra discloses this limitation. *See supra*, §X.A.1.b. Specifically, Svihra published a study aimed at “us[ing] non-invasive stimulation of the tibial nerve with the intention to achieve desired therapeutic effects without iatrogenic nerve damage using a superficial electrostimulation.” *Id.*, 480. Svihra’s goal was to develop a modified, noninvasive version of the SANS treatment. According to Svihra, “Stoller’s stimulation belongs to minimally invasive therapeutic methods because the stimulatory electrode is placed close to the tibial nerve in the region of medial ankle. ***The aim of this research was to produce non-invasive stimulation and achieve comparable effect by superficial electrode without iatrogenic damage to the tibial nerve.*** In 2001, it was for the first time . . . that the superficial stimulation of tibial nerve was used, which tested the effectiveness of modified superficial Stoller’s afferent nerve stimulation (SANS).” *Id.*, 480-81 (emphasis added). Svihra described the procedure as follows:

The original invasive SANS uses the region of medial ankle for percutaneous tibial nerve stimulation using a needle electrode inserted in the vicinity of the nerve. The intensity of stimulation reaches 10mA, the frequency from 1 to 10 Hz and application time is 30 minutes. It uses standard square impulses. When using the modified non-invasive stimulation SANS it is necessary to use surface electrodes for the area of medial ankle and stimulation of tibial nerve with different values, which cannot be set by the original SANS stimulator. We have used an electromyographic device Nicolet Viking

II E. The patient stayed in a horizontal position on her back and ***the electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation we had proceeded on with a therapeutic stimulation of tibial nerve. Intensity of the surface SANS was equal to 70% of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (stimulation by a constant voltage and regulated intensity of direct current).*** Frequency of stimulation was 1 Hz and duration of square impulse was 0.1ms. ***Surface stimulation of 30 minutes duration was repeated once a week*** for a period of 5 weeks.

Id., 481 (emphasis added).

82. In my opinion, Svihra's procedure involved "***non-invasively positioning a first portion of a patient's body relative to an electrical stimulator.***"

Svihra explicitly states the procedure was "non-invasive" in various portions of the publication. See *id.*, 480, 481, 482. Setting that aside, Svihra's explicit goal of the study was to develop a modified version of the SANS procedure, which was a minimally-invasive, percutaneous procedure that required penetrating a patient's skin with a needle electrode. *Id.*, 481. Svihra sought to develop a modified version of the SANS procedure using "superficial" "surface electrodes" in order to not damage the nerve. *Id.* In my opinion, "surface electrodes" in this context would be understood to be electrodes that are placed on the surface of a patient's skin and do not break the patient's skin. Thus, in my opinion, Svihra's procedure was clearly non-invasive.

83. In my opinion, Svihra's "surface electrodes" and/or an electric stimulator source that would necessarily have been connected to the "surface electrodes" are an "electrical stimulator," as claimed. According to Svihra, the electrodes provided "stimulation by a constant voltage and regulated intensity of direct current." *Id.* If the electrodes were not connected to an electrical stimulator source, the electrodes could not provide electrical stimulation "by a constant voltage" and "regulated intensity of direct current" to the patient because the electrodes would have no source of electricity. Thus, in my opinion, the "surface electrodes" and/or the electrical stimulator source are an "electrical stimulator."

84. Svihra explicitly stated that the "surface electrodes" were "placed behind the medial ankle of the left lower extremity." *Id.*, 480, 481. The area of a patient's body "behind the medial ankle of the left lower extremity" is in close proximity to the ankle of the patients' left leg. Given that, as discussed above, the "surface electrodes" and/or the electrical stimulator source are an "electrical stimulator," in my opinion a portion of the patients' bodies were therefore positioned relative to an electrical stimulator.

85. Further, in my opinion, Svihra also discloses "***a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the electrical stimulator.***" Svihra explicitly states "[t]he aim of this study was to use non-invasive stimulation of the ***tibial nerve.***" *Id.*, 480 (emphasis added). Svihra

further explicitly states that “electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.***” *Id.*, 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The “tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia.

86. In my opinion, the electrical stimulator used in Svihra’s procedure was positioned “in proximity” to the patients’ posterior tibial nerve. Based on my review of the ‘477 patent, the patent does not describe what “in proximity to” means in the context of noninvasive electrical stimulation. Rather, the patent simply discloses providing stimulation by placing a wide variety of noninvasive devices – invasive and noninvasive, electrical and magnetic – over or in areas of the body that are intended to be stimulated. For example, Figure 11 of the ‘477 patent is the only embodiment shown in the patent that arguably shows noninvasive electrical stimulation of the posterior tibial nerve. Ex.1001 (‘477 patent), Fig.11. Svihra’s electrical stimulator was positioned “in proximity to” the patients’ posterior tibial nerve in the same way, by placing “surface electrodes” “behind the medial ankle of the left lower extremity” and “proceed[ing] on with a therapeutic stimulation of tibial nerve.” Ex.1004 (Svihra), 481. Given that, as

discussed above, the “surface electrodes” and/or the electrical stimulator source are an “electrical stimulator,” in my opinion Svihra’s electrical stimulator was positioned “in proximity to” the patients’ posterior tibial nerve, as claimed.

c. [1.b] passing a current through the electrical stimulator;

87. As explained above, in my opinion Svihra discloses this limitation. *See supra*, §X.A.1.c. More particularly, Svihra applied stimulation via “surface electrodes,” Ex.1004 (Svihra), 481, which necessarily would have been connected to an electrical stimulator source. The “surface electrodes” and/or the electrical stimulator source are an “electrical stimulator,” as claimed. Svihra explicitly states that the electrodes provided “stimulation by a constant voltage and regulated intensity of direct current.” *Id.*, 481. In order for electrical stimulation to be applied through the electrodes “by constant voltage” and “regulated intensity of direct current,” current would necessarily have had to have been passed through the electrical stimulator source and electrodes. Accordingly, in my opinion and based on Svihra’s explicit disclosures, current was necessarily passed through the electrical stimulator in Svihra’s method.

d. [1.c] delivering an electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof;

88. As explained above, in my opinion Svihra discloses this limitation. *See supra*, §X.A.1.d. Specifically, Svihra discloses “**delivering an electrical**

stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof.” Svihra explicitly states that “electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.*** Intensity of the surface SANS was equal to 70% of intensity, at which the maximal amplitude of response was registered from the abductor hallucis muscle (***stimulation by a constant voltage and regulated intensity of direct current.***)” *Id.*, 481 (emphasis added). In other words, Svihra delivered an electrical stimulus from the “surface electrodes”/electrical stimulator source (*i.e.*, the electrical stimulator) in order to stimulate the posterior tibial nerve. The posterior tibial nerve necessarily received the electrical stimulation, particularly given Svihra’s conclusion that “[n]oninvasive stimulation had improved subjective symptoms related to overactive bladder, had no adverse events, and was well tolerated.” *Id.*, 480. Therefore, in my opinion, Svihra delivered an electrical stimulus from the electrical stimulator to the posterior tibial nerve, as claimed.

- e. ***[1.d] detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body;***
- [1.e] receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy; and***
- [1.f] adjusting the current via a controller in communication with the electrical stimulator based on the feedback.***

89. As explained above, in my opinion Svihra discloses the “detecting...,” “receiving...,” and “adjusting...” limitations of claim 1. *See supra*, §§X.A.1.e-X.A.1.g. To the extent it is determined Svihra does not disclose these limitations, in my opinion it would have been obvious to modify Svihra based on the teachings of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) to arrive at the method of claim 1.

90. Well before 2006, electrical stimulation devices and techniques were known that used sensors to detect patient response to treatment and to use feedback from the sensors to adjust treatment parameters, such as electrical stimulation current or voltage. For example, Mann (Ex.1084) discloses a method and system for treatment of incontinence, urgency, frequency, and/or pelvic pain via electrostimulation of various nerves and branches emanating from the sacral nerve

roots. Ex.1084 (Mann), Abstract, 10:65-11:19, 11:43-12:7. A preferred stimulation location is the tibial nerve (*i.e.*, the posterior tibial nerve). *Id.*, 12:42-54, 16:28-41. Mann's system includes a microstimulator "where current pulses delivered from its electrodes . . . stimulate nerve fibers," as well as electronic circuitry that dictates, among other things, the amplitude of the electrical current pulse. *Id.*, 14:53-15:24. According to Mann, "[i]n order to help determine the strength . . . of electrical stimulation and/or the amount and/or type(s) of stimulating drug(s) required to produce the desired therapeutic effect, in one preferred embodiment, a patient's response to and/or need for treatment is sensed. For instance, the muscle activity produced in response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG). Thus, when electrodes and/or catheters of a stimulator are implanted, for example, near the dorsal nerve of the clitoris (a branch of the pudendal nerve), the signals from an EMG sensor built into the stimulator may be used to adjust stimulation parameters." *Id.*, 23:4-15.

91. Mann further indicates that in some embodiments, "a stimulator, or a group or two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional 'stimulator' (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, the sensed information is transmitted to the stimulating stimulator(s). Preferably, the

parameters used by the stimulator(s) are automatically adjusted based on the sensed information. Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:9.

92. DiLorenzo (Ex.1054) discloses a system that uses sensors to monitor patient signals resulting from electrical stimulation therapy and adjusts treatment parameters based on sensor feedback. Ex.1054(DiLorenzo), 3:35-48. DiLorenzo’s system includes at least one stimulating electrode to deliver neural modulation signals to nervous system components of the patient, at least one sensor “to sense at least one parameter, including but not limited to physiologic values and neural signals, which is indicative of at least one of disease state, magnitude of symptoms, and response to therapy,” and a stimulating and recording unit to generate the neural modulation signal “based upon a neural response sensed by” the sensors. *Id.*, 4:4-18. According to DiLorenzo, the stimulating electrodes can be “implanted within” or be “adjacent to” (*i.e.*, noninvasive) various stimulation sites, including “a peripheral nerve” in the “lower extremities.” *Id.*, 6:38-43, 10:24-42, 28:33-56. The posterior tibial nerve is a peripheral nerve in the lower extremities, *i.e.*, leg. The sensor may include EMG electrodes that detect electrical conduction through a nerve or muscular response caused by electrical conduction through the nerve. *Id.*, 6:58-67, 9:1-14, 9:34-46, 9:54-65, 23:31-24:23, 29:27-44. Based on feedback from

the sensors, the system automatically adjusts control parameters such as electrical stimulation treatment parameters in real-time “to provide optimal control of disease state.” *Id.*, 11:8-42, 13:35-53. Control parameters may include pulse amplitude. *Id.*, 12:18-25, 16:14-26. Pulse amplitude may include adjustment of either pulse voltage or pulse current. *Id.*, 16:24-26, 19:29-67.

93. Similarly, Bourget (Ex.1056) discloses a system that delivers closed-loop therapy (*e.g.*, electrical stimulation) based on patient parameters sensed by a sensor. Ex.1056(Bourget), 3:52-4:14. Bourget’s system includes “a medical device that delivers a therapy to a patient, a sensor that senses a parameter of the patient, a user interface, and a processor. The processor receives a therapy adjustment from the patient via the user interface, determines therapy information based on the therapy adjustment, automatically associates a value of the sensed parameter detected via the sensor with the therapy information in response to receiving the therapy adjustment, subsequently detects the value via the sensor, and automatically controls the medical device to deliver therapy to the patient according to the therapy information associated with the value in response to the detection.” *Id.*, 2:45-57. The system is “applicable to any type of stimulation therapy” for treating a variety of conditions, including incontinence. *Id.*, 4:23-25, 4:47-51. The system includes a medical device for delivering neurostimulation therapy such as electrical stimulation, which can be “[a]ny implantable or external

medical device.” *Id.*, 4:28-35, 4:52-60. The medical device provides therapy according to a program for delivery of stimulation, which may define a voltage or current pulse amplitude for stimulation pulses. *Id.*, 4:61-5:1, 8:32-41. The amplitude adjustment may involve adjustment of voltage or current. *Id.*, 13:19-25. Sensed patient parameters may include, among other things, physiological parameters of a patient, including EMG signals. *Id.*, 7:32-44.

94. Gerber (Ex.1055) likewise discloses a system that provides adaptive neurostimulation therapy via information obtained from sensors to alleviate fecal or urinary incontinence. Ex.1055 (Gerber), 2:1-16. Gerber’s system includes a neurostimulator that provides electrical stimulation to the patient, sensors, and an external monitor/programmer that transmits information such as adjustments to stimulation parameters to the neurostimulator. *Id.*, 3:35-4:18. The sensors “may provide a variety of information indicative of the level of efficacy achieved by the neurostimulation therapy delivered by neurostimulator,” including a physiological state of the patient such as electromyographic activity (*i.e.*, EMG). *Id.*, 5:39-6:7. Stimulation parameters that can be adjusted based on sensor feedback include, among other things, the frequency or amplitude of stimulation. *Id.*, 5:19-38. It would have been readily apparent to a POSA that the “amplitude” of electrical stimulation refers to the voltage and/or current of stimulation, which is a primary determinant of the magnitude of the effect of the stimulation on neural tissue.

Adjusting stimulation voltage necessarily and inherently adjusts the stimulation current, and vice-versa. Ex.1071 (De Lima), 499, Fig.4. The system may “without further input, or authorization from any other source, input and utilize the new stimulation parameters,” or can send proposed new stimulation parameters to a clinician or the patient for approval. Ex.1055 (Gerber), 8:47-67.

95. Each of Mann (Ex.1084), DiLorenzo (Ex.1054), Bourget (Ex.1056), and Gerber (Ex.1055) discloses the “detecting...,” “receiving...,” and “adjusting...” limitations of claim 1 of the ‘477 patent.

96. In particular, Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), and Bourget (Ex.1056) each disclose “***detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body.***” As explained above, based on the claim language, specification, and the knowledge of a POSA regarding detecting electrical conduction and muscular response in the body, a POSA would have understood the claimed “at least one sensor” that “detect[s] electrical conduction through the posterior tibial nerve or branch thereof” or “detect[s] a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof” includes EMG electrodes/sensors. *See supra*, §X.A.1.e.

97. Mann (Ex.1084) discloses the “detecting” limitation of claim 1. As discussed above, Mann’s system includes sensors, including EMG sensors, that provide sensed information “used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:32-34. For example, Mann states “[i]n order to help determine the strength . . . of electrical stimulation and/or the amount and/or type(s) of stimulating drug(s) required to produce the desired therapeutic effect, in one preferred embodiment, a patient's response to and/or need for treatment is sensed. ***For instance, the muscle activity produced in response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG).***” *Id.*, 23:4-15 (emphasis added); *see also id.*, 24:24-28, 25:65-26:20.

98. DiLorenzo (Ex.1054) also discloses the “detecting” limitation of this claim. As discussed above, DiLorenzo’s system includes at least one stimulating electrode to deliver neural modulation signals to nervous system components of the patient, at least one sensor “to sense at least one parameter, including but not limited to physiologic values and neural signals, which is indicative of at least one of disease state, magnitude of symptoms, and response to therapy,” and a stimulating and recording unit to generate the neural modulation signal “based upon a neural response sensed by” the sensors. Ex.1054 (DiLorenzo), 4:4-18. According to DiLorenzo, the sensor may include EMG electrodes that detect electrical conduction through a nerve or muscular response caused by electrical

conduction through the nerve. *Id.*, 6:58-67, 9:1-14, 9:34-46, 9:54-65, 23:31-24:23, 29:27-44.

99. Bourget (Ex.1056) likewise discloses this limitation. Bourget's system includes "a medical device that delivers a therapy to a patient, a sensor that senses a parameter of the patient, a user interface, and a processor." Ex.1056 (Bourget), 2:45-57. Sensed patient parameters may include, among other things, physiological parameters of a patient including EMG signals. *Id.*, 7:32-44.

100. Gerber (Ex.1055) also discloses this limitation. Gerber's system includes a neurostimulator that provides electrical stimulation to the patient, sensors, and an external monitor/programmer that transmits information such as adjustments to stimulation parameters to the neurostimulator. Ex.1055 (Gerber), 3:35-4:18. The sensors "may provide a variety of information indicative of the level of efficacy achieved by the neurostimulation therapy delivered by neurostimulator," including a physiological state of the patient such as electromyographic activity (*i.e.*, EMG). *Id.*, 5:39-6:7.

101. Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), and Bourget (Ex.1056) also disclose "***receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy.***" For example, sensors in Mann's system, such as EMG sensors indicative

of the detected electrical conduction or muscular response, provide sensed information “used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:4-34. According to Mann, “[i]n one preferred embodiment, a stimulator, or a group of two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, **the sensed information is transmitted to the stimulating stimulator(s)**. Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information. Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:20.

102. DiLorenzo’s system receives signals from the sensor(s), such as an EMG sensor, and uses the signals to automatically adjust control parameters of the electrical stimulation in real-time “to provide optimal control of disease state.” Ex.1054 (DiLorenzo), 8:39-50, 11:8-42, 13:35-53. As explained above, a signal from an EMG electrode/sensor is indicative of the detected electrical conduction or muscular response. According to DiLorenzo, the system “considers neural response, in the form of the sensory feedback, as an indication of neurological

disease state and/or responsiveness to therapy, in the determination of treatment parameters.” *Id.*, 3:49-53.

103. Similarly, Bourget’s system “detects [a value of the sensed parameter] via the sensor, and automatically controls the medical device to deliver therapy to the patient according to the therapy information associated with the value in response to the detection.” Ex.1056(Bourget), 2:45-57; *see also id.*, 8:62 (“IMD 12 includes a sensor 40 that senses a patient parameter, and processor 34 detects values of the patient parameter based on the signal generated by sensor 40 as a function of the patient parameter”). The sensor can be an EMG electrode/sensor, *id.*, 7:32-44, which as explained above is indicative of the detected electrical conduction or muscular response.

104. Additionally, Gerber’s system includes an external monitor/programmer that “may receive information from neurostimulator 12 and/or sensor 20 by wireless telemetry” and “may record the received information, analyze the information, and adjust stimulation parameters based on the information or some combination thereof.” Ex.1055 (Gerber), 3:50-4:2; *see also id.*, 5:19-21, 5:39-41, 7:19-23. Given that Gerber’s sensor can be an EMG electrode/sensor, it would be understood that the signal is indicative of the detected electrical conduction or muscular response.

105. Finally, Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1056), and Bourget (Ex.1055) each disclose “***adjusting the current via a controller in communication with the electrical stimulator based on the feedback.***” Mann explicitly states that “[t]he sensed information is preferably used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:4-34. Mann further explains that “[i]n one preferred embodiment, a stimulator, or a group of two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, the sensed information is transmitted to the stimulating stimulator(s). ***Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information.*** Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:9. According to Mann, the “stimulation parameters” that can be adjusted include the amplitude of the electrical current pulse. *Id.*, 15:8-24, 21:48-59.

106. Similarly, according to DiLorenzo, feedback from the sensors is used to determine adjustments to control parameters of the electrical stimulation, which are implemented by a control circuit (*i.e.*, the controller) in communication with a

stimulating and recording unit. Ex.1054 (DiLorenzo), 10:66-11:10, 11:22-12:42.

Control parameters that can be adjusted based on feedback from the sensors include the pulse amplitude, which more specifically may include adjustment of either pulse voltage or pulse current. *Id.*, 12:18-25, 16:14-26, 19:29-67.

107. In Bourget's system, a stimulation pulse generator is controlled by a processor, which detects values of a patient parameter based on sensor signals. Ex.1056 (Bourget), 8:14-62. Based on this sensor feedback, the processor can adjust stimulation parameters by controlling a stimulation pulse generator to deliver neurostimulation therapy according to a program for delivery of stimulation. *Id.* The program may define "a voltage or current pulse amplitude" for stimulation pulses delivered. *Id.*, 4:61-5:1, 8:32-41. The amplitude adjustment may involve adjustment of voltage or current. *Id.*, 13:19-25.

108. Likewise, in Gerber's system, an external monitor/programmer analyzes information from the sensors and automatically generates adjustments to the stimulation parameters to be applied by the neurostimulator, which can be applied without further input or authorization of the patient or clinician. Ex.1055 (Gerber), 2:1-16, 3:66-4:2, 8:47-67. Stimulation parameters that can be adjusted based on sensor feedback include, among other things, the amplitude of stimulation. *Id.*, 5:19-38. It would have been readily apparent to a POSA that the "amplitude" of electrical stimulation refers to the voltage and/or current of

stimulation, which is a primary determinant of the magnitude of the effect of the stimulation on neural tissue. Adjusting stimulation voltage necessarily and inherently adjusts the stimulation current, and vice-versa. Ex.1071 (De Lima), 499, Fig.4.

109. Accordingly, in my opinion, Mann, DiLorenzo, Gerber, and Bourget disclose the “detecting,” “receiving,” and “adjusting” limitations of claim 1.

110. In my opinion, it would have been obvious to modify and improve Svihra’s method to incorporate the teachings of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) described above for a multitude of reasons. First, Svihra, Mann, DiLorenzo, Gerber, and Bourget are each directed at providing electrical stimulation therapy by applying electrical stimulation to a nerve(s) of a patient for the treatment of medical conditions. Indeed, Svihra relates to electrical stimulation therapy for the treatment of overactive bladder. Ex.1004 (Svihra), 480. Likewise, Mann relates to electrical stimulation systems for reducing or eliminating incontinence and/or pelvic pain by stimulating various nerve pathways, including the posterior tibial nerve. Ex1084 (Mann), 10:65-11:19, 12:42-54. Gerber relates to a neurostimulation system for providing adaptive neurostimulation therapy, *i.e.*, electrical stimulation therapy, for treating “urinary control disorders” and “fecal control disorders” such as “urinary incontinence, fecal incontinence, or some combination thereof.” Ex.1055 (Gerber),

3:19-49. DiLorenzo relates to a neurological control system for providing electrical stimulation that can be used for treating a variety of conditions. Ex.1054 (DiLorenzo), 3:35-4:3. Bourget relates to a closed-loop system for providing electrical stimulation therapy for the treatment of various conditions, including incontinence. Ex.1056 (Bourget), 3:52-4:14, 4:41-51. Given that each of these references are directed to similar fields, *i.e.*, electrical stimulation therapy, a POSA would have known of the teachings of Mann, DiLorenzo, Gerber, and/or Bourget and looked to these references when considering modifications or improvements to Svihra's method.

111. Any argument that a POSA would not have considered the teachings of Mann, DiLorenzo, Gerber, or Bourget in combination with Svihra is, in my opinion, incorrect. For example, the fact that Mann, DiLorenzo, Gerber, and/or Bourget may describe embodiments of their systems in the context of invasive electrostimulation does not mean a POSA would not have considered the teachings of these references to modify or improve Svihra's noninvasive method. Similarly, the fact that a reference does not explicitly describe using the system primarily to electrically stimulate the posterior tibial nerve and/or for the treatment of overactive bladder/incontinence likewise does not mean a POSA would not have considered the teachings of these references to modify or improve Svihra's method. The distinctions between invasive and noninvasive electrical stimulation,

the specific target nerve, or the specific condition being treated are irrelevant in the context of the feedback and control systems taught by Mann, DiLorenzo, Gerber, and Bourget, as the features of those systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) could be implemented in either invasive or noninvasive electrical stimulation devices and techniques and could be implemented to target any nerve in the body or treat any condition able to be treated using electrical stimulation. In fact, the references themselves acknowledge that the systems can be applied in a wide variety of different contexts. Indeed, while DiLorenzo describes the invention primarily in the context of intracranial electrical stimulation, DiLorenzo indicates that the stimulating electrodes can be “implanted within” or be “adjacent to” (*i.e.*, noninvasive) various stimulation sites, including “a peripheral nerve” in the “lower extremities.” Ex.1054 (DiLorenzo), 6:38-43, 10:24-42, 28:33-56. The posterior tibial nerve is a peripheral nerve in the lower extremities, *i.e.*, leg. Similarly, Bourget explicitly states that the system is “applicable to any type of stimulation therapy” for treating a variety of conditions, including incontinence, and that “[a]ny implantable or external medical device may deliver closed-loop therapy according to the techniques of the invention.” Ex.1056 (Bourget), 4:23-60. Gerber likewise indicates that the system can be used to provide therapy broadly for “pelvic floor disorders” through stimulation of “nerves of the pelvic floor” including but not limited to the sacral and pudendal nerves.” Ex.1055 (Gerber),

3:19-34. Mann indicates that a variety of nerves can be targeted, including the posterior tibial nerve, to treat a range of conditions. Ex.1084 (Mann), 9:44-10:22, 12:26-54. Thus, a POSA would have considered the teachings of Mann, DiLorenzo, Gerber, and/or Bourget when considering modifications or improvements to Svihra's method.

112. Second, it also would have been obvious to modify or improve Svihra's method based on the teachings of Mann, DiLorenzo, Gerber, or Bourget because using the features of Mann's, DiLorenzo's, Gerber's, and Bourget's systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) would have simply involved the predictable use of elements in the prior art according to their established functions—such as, for example, the use of sensors, sensor feedback, and stimulation parameter adjustment for providing electrical stimulation therapy as described throughout the prior art. The use of these features and elements would have been predictable given the common and successful use of such features in similar electrostimulation devices and procedures as disclosed in the prior art such as the references discussed above.

113. Third, it further would have been obvious to modify or improve Svihra's method based on the teachings of Mann, DiLorenzo, Gerber, or Bourget because the features of Mann's, DiLorenzo's, Gerber's, and Bourget's systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) could simply be substituted for

the control system used by Svihra (*e.g.*, the EMG device, sensors, and intensity adjustment as discussed above, *see supra*, §§X.A.1.e-X.A.1.g). This would have involved nothing more than simply substituting known elements, and the results of such a substitution would have been predictable given, as discussed above, the common and successful use of such features in similar electrostimulation devices and procedures as disclosed in the prior art.

114. Fourth, in my opinion, a POSA would have been motivated to modify Svihra's procedure to incorporate the features of Mann, DiLorenzo, Gerber, or Bourget discussed above for the precise reasons disclosed in those references. Mann, for example, indicates sensed information (such as EMG signals) can be transmitted to the stimulator so that the electrical stimulation parameters "are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the" electrical stimulation. Ex.1084 (Mann), 25:65-26:20. DiLorenzo indicates that the system is beneficial because it, among other things, "incorporat[es] quantitative and qualitative measures of patient symptomatology and neuromotor circuitry function in the regulation of treatment magnitude," performs "automated determination of the optimum magnitude of treatment" in order to "expedite[] achievement of satisfactory treatment of the patient, reducing the time and number of interactions, typically in physician visits, endured by the patient," and "optimizes the efficiency of energy used in the treatment given to the

patient.” Ex.1054 (DiLorenzo), 4:38-5:38. Bourget indicates that the system “may be able to more quickly and easily provide a patient with efficacious therapy through automatically ‘learned’ associations of sensed patient parameter values with therapy information,” because a medical device “may automatically learn to automatically adjust therapy in the manner desired by the patient based on such associations” such that “the patient may no longer need to manually adjust the therapy because the medical device has learned to use values of one or more sensed patient parameters to anticipate any adjustments.” Ex.1056 (Bourget), 2:23-34; *see also id.*, 3:5-14, 3:65-4:14, 7:54-65. Likewise, Gerber states that adjustments to stimulation parameters by the system “provide an adaptive neurostimulation therapy that supports or enhances therapeutic efficacy based on the information obtained.” Ex.1055 (Gerber), 2:14-16. A POSA would have been motivated to incorporate the teachings of Mann, DiLorenzo, Bourget, or Gerber into Svihra’s method to achieve the benefits of those systems, such as improved feedback about the efficacy of the applied electrical stimulation therapy, regulation of treatment magnitude and/or side effects based on quantitative and qualitative measurements, and quicker and more effective treatment for patients by applying adjustments to treatment parameters based on sensor feedback.

C. Ground 3: Claims 2-10 Are Obvious Over Svihra (Ex.1004) Alone or in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), Further in View of the Knowledge of a POSA

115. As explained above, it is my opinion that Svihra (Ex.1004) alone or in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) invalidates claim 1 of the '477 patent. *See supra*, §§X.A and X.B. Based on my review and analysis of Svihra and with reasonable scientific certainty, it is my opinion that it would have further been obvious to modify Svihra's teachings based on the knowledge of a POSA to achieve the methods of claims 2-10 of the '477 patent. I am not aware of any evidence of secondary considerations of nonobviousness, but I reserve the right to respond to any such evidence that EMK may raise in this proceeding. My analysis supporting this opinion is detailed below.

1. Claim 2: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat fecal incontinence.

116. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that

“electrodes were placed behind the medial ankle of the left lower extremity.

Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.***”

Id., 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The “tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia. Although Svihra’s procedure was used to treat patients that “suffered from overactive bladder (OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat other conditions, such as fecal incontinence, based on the knowledge of a POSA.

117. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including fecal incontinence. For example, Queralto (Ex.1016), which was published online in December 2005, discloses a study to “assess the efficiency of posterior tibial nerve (PTN) transcutaneous electrical nerve stimulation (TENS) in the treatment of anal idiopathic incontinence [*i.e.*, fecal incontinence].” Ex.1016 (Queralto), 670. “Stimulation was done on the PTN route using a self-adhesive surface stimulation electrode without an implanted needle electrode. The negative contact electrode was placed on the ankle skin behind the internal malleolus, and the positive electrode, 10 cm above the negative electrode.” *Id.* According to Queralto, “[o]ur

preliminary study suggests that peripheral transcutaneous neuromodulation for fecal idiopathic incontinence is effective, at least in the short term. Its efficacy, morbidity, and cost-effectiveness should then be compared to sacral neuromodulation.” *Id.*, 672. Shafik (Ex.1064), published in 2003, also used posterior tibial nerve stimulation for treating fecal incontinence using a subcutaneous electrode implantation and achieved improvement of fecal incontinence in 78% of patients.” Ex.1064 (Shafik), Abstract.

118. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra’s technique for the treatment of fecal incontinence. First, using Svihra’s technique for the treatment of fecal incontinence would have simply involved applying known techniques (*e.g.*, treating fecal incontinence by stimulating the posterior tibial nerve as taught by, for example, Queralto and Shafik) to improve a known process (*e.g.*, Svihra’s electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of fecal incontinence in the prior art. *E.g.*, Ex.1016 (Queralto), 670; Ex.1064 (Shafik), Abstract.

119. Second, it would have been obvious to try treating fecal incontinence using Svihra’s technique. There were a finite number of known, predictable solutions for the treatment of fecal incontinence. Given that it was known in the

prior art to use electrical stimulation of the posterior tibial nerve to treat fecal incontinence, as taught by, for example, Queralto and Shafik, a POSA would have been motivated to try treating fecal incontinence using Svihra's method. A POSA would have expected success given the successful treatment of fecal incontinence using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating fecal incontinence by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, Shafik discloses an invasive method, this argument is, in my opinion, incorrect. Not only was it known in the art that fecal incontinence could be treated by noninvasively targeting the posterior tibial nerve (*e.g.*, Queralto), the knowledge of the successful use of electrical stimulation to treat fecal incontinence using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

120. Third, a POSA would have found it obvious to treat fecal incontinence using Svihra's method because known work in the field (*e.g.*, Queralto and Shafik) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like fecal

incontinence. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of fecal incontinence using similar methods as was known in the art (*e.g.*, Queralto and Shafik). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of fecal incontinence.

2. Claim 3: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat restless leg syndrome.

121. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that "electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**." *Id.*, 481. By "tibial nerve," Svihra clearly means the "posterior tibial nerve." The "tibial nerve" and "posterior tibial nerve" are interchangeable terms that refer to

the same nerve, which runs down the leg posterior to the tibia. Although Svihra's procedure was used to treat patients that "suffered from overactive bladder (OAB)," *id.*, 480, it would have been obvious to modify Svihra's teachings to treat other conditions, such as restless leg syndrome, based on the knowledge of a POSA.

122. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including restless leg syndrome. For example, DiLorenzo '103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*, nerves, of a patient. Ex.1068 (DiLorenzo '103), Abstract, [0019], [0072]. DiLorenzo '103 indicates the stimulating electrodes can be "implanted within" or be "adjacent to" (*i.e.*, noninvasive) various stimulation sites such as "a peripheral nerve" in the "lower extremities," including explicitly a posterior tibial nerve. *Id.*, [0072], [0093], [0175], [0348]. Claim 131 of DiLorenzo '103 indicates that a disease state that can be treated using the system includes "restless legs syndrome." *Id.*, cls.128-31.

123. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra's technique for the treatment of restless leg syndrome. First, using Svihra's technique for the treatment of restless leg syndrome would have simply involved applying known techniques

(*e.g.*, treating restless leg syndrome by stimulating the posterior tibial nerve as taught by, for example, DiLorenzo '103) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of restless leg syndrome in the prior art. *E.g.*, Ex.1068 (DiLorenzo '103), cls.128-31.

124. Second, it would have been obvious to try treating restless leg syndrome using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of restless leg syndrome. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat restless leg syndrome, as taught by, for example, DiLorenzo '103, a POSA would have been motivated to try treating restless leg syndrome using Svihra's method. A POSA would have expected success given the successful treatment of restless leg syndrome using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating restless leg syndrome by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat restless leg syndrome using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of

electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

125. Third, a POSA would have found it obvious to treat restless leg syndrome using Svihra's method because known work in the field (*e.g.*, DiLorenzo '103) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like restless leg syndrome. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of restless leg syndrome using similar methods as was known in the art (*e.g.*, DiLorenzo '103). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of restless leg syndrome.

3. Claim 4: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat premature ejaculation.

126. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra,

“[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**.”

Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that

“electrodes were placed behind the medial ankle of the left lower extremity.

Cathode was placed proximally and anode distally. After a control stimulation

accompanied by optimalization of the electrode position and set intensity of

stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.***”

Id., 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The

“tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to

the same nerve, which runs down the leg posterior to the tibia. Although Svihra’s

procedure was used to treat patients that “suffered from overactive bladder

(OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat

other conditions, such as premature ejaculation, based on the knowledge of a

POSA.

127. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including premature ejaculation. For example, Gerber ‘372 discloses systems for treating various disorders of the pelvic floor by delivering electrical stimuli to the sacral nerves. Ex.1069 (Gerber ‘372), Abstract, [0002]. Among the pelvic floor disorders that Gerber ‘372’s system treats are sexual dysfunctions including premature ejaculation. *Id.*, Abstract, [0004], [0021], [0047-49], cl.1. Gerber ‘372 states that

“[a]s employed herein, the term ‘sacral nerve []’ means any one of the sacral nerves, portions of the sacral nerve(s), nerves neurologically connected to any one of the sacral nerves and in relatively close physical proximity thereto, and extensions or branches of any one of the sacral nerves.” *Id.*, [0064]. The posterior tibial nerve is a sacral nerve as it reaches the spinal cord via the dorsal roots of the sacral nerves. *See, e.g.*, Ex.1080 (Boveja), Abstract, [0180] (“sacral nerves” include “sacral nerves S1, S2, S3, S4, pudendal nerve, superior gluteal nerve, lumbo-sacral trunk, inferior gluteal nerve, common fibular nerve, **tibial nerve**, posterior femoral cutaneous nerve, sciatic nerve, and obturator nerve.”) (emphasis added).

128. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra’s technique for the treatment of premature ejaculation. First, using Svihra’s technique for the treatment of premature ejaculation would have simply involved applying known techniques (*e.g.*, treating premature ejaculation by stimulating sacral nerves such as the posterior tibial nerve as taught by, for example, Gerber ‘372) to improve a known process (*e.g.*, Svihra’s electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of premature ejaculation in the prior art. *E.g.*, Ex.1069 (Gerber ‘372), Abstract, [0004], [0021], [0047-49], cl.1.

129. Second, it would have been obvious to try treating premature ejaculation using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of premature ejaculation. Given that it was known in the prior art to use electrical stimulation of the sacral nerves such as the posterior tibial nerve to treat premature ejaculation, as taught by, for example, Gerber '372, a POSA would have been motivated to try treating premature ejaculation using Svihra's method. A POSA would have expected success given the successful treatment of premature ejaculation using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating premature ejaculation by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, Gerber '372 discloses an invasive method, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat premature ejaculation using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

130. Third, a POSA would have found it obvious to treat premature ejaculation using Svihra's method because known work in the field (*e.g.*, Gerber '372) would have prompted variations to Svihra's method based on design

incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like premature ejaculation. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of premature ejaculation using similar methods as was known in the art (*e.g.*, Gerber '372). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of premature ejaculation.

4. Claim 5: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat chronic pain.

131. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that "electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**."

Id., 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The “tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia. Although Svihra’s procedure was used to treat patients that “suffered from overactive bladder (OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat other conditions, such as chronic pain, based on the knowledge of a POSA.

132. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including chronic pain. For example, van Balken 2003 (Ex.1065), which was published in 2003, discloses a study to evaluate the results of percutaneous tibial nerve stimulation in patients with chronic pain. Ex.1065 (van Balken 2003), 158. van Balken concluded that percutaneous tibial nerve stimulation “may have a place in the treatment of patients with chronic pelvic pain who have already tried many other therapies and are left with no further option.” *Id.* Similarly, Whitehurst (Ex.1066), published in 2005, discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain. Ex.1066(Whitehurst), [0005], [0015], [0055].

133. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra’s technique for the treatment of chronic pain. First, using Svihra’s technique for the treatment of chronic pain

would have simply involved applying known techniques (*e.g.*, treating chronic pain by stimulating the posterior tibial nerve as taught by, for example, van Balken and Whitehurst) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of chronic pain in the prior art. *E.g.*, Ex.1065 (van Balken 2003), 158; Ex.1066 (Whitehurst), [0005], [0015], [0055].

134. Second, it would have been obvious to try treating chronic pain using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of chronic pain. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat chronic pain, as taught by, for example, van Balken and Whitehurst, a POSA would have been motivated to try treating chronic pain using Svihra's method. A POSA would have expected success given the successful treatment of chronic pain using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating chronic pain by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat chronic pain using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical

stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

135. Third, a POSA would have found it obvious to treat chronic pain using Svihra's method because known work in the field (*e.g.*, van Balken and Whitehurst) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like chronic pain. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of chronic pain using similar methods as was known in the art (*e.g.*, van Balken and Whitehurst). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of chronic pain.

5. Claim 6: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat osteoarthritis or arthritis.

136. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra,

“[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**.”

Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that

“electrodes were placed behind the medial ankle of the left lower extremity.

Cathode was placed proximally and anode distally. After a control stimulation

accompanied by optimization of the electrode position and set intensity of

stimulation ***we had proceeded on with a therapeutic stimulation of tibial nerve.***”

Id., 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The

“tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to

the same nerve, which runs down the leg posterior to the tibia. Although Svihra’s

procedure was used to treat patients that “suffered from overactive bladder

(OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat

other conditions, such as osteoarthritis or arthritis, based on the knowledge of a

POSA.

137. Well before 2006, it was known that many other conditions could be

treated by providing electrical stimulation to the posterior tibial nerve, including

osteoarthritis or arthritis. For example, Jaax (Ex.1067), which was filed in

December 2005, discloses the treatment of osteoarthritis by applying electrical

stimulation to a stimulation site, such as the posterior tibial nerve. Ex.1067 (Jaax),

3:13-21, 5:40-49, 5:50-6:11. Similarly, Whitehurst (Ex.1066) discloses applying an

electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat

chronic pain associated with conditions including rheumatoid arthritis. Ex.1066 (Whitehurst), [0005], [0015], [0017], [0055].

138. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra's technique for the treatment of osteoarthritis or arthritis. First, using Svihra's technique for the treatment of osteoarthritis or arthritis would have simply involved applying known techniques (*e.g.*, treating osteoarthritis or arthritis by stimulating the posterior tibial nerve as taught by, for example, Jaax and Whitehurst) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of osteoarthritis or arthritis in the prior art. *E.g.*, Ex.1067 (Jax), 3:13-21, 5:40-49, 5:50-6:11; Ex.1066 (Whitehurst), [0005], [0015], [0017], [0055].

139. Second, it would have been obvious to try treating osteoarthritis or arthritis using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of osteoarthritis or arthritis. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat osteoarthritis or arthritis, as taught by, for example, Jaax and Whitehurst, a POSA would have been motivated to try treating osteoarthritis or arthritis using Svihra's method. A POSA would have expected success given the successful

treatment of osteoarthritis or arthritis using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating osteoarthritis or arthritis by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat osteoarthritis or arthritis using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

140. Third, a POSA would have found it obvious to treat osteoarthritis or arthritis using Svihra's method because known work in the field (*e.g.*, Jaax and Whitehurst) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like osteoarthritis or arthritis. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of osteoarthritis or arthritis using similar methods as was known in the art (*e.g.*, Jaax and Whitehurst). Accordingly, in my opinion, it would have been

obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of osteoarthritis or arthritis.

6. Claim 7: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof responsible for neuropathic pain to treat neuropathic pain.

141. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that "electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**." *Id.*, 481. By "tibial nerve," Svihra clearly means the "posterior tibial nerve." The "tibial nerve" and "posterior tibial nerve" are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia. Although Svihra's procedure was used to treat patients that "suffered from overactive bladder (OAB)," *id.*, 480, it would have been obvious to modify Svihra's teachings to treat other conditions, such as neuropathic pain, based on the knowledge of a POSA.

142. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including neuropathic pain. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic neuropathic pain. Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0028-29], [0055]. Whitehurst further explicitly discloses delivering the electrical stimulus to the posterior tibial nerve or branch thereof ***responsible for the neuropathic pain***. According to Whitehurst, “a leadless microstimulator (200) may be subcutaneously implanted within the leg (220) of a patient in a location where the patient feels pain. For illustrative purposes, it is assumed in the example of FIG. 4 that the patient feels pain in an upper thigh area (221) of the leg. ***The peripheral nerve causing the pain may be the tibial nerve (210)***. . . . electrical and/or drug stimulation applied to the neural tissue (212) by the subcutaneously implanted microstimulator (200) ***may effectively stimulate the tibial nerve (210) and treat the pain felt by the patient***.” *Id.*, [0055].

143. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra’s technique to deliver electrical stimulation to the posterior tibial nerve or branch thereof responsible for neuropathic pain for the treatment of neuropathic pain. First, using Svihra’s technique for the treatment of neuropathic pain would have simply involved

applying known techniques (*e.g.*, treating neuropathic pain by stimulating the posterior tibial nerve responsible for the pain as taught by, for example, Whitehurst) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of neuropathic pain in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0055].

144. Second, it would have been obvious to try treating neuropathic pain by applying stimulation to the posterior tibial nerve or branch responsible for the pain using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of neuropathic pain. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat neuropathic pain, as taught by, for example, Whitehurst, a POSA would have been motivated to try treating neuropathic pain using Svihra's method. A POSA would have expected success given the successful treatment of neuropathic pain using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating neuropathic pain by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat neuropathic pain

using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

145. Third, a POSA would have found it obvious to treat neuropathic pain by applying stimulation to the posterior tibial nerve or branch responsible for the pain using Svihra's method because known work in the field (*e.g.*, Whitehurst) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like neuropathic pain. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of neuropathic pain using similar methods as was known in the art (*e.g.*, Whitehurst). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of neuropathic pain.

146. Additionally, to the extent that it might be argued that a POSA would not have found it obvious to try treating neuropathic pain by treating the "branch thereof [of the posterior tibial nerve] responsible for neuropathic pain," in addition to or alternatively to the posterior tibial nerve itself, this argument is in my opinion

incorrect. It would be obvious to a POSA that stimulation treatment could be directed toward a specific branch of a nerve structure responsible for pain; the tibial nerve itself is such a branch of a larger nerve structure, the sciatic nerve, which is also itself a branch of a larger nerve structure, the sacral plexus. Thus, it would have been obvious to a POSA to apply electrical stimulation to whatever nerve or branch of nerve is responsible for or causing a patient's neuropathic pain.

7. Claim 8: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat neuralgia.

147. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that "electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimalization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**." *Id.*, 481. By "tibial nerve," Svihra clearly means the "posterior tibial nerve." The "tibial nerve" and "posterior tibial nerve" are interchangeable terms that refer to

the same nerve, which runs down the leg posterior to the tibia. Although Svihra's procedure was used to treat patients that "suffered from overactive bladder (OAB)," *id.*, 480, it would have been obvious to modify Svihra's teachings to treat other conditions, such as neuralgia, based on the knowledge of a POSA.

148. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including neuralgia. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain including neuralgia. Ex.1066 (Whitehurst), [0005], [0015], [0019-20], [0055].

149. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra's technique for the treatment of neuralgia. First, using Svihra's technique for the treatment of neuralgia would have simply involved applying known techniques (*e.g.*, treating neuralgia by stimulating the posterior tibial nerve as taught by, for example, Whitehurst) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of neuralgia in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0055].

150. Second, it would have been obvious to try treating neuralgia using Svihra's technique. There were a finite number of known, predictable solutions for

the treatment of neuralgia. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat neuralgia, as taught by, for example, Whitehurst, a POSA would have been motivated to try treating neuralgia using Svihra's method. A POSA would have expected success given the successful treatment of neuralgia using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating neuralgia by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat neuralgia using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

151. Third, a POSA would have found it obvious to treat neuralgia using Svihra's method because known work in the field (*e.g.*, Whitehurst) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like neuralgia. As indicated above, such a variation to Svihra's method would have been predictable

to a POSA given the successful treatment of neuralgia using similar methods as was known in the art (*e.g.*, Whitehurst). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of neuralgia.

8. Claim 9: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat atrophy.

152. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved delivering electrical stimulus to the posterior tibial nerve. According to Svihra, "[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**." Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that "electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**." *Id.*, 481. By "tibial nerve," Svihra clearly means the "posterior tibial nerve." The "tibial nerve" and "posterior tibial nerve" are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia. Although Svihra's procedure was used to treat patients that "suffered from overactive bladder

(OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat other conditions, such as atrophy, based on the knowledge of a POSA.

153. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including atrophy. It was known, for example, that atrophy can be caused by conditions such as paralysis or osteoarthritis. *E.g.*, Ex.1070 (Davis), [0003] (“Loss of upper motor control due to stroke results primarily in limb paralysis and secondarily in disuse atrophy of the affected muscle and shoulder joint. This atrophy may result in complications such as joint pain and skin breakdown, which may be even more troubling to the patient than the loss of motor function.”); Ex.1067 (Jaax), 1:26-34 (“Non-surgical techniques for treating osteoarthritis include weight loss, rest, physical therapy, orthotics, and heat. Weight loss alleviates stress on an affected joint and is sometimes effective in treating osteoarthritis. Short-term rest of an affected joint may be effective in temporarily relieving pain. However, longer periods of rest may result in muscle atrophy and decreased joint mobility.”). Clearly, treating the underlying condition (*e.g.*, paralysis or osteoarthritis) would eliminate the complications caused by the condition, such as atrophy.

154. Using electrical stimulation of the posterior tibial nerve to treat paralysis and osteoarthritis, conditions that cause atrophy, was known. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to

peripheral nerves, including the posterior tibial nerve, to treat chronic pain causing paralysis. Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]. DiLorenzo ‘103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*, nerves, of a patient. Ex.1068 (DiLorenzo ‘103), Abstract, [0019], [0072]. According to DiLorenzo ‘103, the system can be used for “electrical stimulation of peripheral nerves, such as stimulation of the **tibial** or peroneal nerves for use in **eliciting the flexion withdrawal reflex to facilitate gait restoration in paraplegics.**” *Id.*, [0348]. A paraplegic is a person with paralysis, and therefore DiLorenzo ‘103 discloses electrical stimulation of the tibial nerve to treat paralysis. Moreover, Jaax (Ex.1067) discloses the treatment of osteoarthritis by applying electrical stimulation to a stimulation site, such as the posterior tibial nerve. Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11.

155. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra’s technique for the treatment of atrophy. First, using Svihra’s technique for the treatment of atrophy would have simply involved applying known techniques (*e.g.*, treating conditions responsible for causing atrophy, such as paralysis or osteoarthritis, by stimulating the posterior tibial nerve as taught by, for example, Whitehurst, DiLorenzo ‘103, or Jaax) to improve a known process (*e.g.*, Svihra’s electrical stimulation technique). The

result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of conditions that cause atrophy in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]; Ex.1068 (DiLorenzo '103), Abstract, [0019], [0072], [0348]; Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11.

156. Second, it would have been obvious to try treating atrophy using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of atrophy and conditions that cause atrophy. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat conditions that cause atrophy, as taught by, for example, Whitehurst, DiLorenzo '103, and Jaax, a POSA would have been motivated to try treating atrophy and conditions that cause it using Svihra's method. A POSA would have expected success given the successful treatment of conditions that cause atrophy, such as paralysis and osteoarthritis, using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating atrophy or conditions that cause it by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat paralysis using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of

electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

157. Third, a POSA would have found it obvious to treat atrophy and conditions that cause it using Svihra's method because known work in the field (*e.g.*, Whitehurst, DiLorenzo '103, Jaax) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like atrophy or conditions that cause it. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of conditions that atrophy using similar methods as was known in the art (*e.g.*, Whitehurst, DiLorenzo '103, Jaax). Accordingly, in my opinion, it would have been obvious to use Svihra's technique of electrically stimulating the posterior tibial nerve for the treatment of conditions that can cause atrophy, including paralysis or osteoarthritis.

9. Claim 10: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat paralysis.

158. As explained above, Svihra alone or in combination with Mann, DiLorenzo, Bourget, or Gerber discloses all the limitations of claim 1. *See supra*, §§X.A.1 and X.B.1. Further, as explained above, Svihra's method involved

delivering electrical stimulus to the posterior tibial nerve. According to Svihra, “[t]he aim of this study was to use non-invasive stimulation of the **tibial nerve**.” Ex.1004 (Svihra), 480 (emphasis added). Svihra further explicitly states that “electrodes were placed behind the medial ankle of the left lower extremity. Cathode was placed proximally and anode distally. After a control stimulation accompanied by optimization of the electrode position and set intensity of stimulation **we had proceeded on with a therapeutic stimulation of tibial nerve**.” *Id.*, 481. By “tibial nerve,” Svihra clearly means the “posterior tibial nerve.” The “tibial nerve” and “posterior tibial nerve” are interchangeable terms that refer to the same nerve, which runs down the leg posterior to the tibia. Although Svihra’s procedure was used to treat patients that “suffered from overactive bladder (OAB),” *id.*, 480, it would have been obvious to modify Svihra’s teachings to treat other conditions, such as paralysis, based on the knowledge of a POSA.

159. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including paralysis. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain causing paralysis. Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]. DiLorenzo ‘103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*,

nerves, of a patient. Ex.1068 (DiLorenzo '103), Abstract, [0019], [0072].

According to DiLorenzo '103, the system can be used for “electrical stimulation of peripheral nerves, such as stimulation of the **tibial** or peroneal nerves for use in ***eliciting the flexion withdrawal reflex to facilitate gait restoration in paraplegics.***” *Id.*, [0348]. A paraplegic is a person with paralysis, and therefore DiLorenzo '103 discloses electrical stimulation of the tibial nerve to treat paralysis.

160. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Svihra's technique for the treatment of paralysis. First, using Svihra's technique for the treatment of paralysis would have simply involved applying known techniques (*e.g.*, treating paralysis by stimulating the posterior tibial nerve as taught by, for example, Whitehurst and DiLorenzo '103) to improve a known process (*e.g.*, Svihra's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of paralysis in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]; Ex.1068 (DiLorenzo '103), Abstract, [0019], [0072], [0348].

161. Second, it would have been obvious to try treating paralysis using Svihra's technique. There were a finite number of known, predictable solutions for the treatment of paralysis. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat paralysis, as taught by, for example,

Whitehurst and DiLorenzo '103, a POSA would have been motivated to try treating paralysis using Svihra's method. A POSA would have expected success given the successful treatment of paralysis using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating paralysis by electrically stimulating the posterior tibial nerve using Svihra's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat paralysis using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

162. Third, a POSA would have found it obvious to treat paralysis using Svihra's method because known work in the field (*e.g.*, Whitehurst and DiLorenzo '103) would have prompted variations to Svihra's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like paralysis. As indicated above, such a variation to Svihra's method would have been predictable to a POSA given the successful treatment of paralysis using similar methods as was known in the art (*e.g.*, Whitehurst and DiLorenzo

‘103). Accordingly, in my opinion, it would have been obvious to use Svihra’s technique of electrically stimulating the posterior tibial nerve for the treatment of paralysis.

D. Ground 4: Claim 1 Is Obvious Over Amarenco (Ex.1005) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056)

163. Based on my review and analysis of Amarenco and with reasonable scientific certainty, it is my opinion that it would have been obvious to modify Amarenco’s teachings based on Mann, DiLorenzo, Gerber, and Bourget to achieve the method of claim 1 of the ‘477 patent. I am not aware of any evidence of secondary considerations of nonobviousness, but I reserve the right to respond to any such evidence that EMK may raise in this proceeding. My analysis supporting this opinion is detailed below.

1. Claim 1:

a. *[1.p] A method of performing electrical stimulation therapy, comprising:*

164. Amarenco studied “by urodynamic investigation possible detrusor activity modifications during acute tibial nerve stimulation in a population presenting with symptoms (urge incontinence and frequency) secondary to overactive bladder.” Ex.1005 (Amarenco), 2210. Amarenco performed electrical stimulation of patients’ posterior tibial nerve. Indeed, Amarenco’s procedure involved “left posterior tibial nerve stimulation using a surface self-adhesive

electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” *Id.* Amarenco therefore discloses a method of performing electrical stimulation therapy, *i.e.*, noninvasive electrical stimulation for therapy in patients with OAB.

- b. [1.a] non-invasively positioning a first portion of a patient's body relative to an electrical stimulator such that a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the electrical stimulator;**

165. Amarenco’s procedure involved “left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10Hz. frequency and 200 milliseconds wide.” *Id.* More specifically, Amarenco states:

Stimulation was done using a self-adhesive surface stimulation electrode without an implanted needle electrode. Contact electrodes were placed with electrode gel on the ankle skin with the negative electrode behind the internal malleolus and the positive electrode 10 cm. above the negative electrode. The correct position of the negative electrode was determined by visualization of rhythmic flexion of the toes secondary to plantar muscle contraction during stimulation delivered at 1 hz. The intensity level was then chosen as the intensity immediately under the threshold determining motor contraction. In addition, no pain was to be noted during the stimulation procedure, which necessarily had to be comfortable to the patient. Stimulation frequency during cystometry was then applied at 10 Hz. and a pulse width of 200 milliseconds in continuous mode.

Id., 2211. According to Amarenco, “[t]his technique is cheap, noninvasive and free of pharmaceutical side effects.” *Id.*, 2214.

166. A POSA would understand Amarenco's procedure involved "***non-invasively positioning a first portion of a patient's body relative to an electrical stimulator,***" as claimed. Not only does Amarenco explicitly state the procedure was non-invasive (*see id.*), a POSA would understand that a "self-adhesive surface stimulation electrode" used by Amarenco do not break the patients' skin and therefore, that the procedure was non-invasive. A POSA would further appreciate that electrodes applying stimulation at "10 Hz. and a pulse width of 200 milliseconds in continuous mode" are an "electrical stimulator," as claimed. *Id.* Finally, a POSA would understand that placing electrodes "on the ankle skin with the negative electrode behind the internal malleolus and the positive electrode 10 cm. above the negative electrode" necessarily means that a portion of the patients' bodies was positioned relative to an electrical stimulator, as claimed.

167. Amarenco also discloses "***a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the electrical stimulator,***" as claimed. Amarenco's procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus." *Id.*, 2210. As discussed above, Amarenco's electrodes were "in proximity to" the patients' posterior tibial nerve because the electrodes were placed "on the ankle skin behind the internal malleolus" (*i.e.*, near the ankle) and provided electrical stimulation to the patients' posterior tibial nerve.

c. [1.b] passing a current through the electrical stimulator; and

168. Amarenco's procedure involved applying stimulation "at 10 Hz. and a pulse width of 200 milliseconds in continuous mode" via a "self-adhesive surface stimulation electrode without an implanted needle electrode." Ex.1005 (Amarenco), 2211. Amarenco's "self-adhesive surface stimulation electrodes" would necessarily have been connected to an electrical stimulator source. The "self-adhesive surface stimulation electrodes" and/or the electrical stimulator source are an "electrical stimulator," as claimed. Amarenco explicitly states that the electrodes provided stimulation "at 10 Hz. and a pulse width of 200 milliseconds in continuous mode." *Id.* In order for electrical stimulation to be applied through the electrodes, current would necessarily have had to have been passed through the electrical stimulator source and electrodes. Accordingly, in my opinion and based on Amarenco's explicit disclosures, current was necessarily passed through the electrical stimulator in Amarenco's method.

d. [1.c] delivering an electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof;

169. Amarenco's procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." *Id.*, 2210. Further, Amarenco indicates that "[s]timulation

frequency during cystometry was then applied at 10 Hz. and a pulse width of 200 milliseconds in continuous mode. This second cystometry during posterior tibial nerve stimulation was started immediately after determining the chosen stimulation. Neurostimulation was continuous during the whole second study.” *Id.*, 2211. In other words, Amarenco delivered an electrical stimulus from the “surface self-adhesive electrodes”/electrical stimulator source (*i.e.*, the electrical stimulator) in order to stimulate the posterior tibial nerve. The posterior tibial nerve necessarily received the electrical stimulation, particularly given Amarenco’s conclusion that “[t]hese results suggest an objective acute effect of posterior tibial nerve stimulation on urodynamic parameters. Improved bladder overactivity is an encouraging argument to propose posterior tibial nerve stimulation as a noninvasive treatment modality in clinical practice.” *Id.*, 2210. Therefore, in my opinion, Amarenco delivered an electrical stimulus from the electrical stimulator to the posterior tibial nerve, as claimed.

- e. ***[1.d] detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body;***
- [1.e] receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy; and***
- [1.f] adjusting the current via a controller in communication with the electrical stimulator based on the feedback.***

170. During Amarenco's study, the researchers detected electrical conduction through the posterior tibial nerve and/or muscular response caused by the electrical conduction through the posterior tibial nerve via a sensor, i.e., EMG. Indeed, Amarenco's results included EMG results, clearly indicating that Amarenco measured EMG signals via EMG electrodes/sensors. Ex.1005 (Amarenco), 2212, Figs.3-4. It is not clear whether Amarenco received the EMG feedback or adjusted the current of electrical stimulation based on the feedback. To the extent it is determined Amarenco does not disclose these limitations, in my opinion it would have been obvious to modify Amarenco based on the teachings of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) to arrive at the method of claim 1.

171. Well before 2006, electrical stimulation devices and techniques were known that used sensors to detect patient response to treatment and to use feedback from the sensors to adjust treatment parameters, such as electrical stimulation current or voltage. For example, Mann (Ex.1084) discloses a method and system for treatment of incontinence, urgency, frequency, and/or pelvic pain via electrostimulation of various nerves and branches emanating from the sacral nerve roots. Ex.1084 (Mann), Abstract, 10:65-11:19, 11:43-12:7. A preferred stimulation location is the tibial nerve (*i.e.*, the posterior tibial nerve). *Id.*, 12:42-54, 16:28-41. Mann's system includes a microstimulator "where current pulses delivered from its electrodes . . . stimulate nerve fibers," as well as electronic circuitry that dictates, among other things, the amplitude of the electrical current pulse. *Id.*, 14:53-15:24. According to Mann, "[i]n order to help determine the strength . . . of electrical stimulation and/or the amount and/or type(s) of stimulating drug(s) required to produce the desired therapeutic effect, in one preferred embodiment, a patient's response to and/or need for treatment is sensed. For instance, the muscle activity produced in response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG). Thus, when electrodes and/or catheters of a stimulator are implanted, for example, near the dorsal nerve of the clitoris (a branch of the pudendal nerve), the signals from an EMG sensor built into the stimulator may be used to adjust stimulation parameters." *Id.*, 23:4-15.

172. Mann further indicates that in some embodiments, “a stimulator, or a group or two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, the sensed information is transmitted to the stimulating stimulator(s). Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information. Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:9.

173. DiLorenzo (Ex.1054) discloses a system that uses sensors to monitor patient signals resulting from electrical stimulation therapy and adjusts treatment parameters based on sensor feedback. Ex.1054 (DiLorenzo), 3:35-48. DiLorenzo’s system includes at least one stimulating electrode to deliver neural modulation signals to nervous system components of the patient, at least one sensor “to sense at least one parameter, including but not limited to physiologic values and neural signals, which is indicative of at least one of disease state, magnitude of symptoms, and response to therapy,” and a stimulating and recording unit to generate the neural modulation signal “based upon a neural response sensed by” the sensors. *Id.*, 4:4-18. According to DiLorenzo, the stimulating electrodes can be “implanted

within” or be “adjacent to” (*i.e.*, noninvasive) various stimulation sites, including “a peripheral nerve” in the “lower extremities.” *Id.*, 6:38-43, 10:24-42, 28:33-56.

The posterior tibial nerve is a peripheral nerve in the lower extremities, *i.e.*, leg.

The sensor may include EMG electrodes that detect electrical conduction through a nerve or muscular response caused by electrical conduction through the nerve. *Id.*, 6:58-67, 9:1-14, 9:34-46, 9:54-65, 23:31-24:23, 29:27-44. Based on feedback from the sensors, the system automatically adjusts control parameters such as electrical stimulation treatment parameters in real-time “to provide optimal control of disease state.” *Id.*, 11:8-42, 13:35-53. Control parameters may include, for example, pulse amplitude. *Id.*, 12:18-25, 16:14-26. Pulse amplitude may include adjustment of either pulse voltage or pulse current. *Id.*, 16:24-26, 19:29-67.

174. Similarly, Bourget (Ex.1056) discloses a system that delivers closed-loop therapy (*e.g.*, electrical stimulation) based on patient parameters sensed by a sensor. Ex.1056 (Bourget), 3:52-4:14. Bourget’s system includes “a medical device that delivers a therapy to a patient, a sensor that senses a parameter of the patient, a user interface, and a processor. The processor receives a therapy adjustment from the patient via the user interface, determines therapy information based on the therapy adjustment, automatically associates a value of the sensed parameter detected via the sensor with the therapy information in response to receiving the therapy adjustment, subsequently detects the value via the sensor, and

automatically controls the medical device to deliver therapy to the patient according to the therapy information associated with the value in response to the detection.” *Id.*, 2:45-57. The system is “applicable to any type of stimulation therapy” for treating a variety of conditions, including incontinence. *Id.*, 4:23-25, 4:47-51. The system includes a medical device for delivering neurostimulation therapy such as electrical stimulation, which can be “[a]ny implantable or external medical device.” *Id.*, 4:28-35, 4:52-60. The medical device provides therapy according to a program for delivery of stimulation, which may define “a voltage or current pulse amplitude” for stimulation pulses. *Id.*, 4:61-5:1, 8:32-41. The amplitude adjustment may involve adjustment of voltage or current. *Id.*, 13:19-25. Sensed patient parameters may include, among other things, physiological parameters of a patient, including EMG signals. *Id.*, 7:32-44.

175. Gerber (Ex.1055) likewise discloses a system that provides adaptive neurostimulation therapy via information obtained from sensors to alleviate fecal or urinary incontinence. Ex.1055 (Gerber), 2:1-16. Gerber’s system includes a neurostimulator that provides electrical stimulation to the patient, sensors, and an external monitor/programmer that transmits information such as adjustments to stimulation parameters to the neurostimulator. *Id.*, 3:35-4:18. The sensors “may provide a variety of information indicative of the level of efficacy achieved by the neurostimulation therapy delivered by neurostimulator,” including a physiological

state of the patient such as electromyographic activity (*i.e.*, EMG). *Id.*, 5:39-6:7.

Stimulation parameters that can be adjusted based on sensor feedback include, among other things, details regarding the amplitude of stimulation. *Id.*, 5:19-38. It would have been readily apparent to a POSA that the “amplitude” of electrical stimulation refers to the voltage and/or current of stimulation, which is a primary determinant of the magnitude of the effect of the stimulation on neural tissue.

Adjusting stimulation voltage necessarily and inherently adjusts the stimulation current, and vice-versa. Ex.1071 (De Lima), 499, Fig.4. The system may “without further input, or authorization from any other source, input and utilize the new stimulation parameters,” or can send proposed new stimulation parameters to a clinician or the patient for approval. Ex.1055 (Gerber), 8:47-67.

176. Each of Mann (Ex.1084), DiLorenzo (Ex.1054), Bourget (Ex.1056), and Gerber (Ex.1055) discloses the “detecting...,” “receiving...,” and “adjusting...” limitations of claim 1 of the ‘477 patent.

177. In particular, Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), and Bourget (Ex.1056) each disclose “***detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body.***” As explained above, based on the claim language, specification, and the

knowledge of a POSA regarding detecting electrical conduction and muscular response in the body, a POSA would have understood the claimed “at least one sensor” that “detect[s] electrical conduction through the posterior tibial nerve or branch thereof” or “detect[s] a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof” includes EMG electrodes/sensors. *See supra*, §X.A.1.e.

178. Mann (Ex.1084) discloses the “detecting” limitation of claim 1. As discussed above, Mann’s system includes sensors, including EMG sensors, that provide sensed information “used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:32-34. For example, Mann states “[i]n order to help determine the strength . . . of electrical stimulation and/or the amount and/or type(s) of stimulating drug(s) required to produce the desired therapeutic effect, in one preferred embodiment, a patient's response to and/or need for treatment is sensed. ***For instance, the muscle activity produced in response to stimulation may be detected, e.g., via recording of the associated electromyograph (EMG).***” *Id.*, 23:4-15 (emphasis added); *see also id.*, 24:24-28, 25:65-26:20.

179. DiLorenzo (Ex.1054) also discloses the “detecting” limitation of this claim. As discussed above, DiLorenzo’s system includes at least one stimulating electrode to deliver neural modulation signals to nervous system components of the patient, at least one sensor “to sense at least one parameter, including but not

limited to physiologic values and neural signals, which is indicative of at least one of disease state, magnitude of symptoms, and response to therapy,” and a stimulating and recording unit to generate the neural modulation signal “based upon a neural response sensed by” the sensors. Ex.1054 (DiLorenzo), 4:4-18. According to DiLorenzo, the sensor may include EMG electrodes that detect electrical conduction through a nerve or muscular response caused by electrical conduction through the nerve. *Id.*, 6:58-67, 9:1-14, 9:34-46, 9:54-65, 23:31-24:23, 29:27-44.

180. Bourget (Ex.1056) likewise discloses this limitation. Bourget’s system includes “a medical device that delivers a therapy to a patient, a sensor that senses a parameter of the patient, a user interface, and a processor.” Ex.1056 (Bourget), 2:45-57. Sensed patient parameters may include, among other things, physiological parameters of a patient, including EMG signals. *Id.*, 7:32-44.

181. Gerber (Ex.1055) also discloses this limitation. Gerber’s system includes a neurostimulator that provides electrical stimulation to the patient, sensors, and an external monitor/programmer that transmits information such as adjustments to stimulation parameters to the neurostimulator. Ex.1055 (Gerber), 3:35-4:18. The sensors “may provide a variety of information indicative of the level of efficacy achieved by the neurostimulation therapy delivered by

neurostimulator 12,” including a physiological state of the patient such as electromyographic activity (*i.e.*, EMG). *Id.*, 5:39-6:7.

182. Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), and Bourget (Ex.1056) also disclose “***receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy.***” For example, sensors in Mann’s system, such as EMG sensors, provide sensed information “used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:4-34. According to Mann, “[i]n one preferred embodiment, a stimulator, or a group of two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, ***the sensed information is transmitted to the stimulating stimulator(s).*** Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information. Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:20.

183. DiLorenzo’s system receives signals from the sensor(s), such as an EMG sensor, and uses the signals to automatically adjust control parameters of the

electrical stimulation in real-time “to provide optimal control of disease state.”

Ex.1054 (DiLorenzo), 8:39-50, 11:8-42, 13:35-53. As explained above, a signal from an EMG electrode/sensor is indicative of the detected electrical conduction or muscular response. According to DiLorenzo, the system “considers neural response, in the form of the sensory feedback, as an indication of neurological disease state and/or responsiveness to therapy, in the determination of treatment parameters.” *Id.*, 3:49-53.

184. Similarly, Bourget’s system “detects [a value of the sensed parameter] via the sensor, and automatically controls the medical device to deliver therapy to the patient according to the therapy information associated with the value in response to the detection.” Ex.1056 (Bourget), 2:45-57; *see also id.*, 8:62 (“IMD 12 includes a sensor 40 that senses a patient parameter, and processor 34 detects values of the patient parameter based on the signal generated by sensor 40 as a function of the patient parameter”). The sensor can be an EMG electrode/sensor, which a POSA would understand is indicative of the detected electrical conduction or muscular response.

185. Additionally, Gerber’s system includes an external monitor/programmer that “may receive information from neurostimulator 12 and/or sensor 20 by wireless telemetry” and “may record the received information, analyze the information, and adjust stimulation parameters based on the

information or some combination thereof.” Ex.1055 (Gerber), 3:50-4:2; *see also id.*, 5:19-21, 5:39-41, 7:19-23. As with Mann, DiLorenzo, Bourget, given that Gerber’s sensor can be an EMG electrode/sensor, a POSA would appreciate the signal is indicative of the detected electrical conduction or muscular response.

186. Finally, Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), and Bourget (Ex.1056) each disclose “***adjusting the current via a controller in communication with the electrical stimulator based on the feedback.***” Mann explicitly states that “[t]he sensed information is preferably used to control the stimulation parameters in a closed-loop manner.” Ex.1084 (Mann), 23:4-34. Mann further explains that “[i]n one preferred embodiment, a stimulator, or a group of two or more stimulators, is controlled via closed-loop operation. A need for and/or response to stimulation is sensed by the stimulator(s), or by an additional ‘stimulator’ (which may or may not be dedicated to the sensing function), or another implanted or external device. If necessary, the sensed information is transmitted to the stimulating stimulator(s). ***Preferably, the parameters used by the stimulator(s) are automatically adjusted based on the sensed information.*** Thus, the electrical and/or drug stimulation parameters are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the electrical and/or drug stimulation.” *Id.*, 25:65-26:9. According to Mann, the

“stimulation parameters” that can be adjusted include the amplitude of the electrical current pulse. *Id.*, 15:8-24, 21:48-59.

187. Similarly, according to DiLorenzo, feedback from the sensors is used to determine adjustments to control parameters of the electrical stimulation, which are implemented by a control circuit (*i.e.*, the controller) in communication with a stimulating and recording unit. Ex.1054 (DiLorenzo), 10:66-11:10, 11:22-12:42. Control parameters that can be adjusted based on feedback from the sensors include pulse amplitude. *Id.*, 12:18-25, 16:14-26. Pulse amplitude may include adjustment of either pulse voltage or pulse current. *Id.*, 16:24-26, 19:29-67.

188. In Bourget’s system, a stimulation pulse generator is controlled by a processor, which detects values of a patient parameter based on sensor signals. Ex.1056 (Bourget), 8:14-62. Based on this sensor feedback, the processor can adjust stimulation parameters by controlling stimulation pulse generator to deliver neurostimulation therapy according to a program for delivery of stimulation. *Id.* The program may define “a voltage or current pulse amplitude” for stimulation pulses. *Id.*, 4:61-5:1, 8:32-41. The amplitude adjustment may involve adjustment of voltage or current. *Id.*, 13:19-25.

189. Likewise, in Gerber’s system, an external monitor/programmer analyzes information from the sensors and automatically generates adjustments to the stimulation parameters to be applied by the neurostimulator, which can be

applied without further input or authorization of the patient or clinician. Ex.1055 (Gerber), 2:1-16, 3:66-4:2, 8:47-67. Stimulation parameters that can be adjusted based on sensor feedback include, among other things, the amplitude of stimulation. *Id.*, 5:19-38. It would have been readily apparent to a POSA that the “amplitude” of electrical stimulation refers to the voltage and/or current of stimulation, which is a primary determinant of the magnitude of the effect of the stimulation on neural tissue. Adjusting stimulation voltage necessarily and inherently adjusts the stimulation current, and vice-versa. Ex.1071 (De Lima), 499, Fig.4. Accordingly, in my opinion, Mann, DiLorenzo, Gerber, and Bourget disclose the “detecting,” “receiving,” and “adjusting” limitations of claim 1.

190. In my opinion, it would have been obvious to modify and improve Amarenco’s method to incorporate the teachings of Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) described above for a multitude of reasons. First, Amarenco, Mann, DiLorenzo, Gerber, and Bourget are each directed at providing electrical stimulation therapy by applying electrical stimulation to a nerve(s) of a patient for the treatment of medical conditions. Indeed, Amarenco relates to electrical stimulation therapy for the treatment of overactive bladder. Ex.1005 (Amarenco), 2210. Mann relates to electrical stimulation systems for reducing or eliminating incontinence and/or pelvic pain by stimulating various nerve pathways, including the posterior tibial nerve. Ex.1084

(Mann), 10:65-11:19, 12:42-54. Likewise, Gerber relates to a neurostimulation system for providing adaptive neurostimulation therapy, *i.e.*, electrical stimulation therapy, for treating “urinary control disorders” and “fecal control disorders” such as “urinary incontinence, fecal incontinence, or some combination thereof.”

Ex.1055 (Gerber), 3:19-49. DiLorenzo relates to a neurological control system for providing electrical stimulation that can be used for treating a variety of conditions.

Ex.1054 (DiLorenzo), 3:35-4:3. Bourget relates to a closed-loop system for providing electrical stimulation therapy for the treatment of various conditions, including incontinence. Ex.1056 (Bourget), 3:52-4:14, 4:41-51. Given that each of these references are directed to similar fields, *i.e.*, electrical stimulation therapy, a POSA would have known of the teachings of Mann, DiLorenzo, Gerber, and/or Bourget and looked to these references when considering modifications or improvements to Amarenco’s method.

191. Any argument that a POSA would not have considered the teachings of Mann, DiLorenzo, Gerber, or Bourget in combination with Amarenco is, in my opinion, incorrect. For example, the fact that Mann, DiLorenzo, Gerber, and/or Bourget may describe embodiments of their systems in the context of invasive electrostimulation does not mean a POSA would not have considered the teachings of these references to modify or improve Amarenco’s noninvasive method. Similarly, the fact that a reference does not explicitly describe using a system

primarily to electrically stimulate the posterior tibial nerve and/or for the treatment of overactive bladder/incontinence likewise does not mean a POSA would not have considered the teachings of these references to modify or improve Amarenco's method. The distinctions between invasive and noninvasive electrical stimulation, the specific target nerve, or the specific condition being treated are irrelevant in the context of the feedback and control systems taught by Mann, DiLorenzo, Gerber, and Bourget, as the features of those systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) could be implemented in either invasive or noninvasive electrical stimulation devices and techniques and could be implemented to target any nerve in the body or treat any condition able to be treated using electrical stimulation. In fact, the references themselves acknowledge that the systems can be applied in a wide variety of different contexts. Indeed, while DiLorenzo describes the invention primarily in the context of intracranial electrical stimulation, DiLorenzo indicates that the stimulating electrodes can be "implanted within" or be "adjacent to" (*i.e.*, noninvasive) various stimulation sites, including "a peripheral nerve" in the "lower extremities." Ex.1054 (DiLorenzo), 6:38-43, 10:24-42, 28:33-56. The posterior tibial nerve is a peripheral nerve in the lower extremities, *i.e.*, leg. Similarly, Bourget explicitly states that the system is "applicable to any type of stimulation therapy" for treating a variety of conditions, including incontinence, and that "[a]ny implantable or external medical device may deliver closed-loop therapy

according to the techniques of the invention.” Ex.1056 (Bourget), 4:23-60. Gerber likewise indicates that the system can be used to provide therapy broadly for “pelvic floor disorders” through stimulation of “nerves of the pelvic floor” including but not limited to the sacral and pudendal nerves.” Ex.1055 (Gerber), 3:19-34. Mann indicates that a variety of nerves can be targeted, including the posterior tibial nerve, to treat a range of conditions. Ex.1084 (Mann), 9:44-10:22, 12:26-54. Thus, a POSA would have considered the teachings of Mann, DiLorenzo, Gerber, and/or Bourget when considering modifications or improvements to Amarenco’s method.

192. Second, it also would have been obvious to modify or improve Amarenco’s method based on the teachings of Mann, DiLorenzo, Gerber, or Bourget because using the features of Mann’s, DiLorenzo’s, Gerber’s, and Bourget’s systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) would have simply involved the predictable use of elements in the prior art according to their established functions—such as, for example, the use of sensors, sensor feedback, and stimulation parameter adjustment for providing electrical stimulation therapy as described throughout the prior art. The use of these features and elements would have been predictable given the common and successful use such features in similar electrostimulation devices and procedures as disclosed in the prior art such as the references discussed above.

193. Third, it further would have been obvious to modify or improve Amarenco's method based on the teachings of Mann, DiLorenzo, Gerber, or Bourget because the features of Mann's, DiLorenzo's, Gerber's, and Bourget's systems (*e.g.*, sensors, feedback, parameter adjustment, etc.) could simply be substituted for the control system used by Amarenco (*e.g.*, the EMG device and EMG electrodes/sensors). This would have involved nothing more than simply substituting known elements, and the results of such a substitution would have been predictable given, as discussed above, the common and successful use such features in similar electrostimulation devices and procedures as disclosed in the prior art.

194. Fourth, in my opinion, a POSA would have been motivated to modify Amarenco's procedure to incorporate the features of Mann, DiLorenzo, Gerber, or Bourget discussed above for the precise reasons disclosed in those references. Mann, for example, indicates sensed information (such as EMG signals) can be transmitted to the stimulator so that the electrical stimulation parameters "are adjusted in a closed-loop manner to provide stimulation tailored to the need for and/or response to the" electrical stimulation. Ex.1084 (Mann), 25:65-26:20. DiLorenzo indicates that the system is beneficial because it, among other things, "incorporat[es] quantitative and qualitative measures of patient symptomatology and neuromotor circuitry function in the regulation of treatment magnitude,"

performs “automated determination of the optimum magnitude of treatment” in order to “expedite[] achievement of satisfactory treatment of the patient, reducing the time and number of interactions, typically in physician visits, endured by the patient,” and “optimizes the efficiency of energy used in the treatment given to the patient.” Ex.1054 (DiLorenzo), 4:38-5:38. Bourget indicates that the system “may be able to more quickly and easily provide a patient with efficacious therapy through automatically ‘learned’ associations of sensed patient parameter values with therapy information,” because a medical device “may automatically learn to automatically adjust therapy in the manner desired by the patient based on such associations” such that “the patient may no longer need to manually adjust the therapy because the medical device has learned to use values of one or more sensed patient parameters to anticipate any adjustments.” Ex.1056 (Bourget), 2:23-34; *see also id.*, 3:5-14, 3:65-4:14, 7:54-65. Likewise, Gerber states that adjustments to stimulation parameters by the system “provide an adaptive neurostimulation therapy that supports or enhances therapeutic efficacy based on the information obtained.” Ex.1055 (Gerber), 2:14-16. A POSA would have been motivated to incorporate the teachings of Mann, DiLorenzo, Bourget, or Gerber into Amarenco’s method to achieve the benefits of those systems, such as feedback about the efficacy of the applied electrical stimulation therapy, improved regulation of treatment magnitude and/or side effects based on quantitative and

qualitative measurements, and quicker and more effective treatment for patients by applying adjustments to treatment parameters based on sensor feedback.

E. Ground 5: Claims 2-10 Are Obvious Over Amarenco (Ex.1005) in Combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), Further in View of the Knowledge of a POSA

195. As explained above, Amarenco (Ex.1004) in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056) render obvious claim 1 of the '477 patent (*see supra*, §X.D.1). Based on my review and analysis of Amarenco and with reasonable scientific certainty, it is my opinion that it would have further been obvious to modify Amarenco's teachings based on the knowledge of a POSA to achieve the methods of claims 2-10 of the '477 patent. I am not aware of any evidence of secondary considerations of nonobviousness, but I reserve the right to respond to any such evidence that EMK may raise in this proceeding. My analysis supporting this opinion is detailed below.

1. Claim 2: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat fecal incontinence.

196. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-

adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” Ex.1005 (Amarenco), 2210. Although Amarenco’s procedure was used to treat patients that “with urge incontinence, frequency and urgency secondary to overactive bladder” *id.*, it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as fecal incontinence, based on the knowledge of a POSA.

197. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including fecal incontinence. For example, Queralto (Ex.1016), which was published online in December 2005, discloses a study to “assess the efficiency of posterior tibial nerve (PTN) transcutaneous electrical nerve stimulation (TENS) in the treatment of anal idiopathic incontinence [*i.e.*, fecal incontinence].” Ex.1016 (Queralto), 670. “Stimulation was done on the PTN route using a self-adhesive surface stimulation electrode without an implanted needle electrode. The negative contact electrode was placed on the ankle skin behind the internal malleolus, and the positive electrode, 10 cm above the negative electrode.” *Id.* According to Queralto, “[o]ur preliminary study suggests that peripheral transcutaneous neuromodulation for fecal idiopathic incontinence is effective, at least in the short term. Its efficacy, morbidity, and cost-effectiveness should then be compared to sacral neuromodulation.” *Id.*, 672. Shafik (Ex.1064), published in 2003, also used

posterior tibial nerve stimulation for treating fecal incontinence using a subcutaneous electrode implantation and achieved improvement of fecal incontinence in 78% of patients.” Ex.1064 (Shafik), Abstract.

198. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of fecal incontinence. First, using Amarenco’s technique for the treatment of fecal incontinence would have simply involved applying known techniques (*e.g.*, treating fecal incontinence by stimulating the posterior tibial nerve as taught by, for example, Queralto and Shafik) to improve a known process (*e.g.*, Amarenco’s electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of fecal incontinence in the prior art. *E.g.*, Ex.1016 (Queralto), 670; Ex.1064 (Shafik), Abstract.

199. Second, it would have been obvious to try treating fecal incontinence using Amarenco’s technique. There were a finite number of known, predictable solutions for the treatment of fecal incontinence. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat fecal incontinence, as taught by, for example, Queralto and Shafik, a POSA would have been motivated to try treating fecal incontinence using Amarenco’s method. A POSA would have expected success given the successful treatment of fecal

incontinence using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating fecal incontinence by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, Shafik discloses an invasive method, this argument is, in my opinion, incorrect. Not only was it known in the art that fecal incontinence could be treated by noninvasively targeting the posterior tibial nerve (*e.g.*, Queralto), the knowledge of the successful use of electrical stimulation to treat fecal incontinence using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

200. Third, a POSA would have found it obvious to treat fecal incontinence using Amarenco's method because known work in the field (*e.g.*, Queralto and Shafik) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like fecal incontinence. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of fecal incontinence using similar methods as was known in the art (*e.g.*, Queralto and Shafik). Accordingly, in my opinion, it would have been

obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of fecal incontinence.

2. Claim 3: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat restless leg syndrome.

201. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." Ex.1005 (Amarenco), 2210. Although Amarenco's procedure was used to treat patients that "with urge incontinence, frequency and urgency secondary to overactive bladder" *id.*, it would have been obvious to modify Amarenco's teachings to treat other conditions, such as restless leg syndrome, based on the knowledge of a POSA.

202. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including restless leg syndrome. For example, DiLorenzo '103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*, nerves, of a patient. Ex.1068 (DiLorenzo '103),

Abstract, [0019], [0072]. DiLorenzo '103 indicates the stimulating electrodes can be "implanted within" or be "adjacent to" (*i.e.*, noninvasive) various stimulation sites such as "a peripheral nerve" in the "lower extremities," including explicitly a posterior tibial nerve. *Id.*, [0072], [0093], [0175], [0348]. Claim 131 of DiLorenzo '103 indicates that a disease state that can be treated using the system includes restless leg syndrome. *Id.*, cls.128-31.

203. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco's technique for the treatment of restless leg syndrome. First, using Amarenco's technique for the treatment of restless leg syndrome would have simply involved applying known techniques (*e.g.*, treating restless leg syndrome by stimulating the posterior tibial nerve as taught by, for example, DiLorenzo '103) to improve a known process (*e.g.*, Amarenco's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of restless leg syndrome in the prior art. *E.g.*, Ex.1068 (DiLorenzo '103), cls.128-31.

204. Second, it would have been obvious to try treating restless leg syndrome using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of restless leg syndrome. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to

treat restless leg syndrome, as taught by, for example, DiLorenzo '103, a POSA would have been motivated to try treating restless leg syndrome using Amarenco's method. A POSA would have expected success given the successful treatment of restless leg syndrome using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating restless leg syndrome by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat restless leg syndrome using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

205. Third, a POSA would have found it obvious to treat restless leg syndrome using Amarenco's method because known work in the field (*e.g.*, DiLorenzo '103) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like restless leg syndrome. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful

treatment of restless leg syndrome using similar methods as was known in the art (*e.g.*, DiLorenzo '103). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of restless leg syndrome.

3. Claim 4: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat premature ejaculation.

206. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." Ex.1005 (Amarenco), 2210. Although Amarenco's procedure was used to treat patients that "with urge incontinence, frequency and urgency secondary to overactive bladder" *id.*, it would have been obvious to modify Amarenco's teachings to treat other conditions, such as premature ejaculation, based on the knowledge of a POSA.

207. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including premature ejaculation. For example, Gerber '372 discloses systems for treating

various disorders of the pelvic floor by delivering electrical stimuli to the sacral nerves. Ex.1069 (Gerber '372), Abstract, [0002]. Among the pelvic floor disorders that Gerber '372's system treats are sexual dysfunctions including premature ejaculation. *Id.*, Abstract, [0004], [0021], [0047-49], cl.1. Gerber '372 states that "[a]s employed herein, the term 'sacral nerve []' means any one of the sacral nerves, portions of the sacral nerve(s), nerves neurologically connected to any one of the sacral nerves and in relatively close physical proximity thereto, and extensions or branches of any one of the sacral nerves." *Id.*, [0064]. The posterior tibial nerve is a sacral nerve as it reaches the spinal cord via the dorsal roots of the sacral nerves. *See, e.g.*, Ex.1080 (Boveja), Abstract, [0180] ("sacral nerves" include "sacral nerves S1, S2, S3, S4, pudendal nerve, superior gluteal nerve, lumbo-sacral trunk, inferior gluteal nerve, common fibular nerve, **tibial nerve**, posterior femoral cutaneous nerve, sciatic nerve, and obturator nerve." (emphasis added)).

208. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco's technique for the treatment of premature ejaculation. First, using Amarenco's technique for the treatment of premature ejaculation would have simply involved applying known techniques (*e.g.*, treating premature ejaculation by stimulating sacral nerves such as the posterior tibial nerve as taught by, for example, Gerber '372) to improve a

known process (*e.g.*, Amarenco's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of premature ejaculation in the prior art. *E.g.*, Ex.1069 (Gerber '372), Abstract, [0004], [0021], [0047-49], cl.1.

209. Second, it would have been obvious to try treating premature ejaculation using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of premature ejaculation. Given that it was known in the prior art to use electrical stimulation of the sacral nerves such as the posterior tibial nerve to treat premature ejaculation, as taught by, for example, Gerber '372, a POSA would have been motivated to try treating premature ejaculation using Amarenco's method. A POSA would have expected success given the successful treatment of premature ejaculation using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating premature ejaculation by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, Gerber '372 discloses an invasive method, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat premature ejaculation using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient

and less burdensome for patients, such as noninvasive electrical stimulation techniques.

210. Third, a POSA would have found it obvious to treat premature ejaculation using Amarenco's method because known work in the field (*e.g.*, Gerber '372) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like premature ejaculation. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of premature ejaculation using similar methods as was known in the art (*e.g.*, Gerber '372). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of premature ejaculation.

4. Claim 5: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat chronic pain.

211. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-

adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” Ex.1005 (Amarenco), 2210. Although Amarenco’s procedure was used to treat patients that “with urge incontinence, frequency and urgency secondary to overactive bladder” *id.*, it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as chronic pain, based on the knowledge of a POSA.

212. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including chronic pain. For example, van Balken 2003 (Ex.1065), which was published in 2003, discloses a study to evaluate the results of percutaneous tibial nerve stimulation in patients with chronic pain. Ex.1065 (van Balken 2003), 158. van Balken concluded that percutaneous tibial nerve stimulation “may have a place in the treatment of patients with chronic pelvic pain who have already tried many other therapies and are left with no further option.” *Id.* Similarly, Whitehurst (Ex.1066), published in 2005, discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain. Ex.1066 (Whitehurst), [0005], [0015], [0055].

213. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of chronic pain. First, using Amarenco’s technique for the treatment of

chronic pain would have simply involved applying known techniques (*e.g.*, treating chronic pain by stimulating the posterior tibial nerve as taught by, for example, van Balken and Whitehurst) to improve a known process (*e.g.*, Amarenco's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of chronic pain in the prior art. *E.g.*, Ex.1065 (van Balken 2003), 158; Ex.1066 (Whitehurst), [0005], [0015], [0055].

214. Second, it would have been obvious to try treating chronic pain using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of chronic pain. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat chronic pain, as taught by, for example, van Balken and Whitehurst, a POSA would have been motivated to try treating chronic pain using Amarenco's method. A POSA would have expected success given the successful treatment of chronic pain using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating chronic pain by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat chronic pain using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical

stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

215. Third, a POSA would have found it obvious to treat chronic pain using Amarenco's method because known work in the field (*e.g.*, van Balken and Whitehurst) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like chronic pain. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of chronic pain using similar methods as was known in the art (*e.g.*, van Balken and Whitehurst). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of chronic pain.

5. Claim 6: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat osteoarthritis or arthritis.

216. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the

procedure involved “left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” Ex.1005 (Amarenco), 2210. Although Amarenco’s procedure was used to treat patients that “with urge incontinence, frequency and urgency secondary to overactive bladder” *id.*, it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as osteoarthritis or arthritis, based on the knowledge of a POSA.

217. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including osteoarthritis or arthritis. For example, Jaax (Ex.1067), which was filed in December 2005, discloses the treatment of osteoarthritis by applying electrical stimulation to a stimulation site, such as the posterior tibial nerve. Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11. Similarly, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain associated with conditions including rheumatoid arthritis. Ex.1066 (Whitehurst), [0005], [0015], [0017], [0055].

218. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of osteoarthritis or arthritis. First, using Amarenco’s technique for the treatment of osteoarthritis or arthritis would have simply involved applying known

techniques (*e.g.*, treating osteoarthritis or arthritis by stimulating the posterior tibial nerve as taught by, for example, Jaax and Whitehurst) to improve a known process (*e.g.*, Amarenco's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of osteoarthritis or arthritis in the prior art. *E.g.*, Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11; Ex.1066 (Whitehurst), [0005], [0015], [0017], [0055].

219. Second, it would have been obvious to try treating osteoarthritis or arthritis using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of osteoarthritis or arthritis. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat osteoarthritis or arthritis, as taught by, for example, Jaax and Whitehurst, a POSA would have been motivated to try treating osteoarthritis or arthritis using Amarenco's method. A POSA would have expected success given the successful treatment of osteoarthritis or arthritis using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating osteoarthritis or arthritis by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat osteoarthritis or arthritis using any means, whether

invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

220. Third, a POSA would have found it obvious to treat osteoarthritis or arthritis using Amarenco's method because known work in the field (*e.g.*, Jaax and Whitehurst) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like osteoarthritis or arthritis. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of osteoarthritis or arthritis using similar methods as was known in the art (*e.g.*, Jaax and Whitehurst). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of osteoarthritis or arthritis.

6. Claim 7: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof responsible for neuropathic pain to treat neuropathic pain.

221. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering

electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved “left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” Ex.1005 (Amarenco), 2210. Although Amarenco’s procedure was used to treat patients that “with urge incontinence, frequency and urgency secondary to overactive bladder” *id.*, it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as neuropathic pain, based on the knowledge of a POSA.

222. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including neuropathic pain. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic neuropathic pain. Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0028-29], [0055]. Whitehurst further explicitly discloses delivering the electrical stimulus to the posterior tibial nerve or branch thereof ***responsible for the neuropathic pain.*** According to Whitehurst, “a leadless microstimulator (200) may be subcutaneously implanted within the leg (220) of a patient in a location where the patient feels pain. For illustrative purposes, it is assumed in the example of FIG. 4 that the patient feels pain in an upper thigh area (221) of the leg. ***The peripheral nerve causing the pain may be the tibial nerve (210).*** . . . electrical

and/or drug stimulation applied to the neural tissue (212) by the subcutaneously implanted microstimulator (200) ***may effectively stimulate the tibial nerve (210) and treat the pain felt by the patient.***” *Id.*, [0055].

223. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique to deliver electrical stimulation to the posterior tibial nerve or branch thereof responsible for neuropathic pain for the treatment of neuropathic pain. First, using Amarenco’s technique for the treatment of neuropathic pain would have simply involved applying known techniques (*e.g.*, treating neuropathic pain by stimulating the posterior tibial nerve responsible for the pain as taught by, for example, Whitehurst) to improve a known process (*e.g.*, Amarenco’s electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of neuropathic pain in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0055].

224. Second, it would have been obvious to try treating neuropathic pain by applying stimulation to the posterior tibial nerve or branch responsible for the pain using Amarenco’s technique. There were a finite number of known, predictable solutions for the treatment of neuropathic pain. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to

treat neuropathic pain, as taught by, for example, Whitehurst, a POSA would have been motivated to try treating neuropathic pain using Amarenco's method. A POSA would have expected success given the successful treatment of neuropathic pain using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating neuropathic pain by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat neuropathic pain using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

225. Third, a POSA would have found it obvious to treat neuropathic pain by applying stimulation to the posterior tibial nerve or branch responsible for the pain using Amarenco's method because known work in the field (*e.g.*, Whitehurst) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like neuropathic pain. As indicated above, such a variation to Amarenco's

method would have been predictable to a POSA given the successful treatment of neuropathic pain using similar methods as was known in the art (*e.g.*, Whitehurst). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of neuropathic pain.

226. Additionally, to the extent that it might be argued that a POSA would not have found it obvious to try treating neuropathic pain by treating the "branch thereof [of the posterior tibial nerve] responsible for neuropathic pain," in addition to or alternatively to the posterior tibial nerve itself, this argument is in my opinion incorrect. It would be obvious to a POSA that stimulation treatment could be directed toward a specific branch of a nerve structure responsible for pain; the tibial nerve itself is such a branch of a larger nerve structure, the sciatic nerve, which is also itself a branch of a larger nerve structure, the sacral plexus. Thus, it would have been obvious to a POSA to apply electrical stimulation to whatever nerve or branch of nerve is responsible for or causing a patient's neuropathic pain.

7. Claim 8: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat neuralgia.

227. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering

electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved “left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide.” Ex.1005 (Amarenco), 2210. Although Amarenco’s procedure was used to treat patients that “with urge incontinence, frequency and urgency secondary to overactive bladder” *id.*, it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as neuralgia, based on the knowledge of a POSA.

228. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including neuralgia. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat neuralgia. Ex.1066 (Whitehurst), [0005], [0015], [0019-20], [0055].

229. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of neuralgia. First, using Amarenco’s technique for the treatment of neuralgia would have simply involved applying known techniques (*e.g.*, treating neuralgia by stimulating the posterior tibial nerve as taught by, for example, Whitehurst) to improve a known process (*e.g.*, Amarenco’s electrical stimulation technique). The result of this combination would have been predictable given the

known and successful use of electrical stimulation techniques for the treatment of neuralgia in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0017-18], [0055].

230. Second, it would have been obvious to try treating neuralgia using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of neuralgia. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat neuralgia, as taught by, for example, Whitehurst, a POSA would have been motivated to try treating neuralgia using Amarenco's method. A POSA would have expected success given the successful treatment of neuralgia using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating neuralgia by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat neuralgia using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

231. Third, a POSA would have found it obvious to treat neuralgia using Amarenco's method because known work in the field (*e.g.*, Whitehurst) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like neuralgia. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of neuralgia using similar methods as was known in the art (*e.g.*, Whitehurst). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of neuralgia.

8. Claim 9: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat atrophy.

232. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." Ex.1005 (Amarenco), 2210. Although Amarenco's procedure was used to treat patients that

“with urge incontinence, frequency and urgency secondary to overactive bladder”
id., it would have been obvious to modify Amarenco’s teachings to treat other conditions, such as atrophy, based on the knowledge of a POSA.

233. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including atrophy. It was known, for example, that atrophy can be caused by conditions such as paralysis or osteoarthritis. *E.g.*, Ex.1070 (Davis), [0003] (“Loss of upper motor control due to stroke results primarily in limb paralysis and secondarily in disuse atrophy of the affected muscle and shoulder joint. This atrophy may result in complications such as joint pain and skin breakdown, which may be even more troubling to the patient than the loss of motor function.”); Ex.1067 (Jaax), 1:26-34 (“Non-surgical techniques for treating osteoarthritis include weight loss, rest, physical therapy, orthotics, and heat. Weight loss alleviates stress on an affected joint and is sometimes effective in treating osteoarthritis. Short-term rest of an affected joint may be effective in temporarily relieving pain. However, longer periods of rest may result in muscle atrophy and decreased joint mobility.”). Clearly, treating the underlying condition (*e.g.*, paralysis or osteoarthritis) would eliminate the complications caused by the condition, such as atrophy.

234. Using electrical stimulation of the posterior tibial nerve to treat paralysis and osteoarthritis, conditions that cause atrophy, was known. For

example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain causing paralysis. Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]. DiLorenzo ‘103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*, nerves, of a patient. Ex.1068 (DiLorenzo ‘103), Abstract, [0019], [0072]. According to DiLorenzo ‘103, the system can be used for “electrical stimulation of peripheral nerves, such as stimulation of the **tibial** or peroneal nerves for use in **eliciting the flexion withdrawal reflex to facilitate gait restoration in paraplegics.**” *Id.*, [0348]. A paraplegic is a person with paralysis, and therefore DiLorenzo ‘103 discloses electrical stimulation of the tibial nerve to treat paralysis. Moreover, Jaax (Ex.1067) discloses the treatment of osteoarthritis by applying electrical stimulation to a stimulation site, such as the posterior tibial nerve. Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11.

235. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of atrophy. First, using Amarenco’s technique for the treatment of atrophy would have simply involved applying known techniques (*e.g.*, treating conditions responsible for causing atrophy, such as paralysis or osteoarthritis, by stimulating the posterior tibial nerve as taught by, for example, Whitehurst,

DiLorenzo '103, or Jaax) to improve a known process (*e.g.*, Amarenco's electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of conditions that cause atrophy in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]; Ex.1068 (DiLorenzo '103), Abstract, [0019], [0072], [0348]; Ex.1067 (Jaax), 3:13-21, 5:40-49, 5:50-6:11.

236. Second, it would have been obvious to try treating atrophy using Amarenco's technique. There were a finite number of known, predictable solutions for the treatment of atrophy and conditions that cause atrophy. Given that it was known in the prior art to use electrical stimulation of the posterior tibial nerve to treat conditions that cause atrophy, as taught by, for example, Whitehurst, DiLorenzo '103, and Jaax, a POSA would have been motivated to try treating atrophy and conditions that cause it using Amarenco's method. A POSA would have expected success given the successful treatment of conditions that cause atrophy, such as paralysis and osteoarthritis, using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating atrophy or conditions that cause it by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat paralysis using any means, whether

invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

237. Third, a POSA would have found it obvious to treat atrophy and conditions that cause it using Amarenco's method because known work in the field (*e.g.*, Whitehurst, DiLorenzo '103, Jaax) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like atrophy or conditions that cause it. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of conditions that atrophy using similar methods as was known in the art (*e.g.*, Whitehurst, DiLorenzo '103, Jaax). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of conditions that can cause atrophy, including paralysis or osteoarthritis.

9. Claim 10: The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat paralysis.

238. As explained above, Amarenco in combination with Mann, DiLorenzo, Bourget, or Gerber disclose all the limitations of claim 1. *See supra*, §X.D.1. Further, as explained above, Amarenco's method involved delivering electrical stimulus to the posterior tibial nerve. According to Amarenco, the procedure involved "left posterior tibial nerve stimulation using a surface self-adhesive electrode on the ankle skin behind the internal malleolus with shocks in continuous mode at 10 Hz. frequency and 200 milliseconds wide." Ex.1005 (Amarenco), 2210. Although Amarenco's procedure was used to treat patients that "with urge incontinence, frequency and urgency secondary to overactive bladder" *id.*, it would have been obvious to modify Amarenco's teachings to treat other conditions, such as paralysis, based on the knowledge of a POSA.

239. Well before 2006, it was known that many other conditions could be treated by providing electrical stimulation to the posterior tibial nerve, including paralysis. For example, Whitehurst (Ex.1066) discloses applying an electrical stimulus to peripheral nerves, including the posterior tibial nerve, to treat chronic pain causing paralysis. Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]. DiLorenzo '103 (Ex.1068) discloses electrical stimulation systems that include a neurological control system for modulating nervous system components, *e.g.*,

nerves, of a patient. Ex.1068 (DiLorenzo ‘103), Abstract, [0019], [0072].

According to DiLorenzo ‘103, the system can be used for “electrical stimulation of peripheral nerves, such as stimulation of the **tibial** or peroneal nerves for use in ***eliciting the flexion withdrawal reflex to facilitate gait restoration in paraplegics.***” *Id.*, [0348]. A paraplegic is a person with paralysis, and therefore DiLorenzo ‘103 discloses electrical stimulation of the tibial nerve to treat paralysis.

240. Based on the knowledge of a POSA, in my opinion it would have been obvious for a multitude of reasons to use Amarenco’s technique for the treatment of paralysis. First, using Amarenco’s technique for the treatment of paralysis would have simply involved applying known techniques (*e.g.*, treating paralysis by stimulating the posterior tibial nerve as taught by, for example, Whitehurst and DiLorenzo ‘103) to improve a known process (*e.g.*, Amarenco’s electrical stimulation technique). The result of this combination would have been predictable given the known and successful use of electrical stimulation techniques for the treatment of paralysis in the prior art. *E.g.*, Ex.1066 (Whitehurst), [0005], [0015], [0020], [0055]; Ex.1068 (DiLorenzo ‘103), Abstract, [0019], [0072], [0348].

241. Second, it would have been obvious to try treating paralysis using Amarenco’s technique. There were a finite number of known, predictable solutions for the treatment of paralysis. Given that it was known in the prior art to use

electrical stimulation of the posterior tibial nerve to treat paralysis, as taught by, for example, Whitehurst and DiLorenzo '103, a POSA would have been motivated to try treating paralysis using Amarenco's method. A POSA would have expected success given the successful treatment of paralysis using similar methods in the prior art. To the extent it is argued that a POSA would not have found it obvious to try treating paralysis by electrically stimulating the posterior tibial nerve using Amarenco's method because, for example, the prior art discloses invasive methods, this argument is, in my opinion, incorrect. The knowledge of the successful use of electrical stimulation to treat paralysis using any means, whether invasive or noninvasive, would have suggested to a POSA that other types of electrical stimulation could also be successful and motivated the POSA to try other means that are more convenient and less burdensome for patients, such as noninvasive electrical stimulation techniques.

242. Third, a POSA would have found it obvious to treat paralysis using Amarenco's method because known work in the field (*e.g.*, Whitehurst and DiLorenzo '103) would have prompted variations to Amarenco's method based on design incentives and market forces, such as the need to find an adequate treatment for other conditions that may be affected by electrical stimulation of the posterior tibial nerve like paralysis. As indicated above, such a variation to Amarenco's method would have been predictable to a POSA given the successful treatment of

paralysis using similar methods as was known in the art (*e.g.*, Whitehurst and DiLorenzo '103). Accordingly, in my opinion, it would have been obvious to use Amarenco's technique of electrically stimulating the posterior tibial nerve for the treatment of paralysis.

XI. CONCLUSION

243. Based on my review and above analysis and with reasonable scientific certainty, it is my opinion that claims 1-10 of the '477 patent are invalid based on the following grounds:

- Claim 1 is anticipated under 35 U.S.C. § 102 by Svihra (Ex.1004);
- Claim 1 is rendered obvious under 35 U.S.C. § 103 by Svihra (Ex.1004) in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056);
- Claims 2-10 are rendered obvious under 35 U.S.C. § 103 by Svihra (Ex.1004) alone or in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), further in view of the knowledge of a POSA;
- Claim 1 is rendered obvious under 35 U.S.C. § 103 by Amarenco (Ex.1005) in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056);

- Claims 2-10 are rendered obvious under 35 U.S.C. § 103 by Amarenco (Ex.1005) in combination with Mann (Ex.1084), DiLorenzo (Ex.1054), Gerber (Ex.1055), or Bourget (Ex.1056), further in view of the knowledge of a POSA.

I declare under penalty of perjury that the foregoing is true and correct. I declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and 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.

Executed this 4th day of September, 2024.

A handwritten signature in black ink, appearing to read 'B. Wingeier', is written over a horizontal line.

Dr. Brett Wingeier, PhD

Appendix A:

'477 Patent Claim Appendix

Appendix A – '477 Patent Claims

Claim 1:

[1.p] A method of performing electrical stimulation therapy, comprising:

[1.a] non-invasively positioning a first portion of a patient's body relative to an electrical stimulator such that a posterior tibial nerve or branch thereof within the first portion of the body is in proximity to the electrical stimulator;

[1.b] passing a current through the electrical stimulator;

[1.c] delivering an electrical stimulus from the electrical stimulator to the posterior tibial nerve or branch thereof;

[1.d] detecting electrical conduction through the posterior tibial nerve or branch thereof or detecting a muscular response caused by an electrical conduction through the posterior tibial nerve or branch thereof via at least one sensor positioned along a second portion of the body;

[1.e] receiving a signal from the at least one sensor indicative of the detected electrical conduction or muscular response thereby providing feedback about the efficacy of the applied electrical stimulation therapy; and

[1.f] adjusting the current via a controller in communication with the electrical stimulator based on the feedback.

Claim 2:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat fecal incontinence.

Claim 3:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat restless leg syndrome.

Claim 4:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat premature ejaculation.

Claim 5:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat chronic pain.

Claim 6:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat osteoarthritis or arthritis.

Claim 7:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof responsible for neuropathic pain to treat neuropathic pain.

Claim 8:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat neuralgia.

Claim 9:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat atrophy.

Claim 10:

The method of claim 1, wherein the electrical stimulus is delivered to the posterior tibial nerve or branch thereof to treat paralysis.

Appendix B:

Materials Considered

Exhibit No.	Description
1001	U.S. Patent No. 9,002,477 (“’477 patent”)
1002	File History of U.S. Patent No. 9,002,477 (“’477 patent file history”)
1003	Declaration of Dr. Brett Wingeier in Support of Petition for Inter Partes Review of U.S. Patent No. 9,002,477 (“Wingeier Decl.”)
1004	J. Svihra <i>et al.</i> , “Neuromodulative treatment of overactive bladder – noninvasive tibial nerve stimulation,” <i>Bratisl Lek Listy</i> 103(12):480-483 (2002) (“Svihra”)
1005	G. Amarenco <i>et al.</i> , “Urodynamic Effect of Acute Transcutaneous Posterior Tibial Nerve Stimulation in Overactive Bladder,” <i>J. Urology</i> 169: 2210-2215 (2003) (“Amarenco”)
1008	G. Willy Davila & Minda Neimark, “The Overactive Bladder: Prevalence and Effects on Quality of Life,” <i>Clinical Obstetrics and Gynecology</i> 45(1):173-181 (2002) (“Davila”)
1009	Alan J. Wein & Eric S. Rovner, “Definition and Epidemiology of Overactive Bladder,” <i>Urology</i> 60(Suppl 5A):7-12 (2002) (“Wein”)
1010	Paul Abrams <i>et al.</i> , “Overactive Bladder Significantly Affects Quality of Life,” <i>The American Journal of Managed Care</i> 6(11, Sup.):580-590 (2000) (“Abrams”)
1011	Neeral Kohli & Peter L. Rosenblatt, “Neuromodulation Techniques for the Treatment of the Overactive Bladder,” <i>Clinical Obstetrics and Gynecology</i> 45(1):218-232 (2002) (“Kohli”)
1012	Floor van der Pal <i>et al.</i> , “Current opinion on the working mechanisms of neuromodulation in the treatment of lower urinary tract dysfunction,” <i>Current Opinion in Urology</i> 16(4):261-267 (2006) (“van der Pal”)
1013	Francisco Velasco, “Neuromodulation: An Overview,” <i>Archives of Medical Research</i> 31(3):232-236 (2000) (“Velasco”)
1014	J. Groen & J.L.H.R. Bosch, “Neuromodulation techniques in the treatment of the overactive bladder,” 87(8):723-731 (2001) (“Groen”)

Exhibit No.	Description
1015	Marshall L. Stoller, “Afferent Nerve Stimulation for Pelvic Floor Dysfunction,” <i>Scientific Non Discussion Poster Session</i> 16(257):256 (1999) (“Stoller”)
1016	M. Queralto <i>et al.</i> , “Preliminary results of peripheral transcutaneous neuromodulation in the treatment of idiopathic fecal incontinence,” <i>International Journal of Colorectal Disease</i> 21(2006):670-672 (2006) (“Queralto”)
1017	F. Monti <i>et al.</i> , “Peripheral neuromodulation using surface electrode for treatment of overactive bladder (oab): initial experience,” <i>Clinical Neurophysiology</i> 117(2006):243 (2006) (“Monti”)
1028	Hermie J. Hermens <i>et al.</i> , “Development of recommendations for SEMG sensors and sensor placement procedures,” <i>Journal of Electromyography and Kinesiology</i> 10(5):361-374 (2000) (“Hermens”)
1030	S. Tahseen Hasan <i>et al.</i> , “Transcutaneous Electrical Nerve Stimulation and Temporary S3 Neuromodulation in Idiopathic Detrusor Instability,” <i>The Journal of Urology</i> 155(6):2005-2011 (1996) (“Hasan”)
1041	Edward J. McGuire <i>et al.</i> , “Treatment of Motor and Sensory Detrusor Instability by Electrical Stimulation,” <i>The Journal of Urology</i> 129(1):78-79 (1983) (“McGuire”)
1042	A.L. Hof, “EMG and Muscle Force: An Introduction,” <i>Human Movement Science</i> 3(1-2):119-153 (1984) (“Hof”)
1043	A Martens De Noordhout <i>et al.</i> , “Percutaneous electrical stimulation of lumbosacral roots in man,” <i>Journal of Neurology, Neurosurgery, and Psychiatry</i> 51(2):174-181 (1988) (“Noordhout”)
1048	U.S. Patent App. No. 11/866,329 to Burnett <i>et al.</i> (“‘329 application”)
1051	<i>Avation Medical, Inc. v. EMKinetics, Inc.</i> No. 3:24-cv-01702 (N.D. Cal.) First Amended Complaint, Dkt. No. 5
1053	Declaration of Todd R. Tucker

Exhibit No.	Description
1054	U.S. Patent No. 6,366,813 to DiLorenzo (“DiLorenzo”)
1055	U.S. Patent No. 7,515,965 to Gerber <i>et al.</i> (“Gerber”)
1056	U.S. Patent No. 7,863,322 to Bourget <i>et al.</i> (“Bourget”)
1064	A. Shafik <i>et al.</i> , “Percutaneous Peripheral Neuromodulation in the Treatment of Fecal Incontinence,” <i>European Surgical Research</i> 35(2):103-107 (2003) (“Shafik”)
1065	Michael R. van Balken <i>et al.</i> , “Percutaneous Tibial Nerve Stimulation as Neuromodulative Treatment of Chronic Pelvic Pain,” <i>European Urology</i> 43(2):158-163 (2003) (“van Balken 2003”)
1066	U.S. Patent Pub. App. Pub. No. 2005/0143789 to Whitehurst <i>et al.</i> published June 30, 2005 (“Whitehurst”)
1067	U.S. Patent No. 7,610,100 to Jaax <i>et al.</i> filed Dec. 30, 2005 (“Jaax”)
1068	U.S. Patent App. Pub. No. 2005/0021103 to DiLorenzo published January 27, 2005 (“DiLorenzo ‘103”)
1069	U.S. Patent App. Pub. No. 2005/0033372 to Gerber published February 10, 2005 (“Gerber ‘372”)
1070	U.S. Patent App. Pub. No. 2005/0245989 to Davis filed April 28, 2005 (“Davis”)
1071	Jader A. De Lima <i>et al.</i> , “A Low-Cost Neurostimulator with Accurate Pulsed-Current Control,” <i>IEEE Transactions on Biomedical Engineering</i> 49(5):497-500 (2002) (“De Lima”)
1080	U.S. Patent Pub. App. Pub. No. 2006/0122660 to Boveja <i>et al.</i> filed Dec. 28, 2005, published Jun. 8, 2006 (“Boveja”)
1084	U.S. Patent No. 6,941,171 to Mann <i>et al.</i> (“Mann”)

Appendix C: Curriculum Vitae

BRETT WINGEIER, PHD

RESEARCH AND DEVELOPMENT LEADER

CONTACT

+1 415-690-7358

brett@wingeier.com

San Francisco, CA

SKILLS

App-enabled healthtech and wearables
Applied research
Biosignals, big data, and statistics
Electromechanical device development
Embedded systems design + architecture
Engineering leadership
High-reliability firmware (C + assembly)
International supply chain (Asia, Europe)
IP creation and portfolio management
ML, TensorFlow, Keras, CNNs, Python, more
Medtech and neurotech
Manufacturing ops (consumer + med)
MSP430, STM32, Atmel, BLE, MICS, more
Product design
Product management
Research program / portfolio management
Technical education and communication

CREDENTIALS

Tulane University

PhD Biomedical Engineering 2004
BSE Biomedical Engineering 1996

Electric fields in the brain; numerical
methods and modeling; biosignals and
complex data

Stanford University

Biodesign (professional development) 2005-2006

US registered patent agent

Reg no. 69,895; 70+ US patents issued

SELECTED WORKS

US patent 8,761,889
US patent 9,486,618
US patent 9,630,005
US patent application 17/700451

Bikson et al 2018. *Brain Stimul* 11(1):134-157
Sillay et al 2013. *Brain Stimul* 6(5):718-726
Bronte-Stewart et al 2009. *Exp Neurol* 215(1):20-28
Wingeier et al 2006. *Exp Neurol* 197(1):244-251
Wingeier et al 2001. *Phys Rev E* 64(5) pt 1

PROFILE

Scientist, engineer, and product leader with deep experience in consumer and medtech. I turn data into life-changing products, and specialize in making sense of complex systems and implementing mission-critical, data-intensive technology. I've brought both active implantable and non-invasive healthtech devices to market, designed supply chains, managed P&Ls, negotiated licenses, built teams, supervised clinical trials, mentored data scientists, and published in neurophysiology, neuromodulation, and biosignal processing.

RELEVANT EXPERIENCE

Founder and Managing Engineer

LT2 Labs (previously Wingeier Biomedical) 2008-present

- Conventional and ML (CNN, LSTM, TensorFlow) biosignal analysis
- Development and power reduction for ingestible capsule product
- Architected and developed implantable neurostimulator for cluster headache and migraine, commercialized in EU (Pulsante System)
- Developed predictive models for spinal electrode placement
- Systems engineering, risk, and requirements work: 13485, FDA QSR, 60601, 14971
- Hands-on embedded development for medtech products: bare metal C, MSP430, STM32, CMSIS, inductive comms, cellular comms, MICS, FreeRTOS
- Clinical trial modeling and advanced biostatistics (GEE methods)

CEO / CTO and Co-Founder

Magnus Medical 2020-2023

- Raised \$25M as founding CEO to commercialize SAINT, a data-driven hardware/software platform yielding 90% remission in major depression
- Built and led 25-member team across disciplines, including engineering (software, mechanical, electrical), clinical, research, and regulatory
- Integrated product, regulatory, quality, and clinical work to achieve breakthrough device designation for SAINT and FDA clearance in Sept 2022
- Laid groundwork for NTAP reimbursement, granted August 2023 (first in psychiatry)
- Transitioned to CTO in late 2022 to directly lead engineering and IP
- Architected next-gen system with inlicensed and new tech, lowering BOM cost by ~70%
- Built supply chain across US and Europe, negotiating supply and quality agreements
- Hands-on data analysis and Atmel firmware development (Atmel)

CTO / CEO and Co-Founder

Halo Neuroscience 2013-2020

- As CTO, co-founded Halo and raised \$20M through Series B to develop and market wearable consumer neurotech products. Transitioned to CEO in 2019
- Build and led 35-member team across disciplines including software, hardware, research, operations, sales, and marketing
- Managed multi-year applied research program in neuroscience and human performance
- Led application of machine learning to neurostim research and product monitoring
- Architected and led engineering and operations for Halo Sport headphones and ecosystem
- Hands-on firmware and embedded systems development (MSP430, Bluetooth)
- Developed consumer-electronics supply chain across Asia
- Manufactured and sold 25K Halo Sport units for \$4.3M yearly revenue, 50% YoY growth
- Technical communication, including extensive public speaking and scientific collaboration

Principal Biomedical Engineer

NeuroPace 2001-2013

- Developed and gained FDA approval for the world's first implantable, responsive neurostimulator for epilepsy
- Wrote embedded code still running for decades in thousands of human heads
- Hands-on firmware and embedded systems development (V8, custom ASICs)
- Product manager for next-gen rechargeable system and ML-driven clinician programmer

Petitioner - Avation Medical, Inc.

Ex. 1003, p. 179

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Wingeier, Brett Matthew

eRA COMMONS USER NAME (credential, e.g., agency login): WINGEIER

POSITION TITLE: Principal Consultant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Tulane University, New Orleans	BSE	05/1996	Biomedical Engineering
Brain Sciences Institute, Melbourne, Australia	Postgrad fellow	05/2001	Brain physics / EEG
Tulane University, New Orleans	PhD	05/2004	Biomedical Engineering
Stanford University	N/A	06/2007	Biodesign

A. Personal Statement

I am a scientist, technologist, and R&D executive with 25 years of experience in the field of medical technology, spanning translational research, development, engineering, and program management. Throughout this career, I have specialized in technology related to neural / neuromotor function and analysis of biosignals. In my doctoral work, I studied human EEG data to characterize brain activity as standing waves and traveling waves [1], yielding new insights into the relationship between local and global brain activity. Thereafter I moved into the neurotech industry, joining the team at NeuroPace that created the world's first implanted, responsive neurostimulator for epilepsy, and working as a biomedical engineer, clinical scientist, and data scientist across multiple stages of the project [2]. I was instrumental in gaining FDA approval for this device in 2013, which remains on the market in the US. In parallel with this work, I led the industry side of a collaboration with the Movement Disorders Clinic at Stanford University which resulted in the first observation that subthalamic nucleus stimulation temporarily reduces the pathological beta-band oscillations that characterize Parkinson's disease [3]. Also in parallel, I worked with Autonomic Technologies to develop a novel implant for sphenopalatine ganglion stimulation in cluster headache, marketed in Europe, for which I architected and developed the embedded software and was instrumental in clinical trial planning. In 2013 I co-founded Halo Neuroscience, becoming the industry leader in tDCS and tES research for cognitive and movement training applications, supervising an extensive research program in application of machine learning to tDCS outcomes and modeling of electrical fields during tDCS, and bringing to market two successful non-invasive brain stimulation systems. In 2020, I co-founded Magnus Medical and served as its chief executive officer through 2022, when we gained FDA clearance for the SAINT treatment for major depression. Most recently, I have re-established my consulting practice in order to bring my experience to bear on a variety of scientific challenges in the neurotech field. As a result of these experiences, I am not only expert in the technical details of data-intensive medical device development; I am also familiar with the challenges involved in applied research and the strategies, such as communication and project planning, which mitigate these challenges. In summary, I have the expertise, leadership, training, expertise, and motivation necessary to successfully perform my role in the proposed project.

Citations:

1. Wingeier BM, Nunez PL, and Silberstein RB (2001). Spherical harmonic decomposition applied to spatial-temporal analysis of human high-density EEG. *Physical Review E* 64(5) pt 1.
2. Sillay KA, Rutecki P, Cicora K, Worrell G, Dratzkowski J, Shih JJ, Sharan AD, Morrell MJ, Williams J, Wingeier BM (2013). Long-term measurement of impedance in chronically implanted depth and subdural electrodes during response neurostimulation in humans. *Brain Stimulation* 6(5):718-726.
3. Wingeier B, Tcheng T, Koop MM, Hill BC, Heit G, and Bronte-Stewart HM (2006). Intraoperative STN DBS attenuates the prominent beta rhythm in the STN in Parkinson's Disease. *Experimental Neurology* 197(1):244-251.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024 - Present Founder and Managing Engineer, LT2 Labs, San Francisco, CA
2020 - 2023 Cofounder, CEO, and Chief Technology Officer, Magnus Medical Inc., Burlingame CA
2013 - 2020 Cofounder and Chief Technology Officer, Halo Neuroscience, San Francisco, CA
2008 - 2013 Principal, Wingeier Biomedical Consulting, San Francisco, CA
2001 - 2013 Principal Biomedical Engineer, NeuroPace Inc., Mountain View, CA
1998 - 2001 Visiting Research Fellow, Brain Sciences Institute, Melbourne, Australia
1996 - 2001 NSF Graduate Fellow, Tulane University, Brain Physics Group, New Orleans LA

Honors and Other Experience

U.S. Registered Patent Agent, registration number 69895
Reviewer, *Clinical Neurophysiology*
Past reviewer, AAAS / Michigan Technology Tri-Corridor Fund grant project
Past reviewer, DoD PRMRP/CDMRP epilepsy section
Member, Society of Clinical Research Associates
IEEE Neuroethics Working Group

C. Contributions to Science

Electrical fields and EEG analysis

My early work was focused on analysis of electrical fields - human scalp EEG - as a window into brain dynamics. Using a large, high-density dataset of EEG from healthy human participants, and extensive modeling, we characterized the falloff of coherence due to volume conduction with distance between electrodes and validated algorithms for removing the effect of volume conduction. I developed a new method of describing the spatial properties of EEG using spherical harmonic decomposition, and we demonstrated a frequency-wavelength relationship in EEG suggesting that that alpha-band activity may be consistent with standing wave dynamics.

Wingeier BM (2004). A high-resolution study of large-scale dynamic properties of human EEG. Dissertation, Tulane University.

Nunez PL, Wingeier BM, and Silberstein RB (2001). Spatial-temporal structures of human alpha rhythms: theory, microcurrent sources, multiscale measurements, and global binding of local networks. *Human Brain Mapping* 13(3):125-164.

Wingeier BM, Nunez PL, and Silberstein RB (2001). Spherical harmonic decomposition applied to spatial-temporal analysis of human high-density EEG. *Physical Review E* 64(5) pt 1.

Neurostimulation for epilepsy and other indications

Much of my later work focused on issues related to neurostimulation for epilepsy. As a principal engineer and clinical scientist at NeuroPace, I led studies of algorithmic methods to identify seizure onset in real-time from measurements of cortical electrical activity, confirming that several simplified algorithms capable of implementation in implantable devices would be robust in the presence of noise. I also led efforts to characterize the performance and impedance of electrodes across years post-implant. For the first time, we showed in detail differences between short-term and long-term impedance shift of surface and depth electrodes, and demonstrated long-term stability of macro-scale platinum-iridium electrodes implanted on the cortical surface.

Sillay KA, Rutecki P, Cicora K, Worrell G, Drazkowski J, Shih JJ, Sharan AD, Morrell MJ, Williams J, Wingeier BM (2013). Long-term measurement of impedance in chronically implanted depth and subdural electrodes during response neurostimulation in humans. *Brain Stimulation* 6(5):718-726.

Wingeier BM, Sillay KA (2011). Robustness of implantable algorithms to detect epileptiform activity in the presence of broad-spectrum background noise. *Conf Proc IEEE Eng Med Biol Soc* 2011:7537-40.

Chan AC, Sun FT, Boto EH, and Wingeier B (2008). Automated seizure onset detection for accurate onset time determination in intracranial EEG. *Clinical Neurophysiology* 119(12):2687-2696.

Drazkowski J, Zimmerman R, Worrell G, Chabolla D, Sirven J, Cascino G, Marsh R, Wharen R, Mirro E, and Wingeier BM (2005). Total charge delivered with responsive neurostimulation correlates with degree of seizure reductions. *Epilepsia* 46 supp 8:335.

Neurostimulation and biomarkers for Parkinson's disease

In a parallel collaboration, I worked with Stanford's movement disorders team to investigate the underlying mechanism of neurostimulation in Parkinson's disease. By analyzing intra-operative recordings of electrical local field potentials before, during, and after stimulation, we showed for the first time that STN DBS reduces the pathological beta rhythm correlated with Parkinsonian symptoms, and characterized the beta rhythm as a stationary, useful biomarker.

Bronte-Stewart HM, Barberini C, Koop MM, Hill BC, Henderson JM, and Wingeier B (2009). The STN beta-band profile in Parkinson's disease is stationary and shows prolonged attenuation after deep brain stimulation. *Experimental Neurology* 215(1):20-28.

Wingeier B, Tcheng T, Koop MM, Hill BC, Heit G, and Bronte-Stewart HM (2006). Intraoperative STN DBS attenuates the prominent beta rhythm in the STN in Parkinson's Disease. *Experimental Neurology* 197(1):244-251.

Medical device product development

Most recently, my contributions to science have focused on analysis, optimization, and effectiveness of non-invasive electromagnetic brain stimulation (tDCS, tES, and TMS), and particularly in product development in this field to make devices both effective and usable. Key research products for which I served as chief technologist and product manager, including leading usability and transfer-to-manufacturing efforts, are the following:

Halo Sport tES neurostimulation system (released in 2016)

Halo Sport II tES neurostimulation system (released in 2019)

Halo Mind tES neurostimulation system (clinical trial use initiated 2020)

SAINT Neuromodulation System (FDA clearance in 2022)

Intellectual property development in neuromodulation and biosignals

Throughout my career, I have developed extensive intellectual property in the area of methods, systems, and devices for neuromodulation, and currently hold over 70 issued US patents. Below are several key patent families.

- 8,761,889 Systems, methods, and devices for a skull/brain interface, to B Wingeier and BD Pless
- 9,486,618 Electrode system for electrical stimulation, to B Wingeier, T Bar-Or, C Davis, V Hammett, and R Lin
- 9,630,005 Method and system for providing electrical stimulation to a user, to B Wingeier, DS Chao, L Von Kraus, A Sarva, and S Sanchez
- 17/700451 Methods and systems for long term treatment of neuropsychiatric disorders (pending); A Maron-Katz, BS Bentzley, B Wingeier