UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

_____

NYXOAH, INC., and
NYXOAH SA,
Petitioner,

v.

INSPIRE MEDICAL SYSTEMS, INC.,
Patent Owner.

_____

IPR2026-00091
Patent 11,806,526

_____

PATENT OWNER'S PRELIMINARY RESPONSE

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Cambridge Mobile Telematics, Inc. v. Sfara, Inc., IPR2024-00952, Paper 12 (PTAB Dec. 13, 2024) 25

PATENT OWNER'S EXHIBIT LIST

Exhibit No.	Description
2001	Complaint, *Inspire Medical Systems, Inc. v. Nyxoah, Inc. et al.*, Case No. 1:25-cv-00667-RGA (D. Del.)
2002	Answer, *Inspire Medical Systems, Inc. v. Nyxoah, Inc. et al.*, Case No. 1:25-cv-00667-RGA (D. Del.)
2003	Letter to The Honorable Richard G. Andrews regarding proposed revised case schedules (D.I. 70)
2004	Order Lifting Stay, entered March 2, 2026 (D.I. 71)

Nyxoah, Inc. and Nyxoah SA ("Petitioners" or "Nyxoah") have concurrently filed three IPR petitions, including the instant Petition, challenging three related patents owned by Patent Owner Inspire Medical Systems, Inc. ("Inspire"), in the District of Delaware. The challenged patents are U.S. Patent Nos. 10,898,709 (IPR2026-00090), 11,806,526 (IPR2026-00091), and 11,850,424 (IPR2026-00092). All three patents are titled "Stimulation for Treating Sleep Disordered Breathing" and have the same specification. All three IPR petitions include the same references used in two invalidity grounds:

Ground I: Durand (Ex. 1006) in view of Hoegh (Ex. 1007); and

Ground II: Headley (Ex. 1008) in view of Tran-I (Ex. 1009) and Tran-II (Ex. 1010).

I. INTRODUCTION

The '526 Patent claims a device for treating obstructive sleep apnea (OSA). Unlike certain prior art closed-loop systems that actively sense the patient's breathing to synchronize stimulation, the claimed device achieves reliable therapeutic stimulation of an upper-airway-patency-related nerve during the inspiratory phase through carefully designed timing relationships using asymmetric stimulation and non-stimulation period durations based on reference respiratory cycle information.

The Petition suffers from a threshold procedural deficiency that independently warrants denial of institution under 37 C.F.R. § 42.104(b)(3): Petitioners have entirely failed to address the construction of the "means for stimulating" limitations that appear in every challenged claim.

Despite the extended time and resources at their disposal, Petitioners have failed to uncover any prior art that even recognizes—let alone solves—a specific problem the '526 Patent addresses. Not one of the five references Petitioners cite grapples with the challenge of designing an asynchronous nerve stimulation protocol that reliably ensures therapeutic inspiratory phase overlap without active sensing. Petitioners' collection of references either mention asynchronous stimulation only in passing, limit it to non-therapeutic contexts, or are directed to an entirely different therapeutic approach altogether.

Ground 1 is, at its core, a retread of the original prosecution. Durand was considered during prosecution. For all purposes relevant to this proceeding, Hoegh is the same as Bolea (Ex. 1012), which the Office applied in an office actions under obviousness, and ultimately concluded that it failed to render the claims unpatentable. Every figure and passage Petitioners cite from Hoegh appears in Bolea. Petitioners' reliance on Hoegh rather than Bolea is transparent gamesmanship and a calculated attempt to disguise the fact that they are relying on art the Office already extensively considered and found insufficient, while

ostensibly claiming to present a "new" reference. Hence, Ground 1 presents nothing that the Office has not already thoroughly considered and rejected during prosecution.

Ground 2 fares even worse. Petitioners' combination of Headley, Tran-I, and Tran-II fails at the most basic threshold: not one of the three cited references discloses stimulating a nerve. All three disclose direct intramuscular stimulation, and, in fact, two of them expressly teach away from nerve stimulation.

Petitioners' reliance on Tran-II is further undermined by material mischaracterizations that attempt to transform a preliminary single-subject simulation study into a validated clinical demonstration—a distortion made all the more troubling by Petitioners' use of Dr. Loeb, a named co-author of both Tran references, as their expert witness. Central to Petitioners' argument is a single low-resolution screen capture—FIG. 4 of Tran-II—from which Petitioners purport to extract specific timing parameter values that are critical to their invalidity challenge. However, those values appear nowhere in Tran-II's text and cannot be reliably derived from the low-resolution screen capture itself. Indeed, the Petition provides internally inconsistent values for the same parameter allegedly extracted from that figure, confirming that Ground 2 rests on a factually unreliable foundation.

Patent Owner respectfully requests that the Board deny institution of *inter*

partes review.

II. LEVEL OF ORDINARY SKILL IN THE ART

Only for purposes of this Preliminary Response, Patent Owner adopts Petitioners' proposed definition of a person of ordinary skill in the art ("POSITA"). Patent Owner reserves the right to propose an alternative definition of a POSITA should the Board grant institution.

III. OVERVIEW OF U.S. PATENT NO. 11,806,526

A. The Challenge of Asynchronous Stimulation for OSA Therapy

The '526 Patent is directed to a device for treating OSA through asynchronous neurostimulation of an upper-airway-patency-related nerve, such as the hypoglossal nerve. Ex. 1001, 4:24–36; 7:50–58. OSA is caused by repeated collapse of the upper airway during sleep, which obstructs airflow and forces the patient to repeatedly arouse from sleep to resume breathing.

Certain prior art references for treating OSA typically described so-called "closed-loop" systems that sensed the patient's respiration and synchronized stimulation to the inspiratory phase. Asynchronous systems, on the other hand, apply stimulation without using actively sensed respiratory information.

For context, FIG. 3A illustrates a normal breathing pattern 150 consisting of a respiratory cycle 160.

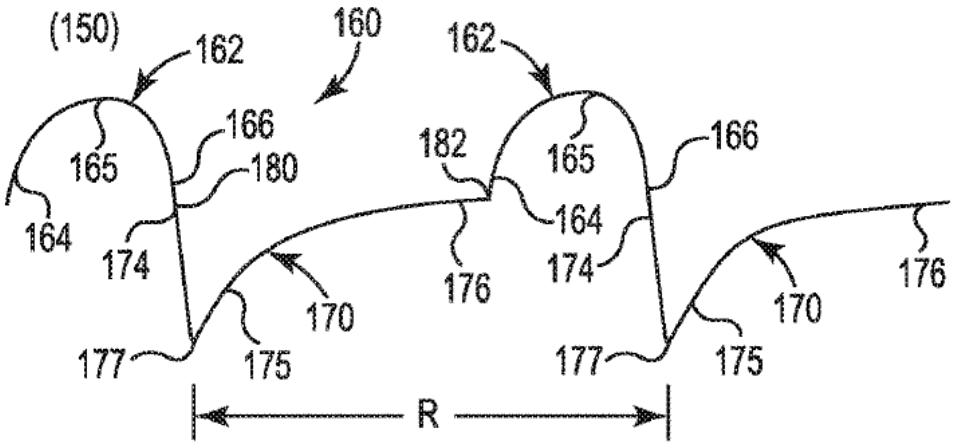


Fig. 3A

FIG. 3A of ’526 Patent

The respiratory cycle 160 includes:

- Inspiratory phase 162: The breathing-in phase, comprising an initial portion 164, intermediate portion 165, and end portion 166. Ex. 1001, 12:45–47.
- Expiratory phase 170: The breathing-out phase, comprising an initial portion 174, intermediate portion 175, end portion 176, and expiratory peak 177. Ex. 1001, 12:47–49.

For OSA patients, the upper airway collapse occurs during inspiration, when negative pressure draws soft tissue into the airway.

An asynchronous stimulation system cannot detect when inspiration begins because it lacks active sensing. Unlike the cited references in the Petition—which relegate asynchronous stimulation to only a cursory paragraph, a brief

familiarization mode, or a preliminary single-subject simulation—the ’526 Patent directly confronts the central challenges of asynchronous OSA therapy: ensuring that stimulation reliably occurs during the inspiratory phase, when airway patency is most critical, without requiring active synchronization to the patient’s breathing and without causing nerve fatigue from overstimulation. *See*, *e.g.*, *id*. at 14:62–15:2.

B. Claimed Invention

The’526 Patent claims a device that provides a stimulation protocol specifically designed so that the stimulation periods reliably overlap with a significant portion of the inspiratory phases to maintain or increase upper airway patency during OSA therapy without causing nerve fatigue. Ex. 1001, 14:56–15:2; 5:40–42. The ’526 Patent includes twenty-three total claims, with independent claims 1, 16, and 22.

Independent claim 1 of the ’526 Patent recites:

1.pre	*A device for treating obstructive sleep apnea, comprising:*
1.a1	*a non-cardiac stimulation means for stimulating an upper airway patency-related nerve,*
1.a2	*according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing,*

1.b	*wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and*
1.c	*wherein the duration of each respective stimulation period is based on a reference respiration-related parameter,*
1.d	*wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.*

Independent claim 16 of the'526 Patent recites:

16.pre	*A device for treating obstructive sleep apnea, comprising:*
16.a1	*a non-cardiac means for stimulating an upper airway patency-related nerve,*
16.a2	*according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing,*
16.b	*wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period,*
16.c	*wherein each stimulation period comprises continuous pulsed stimulation,*
16.d	*wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle,*
16.e	*wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.*

Independent claim 22 of the'526 Patent recites:

22.pre	*A device for treating obstructive sleep apnea, comprising:*
22.a1	*a non-cardiac means for stimulating an upper airway patency-related nerve,*
22.a2	*according to a first stimulation therapy protocol including alternating stimulation periods and non-stimulation periods in which a timing of the stimulation periods is asynchronous relative to patient breathing,*
22.b	*wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period, and*
22.c	*wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle,*
22.d	*wherein, the non-cardiac stimulation means for stimulating comprises an implantable electrode and/or an implantable pulse generator electrically connectable to the implantable electrode.*

FIGS. 3B–3E and 16A–16B disclose timing diagrams of different embodiments of asynchronous stimulation protocols. For example, FIG. 3B illustrates an embodiment of the claimed stimulation protocol and its relationship to the reference respiratory cycle:

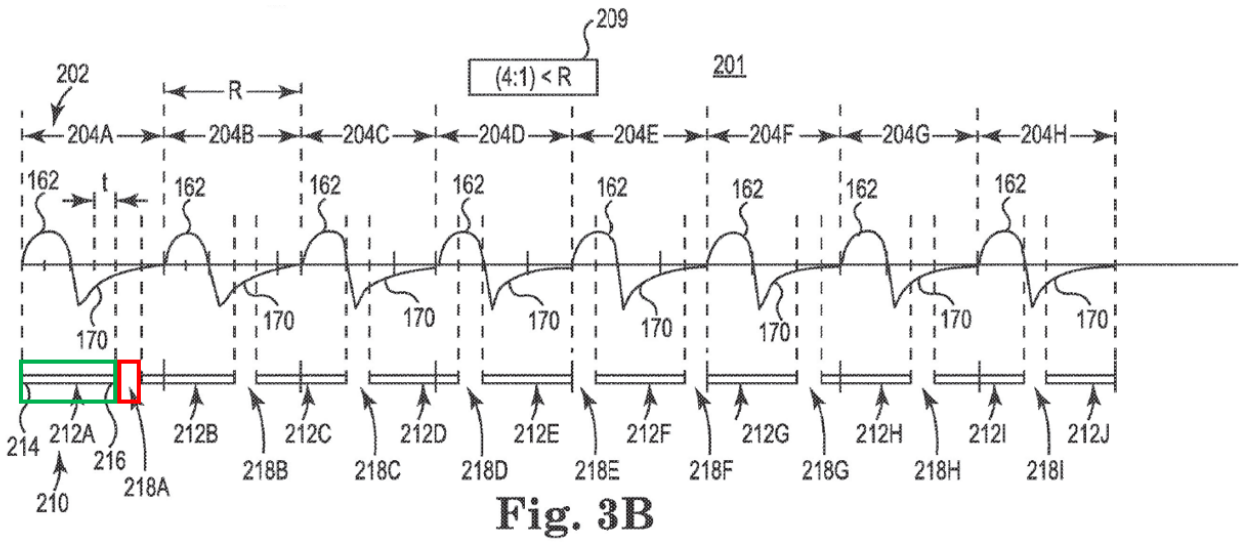


Fig. 3B

Annotated FIG. 3B of ’526 Patent

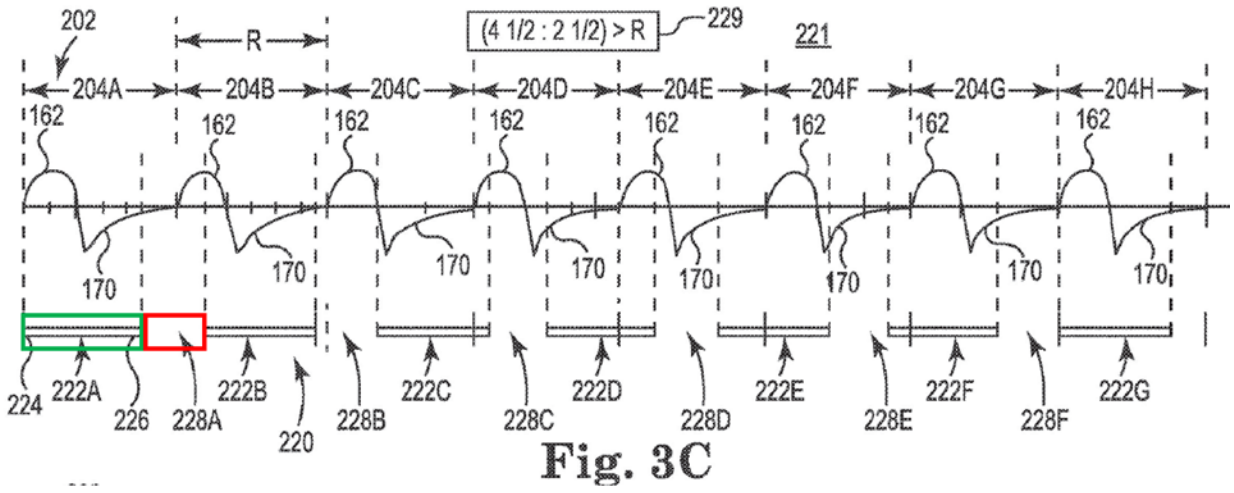
“FIG. 3B illustrates a respiratory pattern 202 including a series of reference respiratory cycles 204A-204H … each reference respiratory cycle 204A-204H has a duration R.” Ex. 1001, 12:66–13:3. “[B]ecause stimulation via the stimulation protocol 210 is not synchronized relative to characteristics of actively-sensed respiratory cycles (such as via real-time measure of respiratory effort), the stimulation protocol 210 operates based on a reference respiratory cycle.” *Id*., 13:8–12.

Per the color-coded annotations above, the “stimulation protocol 210 includes a series of separate stimulation periods (e.g., pulses) 212A-212J spaced apart by a non-stimulation periods 218A-218J.” *Id*. at 13:21–24. “[E]ach respective non-stimulation period 218A-218I has duration less than a duration of each respective stimulation periods 212A-212J.” *Id.* at 14:33–36. In the example shown

in FIG. 3B, "the stimulation period and the non-stimulation period are in a proportion of 4 to 1." *Id*. at 14:2–4.

These carefully designed timing parameters solve the asynchronous overlap challenge: "[E]ven though the stimulation is not synchronized relative to a characteristic (e.g., inspiration) of the respiratory waveform, no matter where the stimulation protocol 210 is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference cycles for a significant majority of the treatment period." *Id*. at 14:62–15:2.

FIG. 3C illustrates another embodiment of the claimed stimulation protocol and its relationship to the reference respiratory cycle:



Annotated FIG. 3C of '526 Patent

The stimulation protocol 220 still includes a stimulation period 222A greater

than a non-stimulation period 228A. *Id*. at 17:8–12. The stimulation protocol 220 of FIG. 3C differs from the stimulation protocol 210 of FIG. 3B in that "the duration of the stimulation cycle is greater than the duration (R) of the reference respiratory cycle." *Id.* at 16:39–42. Nonetheless, the result is substantially the same:

> In a manner substantially the same as previously noted for stimulation protocol 210, even though stimulation protocol 220 is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 220 is started relative to a series of respiratory cycles, the stimulation periods will overlap with at least a portion of the inspiratory phase of the respective reference respiratory cycles for a significant majority of the treatment period."
>
> *Id.* at 16:52–60.

FIG. 16B illustrates another embodiment of the claimed stimulation protocol and its relationship to the reference respiratory cycle:

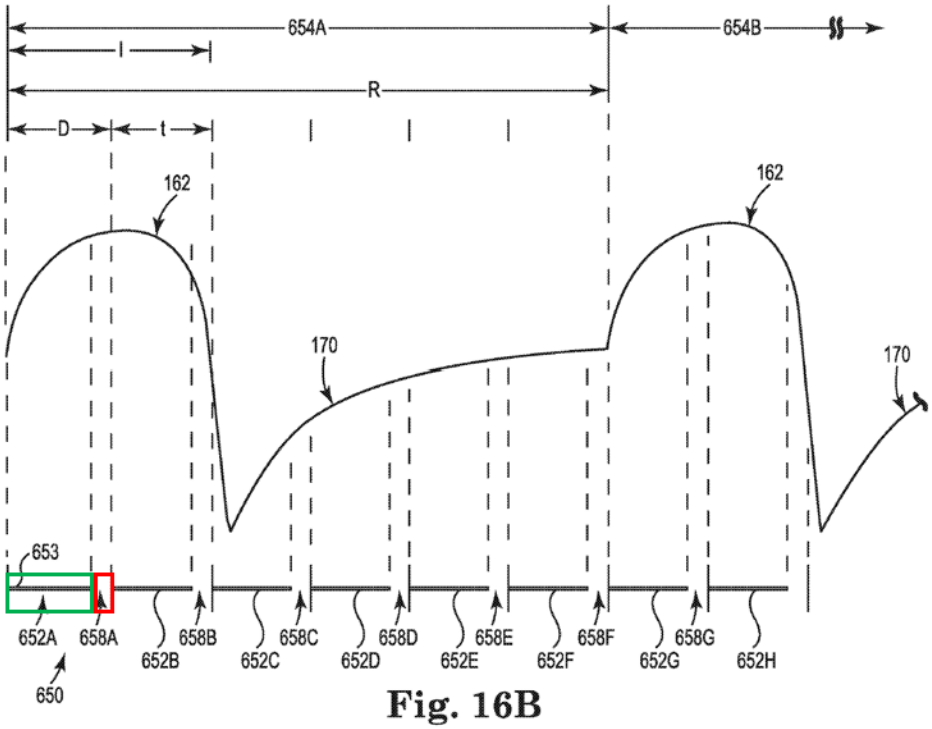


Fig. 16B

Annotated FIG. 16B of ’526 Patent

“[T]he stimulation protocol 650 operates according to stimulation cycles in which the duration (D) of each stimulation cycle is less than the duration (R) of the reference respiratory cycles 654A, 654B.” Ex. 1001 at 37:63–66. Hence, “several stimulation cycles will be repeated within a single respiratory cycle.” Ex. 1001at 39:2–4. Nonetheless, the benefit is substantially the same:

> Accordingly, even though the stimulation is not synchronized relative to a characteristic (e.g. inspiration) of the respiratory waveform, no matter where the stimulation protocol 650 is started relative to a series of respiratory cycles, the short duration (D) of the stimulation cycle (relative to the longer duration R of the respiratory cycle) ensures that at least a portion of two stimulation periods (e.g. 652A, 652B) will

significantly overlap (at least a majority) the inspiratory phase 162 of the respective reference respiratory cycles throughout the portion of the treatment period during which stimulation protocol 650 is applied. *Id.* at 39:18–28.

IV. SUMMARY OF ASSERTED REFERENCES

A. Durand (Ex. 1006)

Durand is a patent application publication titled "Method of Treating Obstructive Sleep Apnea Using Electrical Nerve Stimulation." Ex. 1006. Petitioners admit that Durand was considered during prosecution of the '526 Patent because U.S. Patent. No. 7,680,538 that was issued from Durand was cited in an IDS and considered by the Examiner. Pet. at 19.[1]

Durand describes three embodiments for treating OSA, each representing a different stimulation approach, with only the last embodiment being cited by the Petition. Ex. 1006, Abstract. The first embodiment is directed to "continuous low-level electrical stimulation." *Id*. The second embodiment is directed to "electrical stimulation synchronized with a physical process, such as inspiration." *Id*.

The third embodiment—the only embodiment that Petitioners rely upon for Ground 1—is directed to "intermittent electrical stimulation at controlled intervals

[1] In addition, the Durand patent subsequently appeared in the Examiner's PE2E search history, *see* Ex. 1002 at 104.

based on the patient's metabolism." *Id*. In contrast to the detailed discussion of asynchronous stimulation in the '526 Patent, Durand's third embodiment is described in essentially a single paragraph. Ex.1006, ¶25. That single paragraph states in its entirety:

> In a third embodiment of the method, the controller can be programmed to provide stimulation at a predetermined interval without either detecting a physical process or requiring feedback from the nerve being stimulated. In this method, the stimulation interval can be determined from the patient's nighttime basal metabolism, e.g., based on the patient's observed nighttime resting respiratory rate. The resultant timing of the stimulation pulse trains will closely simulate the patient's normal nighttime respiration cycle. For example, a train of stimulus pulses can be applied for about 2 seconds to about 3 seconds, and more particularly, for about 2½ seconds, with a wait of at least 2 seconds to about 3 seconds between the pulse trains. The pulse trains can each have an amplitude that is at or greater than the patient's activation threshold, up to about 20% above the patient's activation threshold, for example. In this embodiment, the stimulation is provided at predetermined rate or pace without the added complexity of closed-loop feedback.
> Ex. 1006, ¶25.

As discussed below in Sections VIII.A and VIII.B, Durand lacks any discussion of important claim elements, such as respiratory-related parameters and unequal stimulation and non-stimulation durations as recited in the claims.

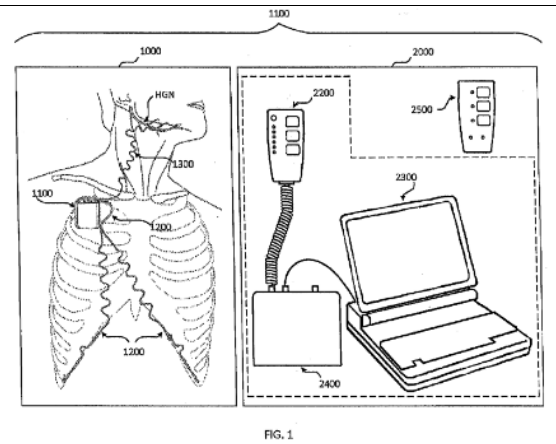
B. Hoegh (Ex. 1007)

Hoegh is a patent application publication titled "Obstructive Sleep Apnea Treatment Screening Methods." Ex. 1007.

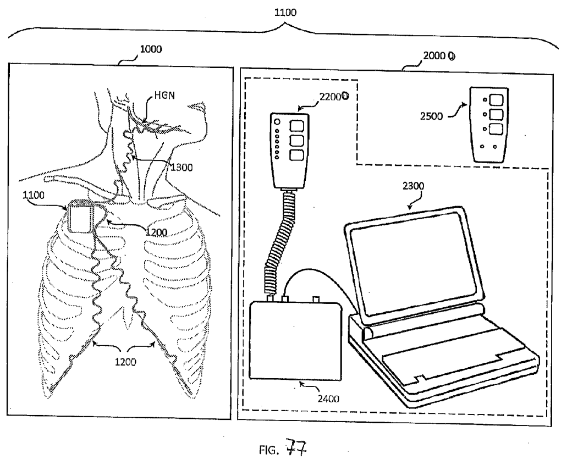
1. Hoegh Is the Same as Bolea (Ex. 1012)

As cited in the Petition, Hoegh is the same as Bolea (U.S. Patent Application Publication No. 2014/0228905, Ex. 1012), which was extensively applied by the Examiner during prosecution. Hoegh and Bolea share the same listed assignee, Cyberonics, Inc., and both applications share common subject matter. Critically, ***all*** portions of Hoegh relied upon by Petitioners in this Petition are found ***almost verbatim*** in Bolea.

The Petition exclusively cites Hoegh's discussion of stimulation techniques, which was reproduced entirely from Bolea (Ex. 1012). The Petition cites FIG. 1 from Hoegh; which is taken directly from Bolea (even the reference numbers are the same):



Hoegh's FIG. 1 (cited in Pet. at 25, 28)



Bolea's FIG. 77

The Petition quotes Hoegh for various claim elements. Each of these quotes are found verbatim or near verbatim in Bolea. For example, the Petition quotes paragraph 97 of Hoegh for element 1.b, Pet. at 30; however, paragraph 97 of Hoegh is a near verbatim copy of paragraph 498 of Bolea with only minor stylistic difference:

The stimulation duty cycle may be fixed or adaptive. In the fixed mode, *the stimulation duty cycle may be set* using the programmer system 2100 to designate a fixed percentage value. This fixed value may be increased when the respiratory period signal is lost, increasing the likelihood of aligning with actual inspiration… Thus, in some instances, the stimulation duty cycle may run above normal (e.g., above 50% to 60%) to achieve a better likelihood of covering the inspiratory phase.	The stimulation duty cycle may be fixed or adaptive. In the fixed mode, *the stimulation duty cycle is set* using to programmer system 2100 to a fixed percentage value. This fixed value may be increased when the respiratory signal is lost, increasing the likelihood of aligning with actual inspiration… Thus, in some instances, the stimulation duty cycle may run above normal (e.g., above 50% to 60%) to achieve a better likelihood of covering the inspiratory phase.
Pet. at 30 quoting Hoegh ¶97 (original emphasis removed; emphasis added)	Bolea at ¶498

As another example, consider paragraph 92 of Hoegh, which was quoted by the Petition for element 1.b, Pet. at 30, and the corresponding near verbatim disclosure in Bolea with only a minor stylistic difference:

To mimic this natural physiology, *stimulation may be delivered* to the hypoglossal nerve during the inspiratory phase plus a brief pre-inspiratory period of about 300 ms.	To mimic this natural physiology, *it is desirable to deliver stimulation* to the hypoglossal nerve during the inspiratory phase plus a brief pre-inspiratory period of about 300 ms.
Pet. at 30 quoting Hoegh ¶92 (original emphasis removed; emphasis added)	Bolea at ¶493

Indeed, ***every citation to Hoegh in the Petition is found in Bolea***:

Hoegh (Ex. 1007) citations	Bolea (Ex. 1012) matching disclosure	Hoegh (Ex. 1007) citations	Bolea (Ex. 1012) matching disclosure
FIG. 1 (Pet. at 25 and 28)	FIG. 77	¶92 (Pet. at 5, 25, 26, 30, 32, 37, 39, 46, 48 and 49)	¶493
¶50 (Pet. at 23 and 26)	¶423, 657	¶93 (Pet. at 32 and 38)	¶494
¶51 (Pet. at 26)	¶424, 658	¶96 (Pet. at 25, 41, 43, 46, 47, and 49)	¶497
¶53–59 (Pet. at 24)	¶427–433	¶97 (Pet. at 31, 37 and 40)	¶473, 498
¶69 (Pet. at 41)	¶450	¶98 (Pet. at 5, 25, 26, 41, 43, 46, and 52)	¶474, 499
¶82 (Pet. at 44)	¶483	¶114 (Pet. at 5, 23, 25, 32, 39, 40, 46, 49, 51 and 52)	¶515
¶85 (Pet. at 44)	¶486	¶134-137 (Pet. at 26)	¶589–592

That is, the ***Petition cites no portion of Hoegh which cannot also be found in Bolea***.

2. Bolea/Hoegh Was Cited Extensively in the Prosecution History

Importantly, the Examiner specifically applied the cited subject matter of

Bolea/Hoegh during prosecution and found the claims allowable over that subject matter. Petitioners' summary of the prosecution history is lacking with respect to its discussion of Bolea/Hoegh.

The Examiner issued a Non-Final Office Action on November 2, 2022. Ex. 1002 at 155–163. This Non-Final Office Action marked the Examiner's use of Bolea. Specifically, the Examiner applied Bolea in § 103 rejections of all claims. *Id*. Notably, the Examiner cited the same passages of Bolea, including paragraph 473, that correspond to the cited portion of Hoegh in the Petition. *Id.* at 158; *see also* Table, *supra.*

In response to the Non-Final Office Action, Patent Owner filed claim amendments and arguments distinguishing Bolea. *Id.* at 128–145. Patent Owner amended the claims to clarify that the first stimulation protocol was a "first stimulation therapy protocol" and argued that Bolea discloses asynchronous stimulation only for daytime familiarization purposes, not as a therapy for sleep apnea. *Id.* at 134–136. Daytime familiarization is used "during wakefulness to introduce the sensation of stimulation." Ex. 1012, ¶591, Ex. 1007, ¶136. Patent Owner argued that Bolea relies on inspiratory synchronous stimulation as its therapeutic modality and does not disclose using asynchronous stimulation as the claimed "first stimulation therapy protocol." *Id*. at 136

Based on the amendments and arguments, the Examiner found the Patent

Owner's arguments persuasive, and allowed the claims along with an Examiner's amendment. *Id*. at 93–95. In the reasons for allowance, The Examiner stated: "none of the prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing," indicating that the closest prior art would be Bolea. *Id*. at 95.

As discussed below in Section VIII.C, Bolea/Hoegh describes a hypoglossal nerve stimulation ("HGNS") system built around a respiratory sensing lead that enables synchronous, inspiration-triggered stimulation. Asynchronous stimulation plays only a minor, non-therapeutic role in Hoegh's disclosure, limited to daytime familiarization before therapeutic use begins.

C. Headley (Ex. 1008)

Headley is an international patent application publication titled "Sleep Apnea Device and Method." Ex. 1008. Headley's Background section identifies prior art nerve stimulation approaches and explains why they are inferior:

> Some have proposed implanting a cuff electrode around the hypoglossal nerve (U.S. Patent 5,522,862, U.S. patent 5,549,655, U.S. patent 5,540,733, incorporated by reference herein in their entirety). **However, this requires a major surgical operation and there is great risk since there is a vital vein immediately adjacent [to] the target nerve**.
>
> Ex. 1008, ¶6 (emphasis added).

Headley then presents its intramuscular stimulation approach as the solution to the risks and burdens of nerve stimulation, stating that its device "will allow stimulation of existing tissue and avoids the current methods of treatment which are quite uncomfortable." Ex. 1008, ¶27.

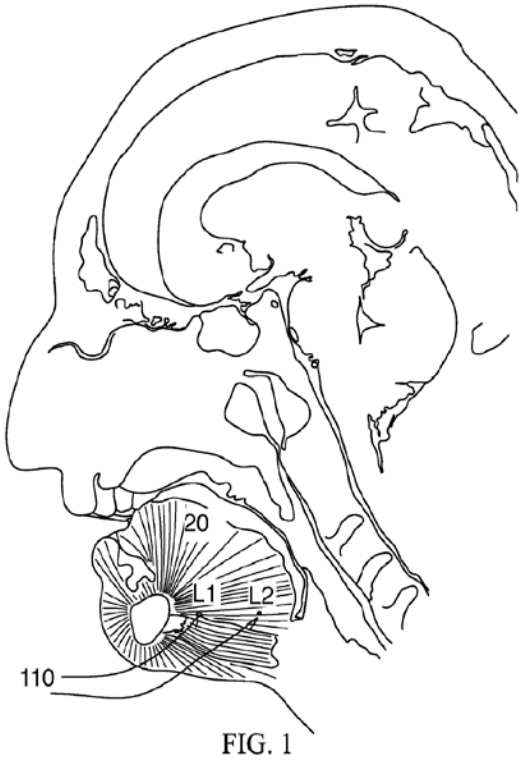


FIG. 1 of Headley

Headley's stimulation timing parameters are similarly based on patient comfort and muscle fatigue management, not respiratory physiology. Headley includes a single paragraph for wide-ranging stimulation parameters:

> In use, the device as described herein and/or the method as described herein provides for alternating on/off "intermittent" treatment wherein the tissue is stimulated for a given period, and then the tissue is allowed

> to rest for a given period. In one preferred embodiment, the device or method applies stimulation for 5 seconds, and then stimulation is turned off for 5 seconds. In another preferred embodiment, the period of stimulation ranges from 1 to 20 seconds, with varying rest periods. In another preferred embodiment, the period of stimulation is 20 seconds and the rest period is 5 seconds. In yet another preferred embodiment, the period is 60 seconds on with 60 seconds off. On periods may range, without limitations from 1 to 120 seconds, and off periods similarly. On/off intermittent periods include from 5/5, 20/5, 10/10, 5/60, 60/5, 20/20, 30/30, 40/40, 50/50, 60/60, and so forth.
> Ex. 1008, ¶48.

D. Tran-I (Ex. 1009)

Tran-I is a conference paper titled "Development of Asynchronous, Intralingual Electrical Stimulation to Treat Obstructive Sleep Apnea." Ex. 1009. The paper was authored by W.H. Tran, G.E. Loeb, F.J.R. Richmond, A.C. Dupont, K.C. Mahutte, C. S.H. Sassoon, and M.J. Dickel. Ex.1009 at 375. Notably, Dr. Gerald Loeb—one of the named authors of Tran-I—serves as Petitioners' expert witness in this proceeding. Ex. 1003, ¶1.

Tran-I describes a feasibility study evaluating the possible use of a BION™ microstimulator implanted directly into the posterior genioglossus muscle for direct intramuscular stimulation—not nerve stimulation—for the treatment of OSA. Ex. 1009 at 375. Tran-I describes preliminary testing using gated continuous positive airway pressure (CPAP) therapy—not actual electrical stimulation—with

results from only two patients. Ex. 1009 at 377. FIG. 5 of Tran-I illustrates the model of the gated CPAP machine used in the testing.

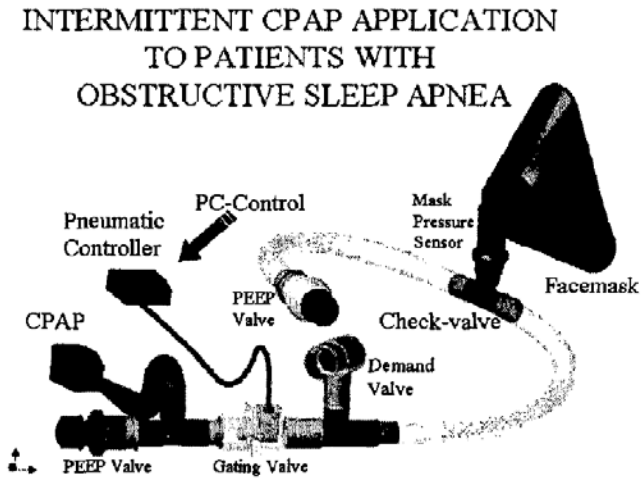


Fig. 5. Model to study rhythmically entrained breathing. Computer gating of CPAP machine in breathing circuit with pressure regulating valves to deliver intermittent positive pressure to open patient's airway.

FIG. 5 of Tran-I

No specific implantable device stimulation parameters are described in Tran-I, and no specific numerical values for stimulation period, non-stimulation period, or their relationship to inspiratory phase duration are disclosed. Ex. 1009 at 375–378.

E. Tran-II (Ex. 1010)

Tran-II is a conference paper titled "First Subject Evaluated with Simulated BION™ Treatment in Posterior Genioglossus to Prevent Obstructive Sleep Apnea." Ex. 1010. Tran-II was authored by a different set of authors than Tran-I: W.H. Tran, G.E. Loeb, F.J.R. Richmond, R. Ahmed, G.T. Clark, and P.B. Haberman. Ex. 1010 at 4287. As with Tran-I, Dr. Gerald Loeb—Petitioners' expert

witness in this proceeding—is a named co-author of Tran-II. Ex. 1003, ¶1.

Tran-II describes using temporary bipolar hooked wire electrodes inserted percutaneously into the genioglossus muscle to simulate what an implanted BION™ device might do: "*Bipolar hooked wires* are inserted percutaneously into the tongue muscle, from under the chin at midline, and used for neuromuscular stimulation." Ex. 1010 at 4287 (emphasis added); *see also id*. at 4288. Tran-II describes results of using the wire electrodes (not a BION™ device) from a single human subject evaluated in a single overnight session. *See* Ex. 1010 at 4287–4288.

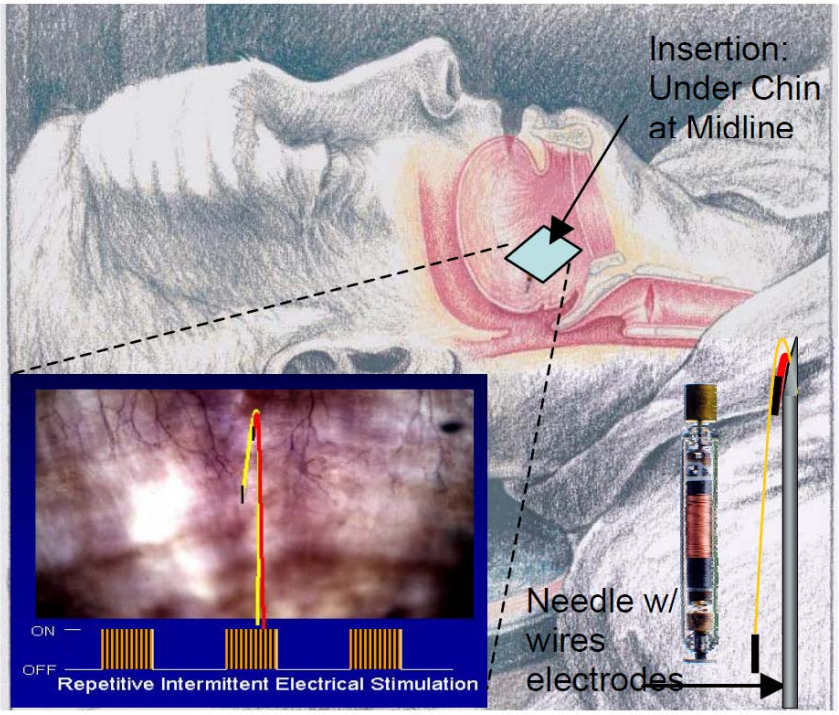


Fig. 2. Bipolar hooked wire electrodes inserted at midline of posterior genioglossus. *Right:* Bare tips of wire electrodes are separated at the same distance as the BION's electrodes. *Left:* Coronal/Horizonal section of wire electrodes in posterior genioglossus at midline. Repetitive intermittent electrical stimulation is used to activate motor endplates to produce the desired tongue movement.

FIG. 2 of Tran-II

Tran-II's results were inconclusive, at best:

> We were not able to assess the effects of repetitive intermittent neuromuscular stimulation on OSA adequately. The participant had many fewer episodes of apnea during the night than when he was diagnosed. The few obstructive sleep apneas that occurred did not provide enough opportunity to properly evaluate the effects of stimulation.

Ex. 1010 at 4289.

V. CLAIM CONSTRUCTION

Petitioners state that "[e]ach claim term in the Challenged Claims should be given its plain and ordinary meaning in this proceeding." Pet. at 14. Only for the purposes of this Preliminary Response, Patent Owner has applied Petitioners' "plain and ordinary meaning," as best understood. Patent Owner reserves the right to propose alternative claim constructions should the Board grant institution. Under any reasonable construction of the claim terms, Petitioners have failed to demonstrate that the prior art discloses or suggests the challenged claims.

VI. THE PETITION IS DEFICIENT UNDER 37 C.F.R. § 42.104(B)(3)

Pursuant to 37 C.F.R. § 42.104(b)(3), Petitioner must identify "[h]ow the challenged claim is to be construed." All challenged claims of the '526 Patent recite "means for stimulating" elements:

- Claim 1: "non-cardiac stimulation means for stimulating"

- Claims 16 and 22: "non-cardiac means for stimulating"

The Board has made clear that a petitioner who fails to address "means" elements does so at its peril regardless of whether it believes 35 U.S.C. § 112(f) "should or should not apply":

> The Consolidated Trial Practice Guide ("CTPG") . . . instructs that "[w]here claim language *may* be construed according to 35 U.S.C. § 112(f), a petitioner *must* provide a construction." CTPG 45 (emphases added) (citing 37 C.F.R. § 42.104(b)(3)). The CTPG advises that a party "may choose to elaborate why § 112(f) should or should not apply to the limitation at issue." *Id.* Notably, the CTPG warns that "[a] petitioner who chooses not to address construction under § 112(f) risks failing to satisfy the requirement of 37 C.F.R. § 42.104(b)(3)." *Id.*

Cambridge Mobile Telematics, Inc. v. Sfara, Inc., IPR2024-00952, Paper 12 at 6 (PTAB Dec. 13, 2024) (designated Informative Mar. 20, 2025); *see also 10x Genomics, Inc. v. Pres. and Fellows of Harvard Coll.*, IPR2023-01299, Paper 15 at 2, 7–8 (PTAB Mar. 14, 2024) (denying institution under 37 C.F.R. § 42.104(b)(3)).

Here, Petitioners have chosen not to address the construction of the "means for stimulating" elements, asserting instead that "[e]ach claim term in the Challenged Claims should be given its plain and ordinary meaning in this proceeding." Pet. at 13. Petitioners have failed to: (1) identify why the "means for stimulating" terms are not means-plus-function limitations under 35 U.S.C. § 112(f), or in the alternative, (2) "identify the specific portions of the specification

that describe the structure, material, or acts corresponding to each claimed function." 37 C.F.R. § 42.104(b)(3).

Although claim construction briefing has not yet begun in the district court case involving the same asserted patents, Petitioners have averred their products do not have the "means for stimulating" elements in the '526 Patent, likely indicating that Petitioners will take a different claim construction position in the district court case. Ex. 2002 at 52. The rules require Petitioners to address the "means for stimulating" term regardless of whether it believes 35 U.S.C. § 112(f) "should or should not apply"—not to remain silent in an attempt to preserve conflicting claim scope positions across forums.

Therefore, Petitioners have failed to comply with 37 C.F.R. § 42.104(b)(3), and institution should be denied.

VII. THE PETITION PROVIDES NO NEW EVIDENCE TO DISTURB THE OFFICE'S PREVIOUS FINDINGS ABOUT DURAND AND HOEGH (GROUND 1)

The Office has already considered both Durand and Hoegh during prosecution of the '526 Patent and found them insufficient to render the claims unpatentable. With respect to Durand, the patent corresponding to Durand—U.S. Patent No. 7,680,538—was before the Examiner. See Section IV.A.

Petitioners' decision to rely on Hoegh rather than Bolea is transparent gamesmanship that the Board should not countenance. Hoegh, as cited in the

Petition, is the same as Bolea, and Petitioners provide no reasoning or explanation why Hoegh provides better evidence of the prior art than Bolea. See Section IV.B.1. Petitioners' strategic and deliberate choice to cite Hoegh rather than Bolea allowed them to ostensibly claim that they are citing a "new" reference, when it is clearly gamesmanship to avoid confronting the inconvenient fact that the Office already extensively considered Bolea/Hoegh and found it insufficient to render the claims unpatentable. See Section IV.B.2.

For example, in the "Reasons for Allowance," the Examiner stated that "none of the cited prior art discloses a first stimulation therapy protocol with alternating stimulation periods and non-stimulation periods in which a timing of stimulation periods is asynchronous relative to patient breathing." Ex. 1002 at 95. Petitioners cite Bolea/Hoegh for allegedly teaching this claim element, citing passages (e.g., Hoegh ¶97/Bolea ¶473) already expressly considered by the Examiner. Pet. at 30; Ex. 1002 at 157–163; *see also* Table, *supra.*

Ground 1 does not cite a single reference, identify a single teaching, or advance a single argument that was not available to and considered by the Office during prosecution. Therefore, Petitioners provide no new evidence to disturb the Office's findings of Ground 1, and Ground 1 should be denied.

VIII. GROUND 1 (DURAND-HOEGH) FAILS TO DISCLOSE THE CLAIMED TIMING RELATIONSHIPS

As the Office has already concluded, Petitioners' Ground 1 fails to establish

obviousness because neither Durand nor Hoegh, alone or in combination, discloses or renders obvious the specific asynchronous therapy protocol recited in the challenged claims.

All claims recite, *inter alia*: "wherein a duration of each respective stimulation period is greater than a duration of each respective non-stimulation period." Claims 1, 16, and 22. Further, each of the independent claims recite a different element directed to a relationship with reference cycle related timing:

- Claim 1: "wherein the duration of each respective stimulation period is based on a reference respiratory-related parameter"
- Claim 16: "wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle"
- Claim 22: "wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle"

Thus, each of the independent claims requires two concurrent timing relationships with respect to a stimulation cycle:

1. stimulation period > non-stimulation period

2. reference respiratory relationship where:

a. stimulation period is based on a reference respiratory-related parameter (claim 1);

b. multiple stimulation periods within a reference respiratory cycle R (claim 16); or

c. stimulation cycle (stimulation period + non-stimulation period) > reference respiratory cycle R (claim 22)

As described in the specification, these timing relationships ensure that even in an asynchronous stimulation system (where stimulation is not synchronized to actively sensed respiration), the stimulation has a high probability of overlapping with the patient's inspiratory phase for a therapeutically effective proportion of respiratory cycles. See Section III.B, *supra*. Neither Durand nor Bolea/Hoegh, alone or in combination, discloses these claim elements.

A. Durand Fails to Teach That Stimulation Period Is Based on a Reference Respiratory-Related Parameter

Petitioners concede that Durand does not disclose this limitation in claim 1. The Petition admits: "Durand does not expressly disclose basing the duration of the stimulation period on a reference respiratory related parameter, …" Pet. at 4–5 (emphasis removed). Durand also does not teach "wherein the first stimulation protocol is to deliver multiple stimulation periods within a duration of a reference respiratory cycle" (claim 16) and "wherein a combined duration of a respective one of the stimulation periods and a respective one of the non-stimulation periods is greater than a duration of a reference respiratory cycle." (claim 22). *See* Pet. at 46, 51 (not citing Durand for these claim elements).

B. Durand Also Fails to Teach a Stimulation Period Being Greater Than a Non-Stimulation Period and, in Fact, Suggests the Opposite

1. Durand Does Not Disclose a Stimulation Period Greater Than a Non-Stimulation Period

Durand's disclosure indicates equal durations for the stimulation and non-stimulation periods, not the claimed inequality. Durand states:

> For example, **a train of stimulus pulses can be applied for about 2 seconds to about 3 seconds**, and more particularly, for about 2½ seconds, with a **wait of at least 2 seconds to about 3 seconds** between the pulse trains.
>
> Ex. 1006, ¶25 (emphasis added).

Durand provides corresponding duration ranges for the two relevant parameters: "about 2 seconds to about 3 seconds" for stimulation and "**at least** 2 seconds to about 3 seconds" for the wait period. *Id.* (emphasis added). That is, Durand defines the wait period relative to the respective stimulation period and to be "at least" the duration of the stimulation period.

In this context, Durand's reference to a particular 2.5 second stimulation period implies that the non-stimulation period would also be at least 2.5 seconds. This is consistent with the conventional understanding of asynchronous stimulation systems in the prior art such as the references cited in the Petition. For example, when Hoegh/Bolea describes its own asynchronous mode (for daytime familiarization), it teaches the same configuration of 2.5 seconds on and 2.5

seconds off: "Asynchronous mode (fixed mode) is when stimulation is delivered at regular programmable intervals (e.g., **2.5 seconds of stimulation, followed by 2.5 seconds off**)." Ex. 1007, ¶114 (emphasis added); *see also* Pet. at 67–68 (characterizing Tran-II as disclosing 2.5 seconds on/2.5 seconds off). The convergence of multiple references on identical parameters demonstrates this was the conventional design approach for asynchronous stimulation. *See Randall Mfg. v. Rea,* 733 F.3d 1355, 1363 (Fed. Cir. 2013*)*.

2. Durand, at Best, Suggests a Stimulation Period Being Shorter Than a Non-Stimulation Period to Simulate the Patient's Normal Nighttime Respiration Cycle

More fundamentally, when read in full context, Durand, if anything, would teach away from the claimed relationship. Durand states:

> In this method, the stimulation interval can be determined from the patient's nighttime basal metabolism, e.g., based on the patient's observed nighttime resting respiratory rate. **The resultant timing of the stimulation pulse trains will closely simulate the patient's normal nighttime respiration cycle**.
> Ex. 1006, ¶ 25 (emphasis added).

The resultant timing of the pulse trains is created by pulses generated during the stimulation period separated by the respective wait period. The directive to "closely simulate the patient's normal nighttime respiration cycle" suggests matching the natural respiratory pattern, including its temporal structure.

Normal respiratory physiology features a shorter inspiration interval than the

expiration interval. As Petitioners' own expert acknowledges: "In people without OSA, inspiration is typically 25-50% of the respiratory cycle." Ex. 1003, ¶105 (quoting Ex. 1007, ¶92). This means that, according to Petitioners' expert, inspiration is 25-50% (shorter phase) of the cycle while non-inspiration/expiration is 50-75% (longer phase).

To "closely simulate the patient's normal nighttime respiration cycle," a POSITA, assuming a POSITA would be motivated to use unequal durations, would design the stimulation protocol to reflect the natural respiratory pattern—using a shorter stimulation period (mimicking shorter inspiration) and a longer non-stimulation period (mimicking longer expiration). This is the opposite of the claimed relationship (stimulation period > non-stimulation period). *W.L. Gore & Assoc., Inc. v. Garlock, Inc.,* 721 F.2d 1540, 1550–51 (Fed. Cir. 1983) (holding the district court erred by "considering the references in less than their entireties, i.e., in disregarding disclosures in the references that diverge from and teach away from the invention at hand"); *see also Arctic Cat Inc. v. Bombardier Recreational Prods. Inc.*, 876 F.3d 1350, 1360 (Fed. Cir. 2017).

Moreover, a reference whose disclosure encompasses alternatives to the claimed invention does not render the claim obvious when the reference teaches away from the claimed configuration. *See Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 141 F.4th 1367, 1382–83 (Fed. Cir. 2025).

C. Hoegh Does Not Cure Durand's Deficiencies

Petitioners attempt to remedy Durand's failures by combining it with Hoegh. As the Office has already found, Hoegh/Bolea does not disclose the claimed timing parameters. *See* Section VII, *supra*.

First, Hoegh's primary focus is synchronous stimulation, which is fundamentally incompatible with the claimed asynchronous therapy protocol. Second, Hoegh's limited asynchronous disclosure pertains to non-therapeutic daytime familiarization and uses only equal stimulation and non-stimulation periods, failing to remedy Durand's deficiencies. Third, the specific teachings Petitioners selectively cite from Hoegh (300 ms pre-inspiratory extension, variable duty cycles) cannot be transplanted to an asynchronous system because those teachings are inextricably tied to synchronous operation with active respiratory sensing. Each of these failures independently defeats Ground 1. Collectively, these clear gaps in the teachings of Hoegh demonstrate that Petitioners' combination is an impermissible hindsight reconstruction.

1. Hoegh is Directed to Synchronous Stimulation with Respiratory Sensing

Hoegh's core disclosure is synchronous stimulation triggered by actively sensed respiratory information, not asynchronous stimulation. Hoegh's FIG. 1 "illustrates an exemplary hypoglossal nerve stimulation (HGNS) system 100" where "[s]timulation may be generated by an implantable neurostimulator (INS)

1100, for example **synchronized with inspiration as measured by the respiration sensing lead (RSL) 1200 using bio-impedance**." Ex. 1007, ¶50 (emphasis added).

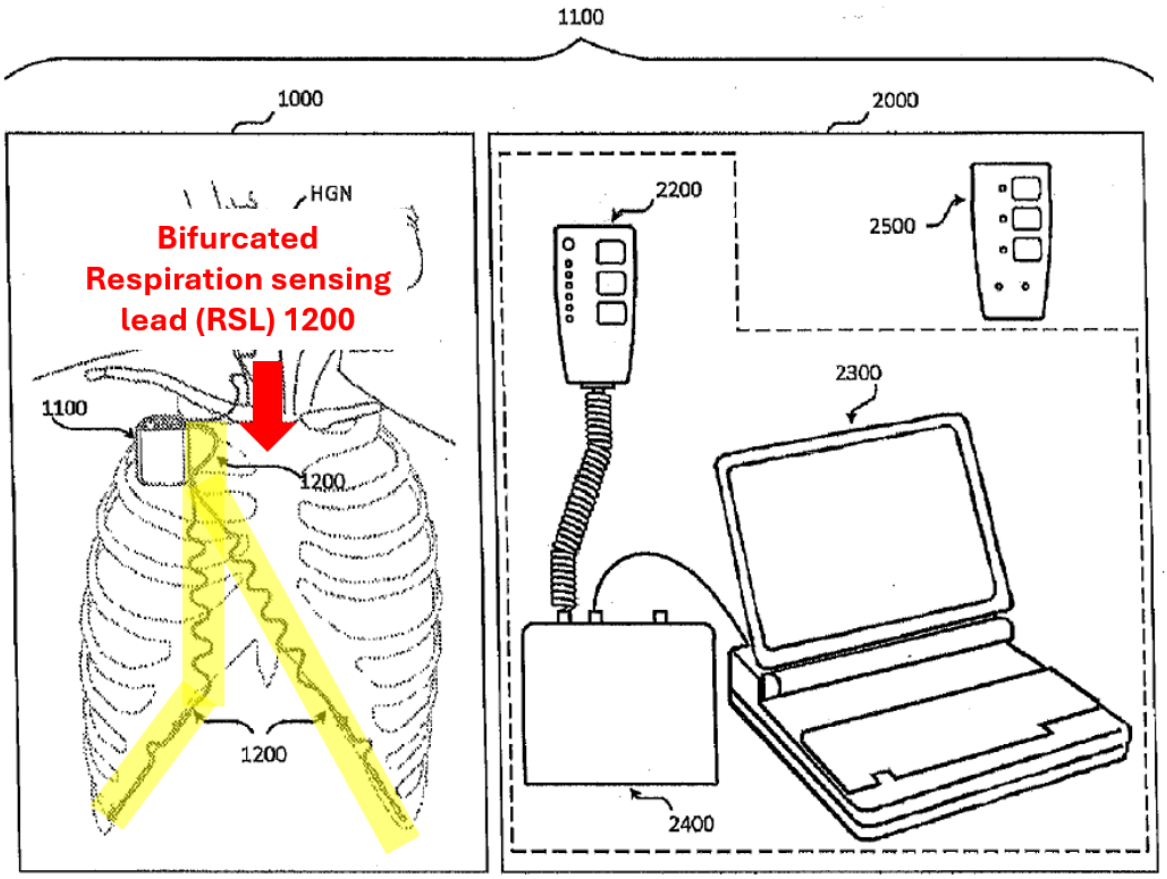


FIG. 1

Annotated FIG. 1 of Hoegh

The RSL is central, not optional, in Hoegh's system. The centrality of the RSL in Hoegh is shown by the fourteen figures and entire section expressly entitled "Respiration Sensing Lead (RSL)" detailing the specifics of the RSL design. Ex. 1007, ¶¶60–73, FIGS. 4A–4H.

In addition, Hoegh's detailed stimulation algorithms and therapeutic stimulation modes are uniformly synchronous to the actively sensed respiratory information by the RSL. Ex. 1007, ¶¶92–112. Hoegh describes sophisticated predictive algorithms for synchronous stimulation: "Accordingly, an algorithm may be used to predict respiratory period and determine the start of the stimulation burst. The predictive algorithm may be contained in software and executed by a microprocessor resident in the INS circuitry 1130, **thus enabling the INS 1100 to generate stimulation synchronous with inspiration**." Ex. 1007, ¶93 (emphasis added). These algorithms detect expiratory onset (peak P) via bio-impedance signal, predict future peaks, and time stimulation accordingly, which is quintessentially synchronous operation.

Hoegh's therapeutic stimulation modes are exclusively synchronous. FIG. 6I (traces 1-8) describes various therapeutic modes: Hoegh expressly labels all eight traces "inspiratory synchronous." "FIG. 6I (traces 1-8) illustrates some commonly used modes, **all of which are inspiratory synchronous**, meaning stimulation is automatically delivered according to an algorithm that predicts the inspiratory phase and initiates stimulation delivery at a desired time relative to inspiration, such as centered on the predicted inspiration." Ex. 1007, ¶104 (emphasis added).

In contrast, Hoegh mentions asynchronous mode in just two paragraphs with minimal technical detail, reproduced here in their entirety:

Stimulation may also be delivered in two modes which are not inspiratory synchronous: manual stimulation and asynchronous (fixed) stimulation. Manual mode delivers stimulation at any frequency, pulse width, amplitude, pulse configuration, and/or duration (e.g., up to 12 seconds). In manual mode, stimulation is delivered by manually entering a command via the programmer system to initiate delivery of a stimulation burst or bursts. The stimulation continues until the burst duration expires or stimulation stop is commanded via the programmer system. Manually delivered stimulations may be delivered in any available pulse configuration.

Asynchronous mode (fixed mode) is when stimulation is delivered at regular programmable intervals (e.g., 2.5 seconds of stimulation, followed by 2.5 seconds off). The intervals may be set to a rate similar to a respiratory cycle, (e.g. 5 seconds). Alternatively, longer intervals (e.g. 8 seconds) may decrease the probability of missing two consecutive inspirations, and increase the probability of providing the patient with stimulation during an entire respiratory cycle. **This may be used during daytime familiarization, ensuring that the patient receives stimulation in a regular fashion, as breathing patterns during wakefulness may be more irregular and difficult to predict than during sleep**. In addition, this mode may be used to test the benefits of asynchronous stimulation compared to inspiratory synchronous stimulation. Asynchronous stimulation may be initiated by programming the device to fixed mode and starting a therapy session. Fixed mode stimulations may be in any available pulse train configuration.

Ex. 1007, ¶¶113–114 (emphasis added).

2. Hoegh Discloses Asynchronous Mode Only for Non-Therapeutic Daytime Familiarization or Testing

As the Office has already correctly considered and found during prosecution, Hoegh's asynchronous mode is "used during daytime familiarization" or testing, not therapeutic treatment for OSA during sleep. *See* Ex. 1002 at 95, 136 (citing Ex. 1012, ¶515 which is analogous to Ex. 1007, ¶114). Hoegh's treatment protocol differentiates pre-therapeutic processes (including familiarization) from actual therapeutic use by segregating the processes from each other.

This segregation can be seen in Hoegh's "FIG. 12A [which] illustrates a treatment overview from implant 10100, to awake titration 10200, to **daytime familiarization 10400**, to sleep titration 10500, to nighttime familiarization 10700, to up-titration 10800, and finally to **regular therapeutic use 11000** and therapy assessments 11100" (Ex. 1007, ¶134) (emphasis added):

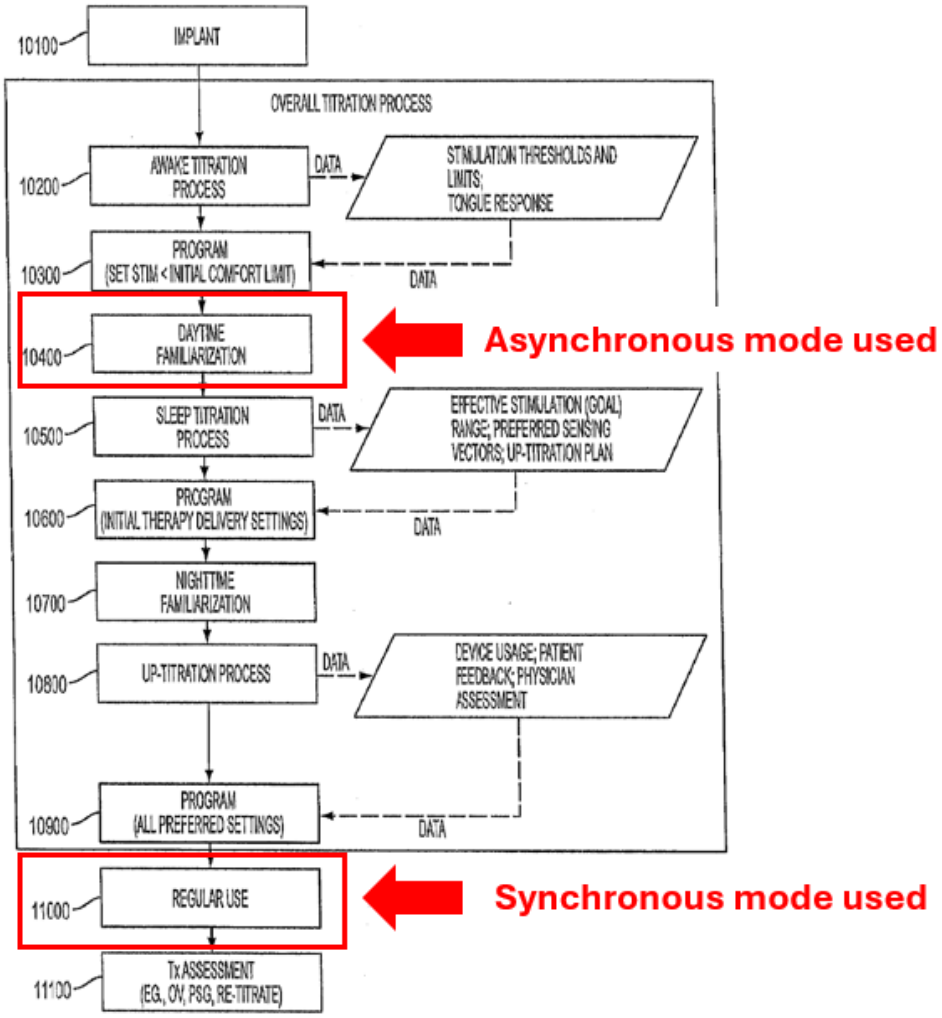


FIG. 12A

Annotated FIG. 12A of Hoegh

The flowchart in FIG. 12A of Hoegh clearly delineates "OVERALL TITRATION PROCESS," including daytime familiarization 10400, nighttime familiarization 10700, and multiple titration processes (e.g., 10200, 10500, 10800) from regular use 1100, which uses synchronized stimulation as described above.

Daytime familiarization occurs "during wakefulness," not during sleep when therapeutic therapy is needed to treat OSA. Ex. 1007, ¶114. The purpose of

daytime familiarization is "to introduce the sensation of stimulation," not treat OSA. Ex. 1007, ¶136. Importantly, daytime familiarization occurs before sleep titration 10500 where "efficacious settings" for therapy "during sleep" are determined. *Id*.

Hoegh states that "This [asynchronous mode] may be used during daytime familiarization, ensuring that the patient receives stimulation in a regular fashion, as breathing patterns during wakefulness may be more irregular and difficult to predict than during sleep." Ex. 1007, ¶114. In light of this context, Hoegh's reference to "therapy session" in "[a]synchronous stimulation may be initiated by programming the device to fixed mode and starting a therapy session," is reference to the start of the daytime familiarization session. Ex. 1007, ¶114. Hoegh uses "therapy session" to refer to any period of stimulation therapy, including pre-therapeutic processes. Hoegh's use of "therapy session" as inclusive of the multiple titration processes (e.g., 10200, 10500, 10800) where the physician starts the therapy session, and daytime familiarization 10400 where the patient starts the therapy session, is confirmed by the very next paragraph of Hoegh, which states, "[t]he patient **or physician may start a therapy session** using the therapy controller 2500 or programmer system 2100." Ex. 1007, ¶115 (emphasis added). *See also* Ex. 1007, ¶¶134, 190, 194, 195, 205, 206.

3. Hoegh's "300 ms Pre-Inspiratory Period" Teaching Is Exclusively for Synchronous Stimulation and Cannot Be Applied to Asynchronous Stimulation

Petitioners rely on Hoegh ¶92's teaching about delivering stimulation "during the inspiratory phase plus a brief pre-inspiratory period of about 300 ms" to argue that stimulation duration exceeds inspiratory phase duration. Pet. at 30. However, Petitioners' reliance on this teaching of Hoegh is misplaced because the "300 ms pre-inspiratory period" is inextricably linked to synchronous operation with active respiratory sensing and cannot be applied to asynchronous stimulation.

Petitioners omit critical context by quoting only a small portion of Hoegh ¶92 in the Petition:

> In people without OSA, inspiration is typically 25-50% of the respiratory cycle, with variations in respiration rate being common. Variations may cause actual inspiration to differ from predicted inspiration. The hypoglossal nerve usually activates approximately 300 ms before inspiration and remains active for the entire inspiratory phase. *To mimic this natural physiology, stimulation may be delivered to the hypoglossal nerve during the inspiratory phase plus a brief pre-inspiratory period of about 300 ms.* **To maximize stimulation coverage of actual inspiration and to account for this variability, stimulation may be centered on the predicted inspiration. As mentioned previously, there are reliable fiducials for the beginning of the expiratory phase (peak P) which may be used to deliver stimulation to cover the inspiratory phase plus brief pre and/or post-inspiratory periods.**"

Ex. 1007, ¶92 (emphasis added; emphasis added; italics indicate portion quoted in the Petition, bold indicates omitted context).

These next two sentences after Petitioners' excerpt make plain that the 300 ms teaching is linked with a synchronized stimulation protocol. Hoegh explains that the "stimulation may be centered on the predicted inspiration," and "reliable fiducials for the beginning of the expiratory phase (peak P) which may be used to deliver stimulation to cover the inspiratory phase plus brief pre and/or post-inspiratory periods," meaning the system predicts when inspiration will occur based on respiratory sensing and times stimulation accordingly. Ex. 1007, ¶92.

Indeed, the following paragraphs of Hoegh (¶¶93–95) further describe the predictive algorithms using synchronized stimulation implementing the "pre and/or post-inspiratory periods," referencing, e.g., FIG. 6B:

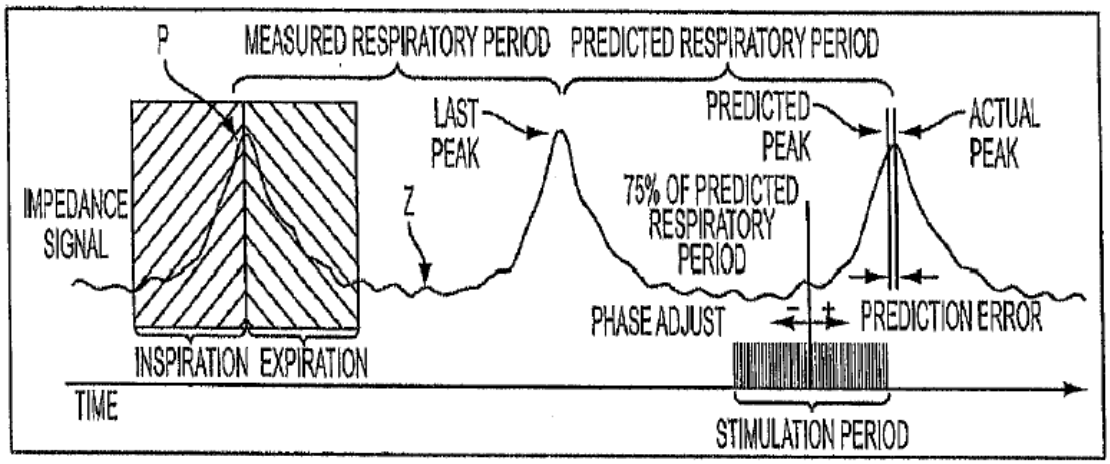


FIG. 6B

FIG. 6B of Hoegh

When describing FIG. 6B, Hoegh explains "[a]ccordingly, **an algorithm may be used to predict respiratory period and determine the start of the stimulation burst** … enabling the INS 1100 to generate **stimulation synchronous with inspiration**." Ex. 1007, ¶93 (emphasis added). Hoegh further states with reference to FIG. 6B that "[i]n this example, the stimulation period is centered about a percentage (e.g., 75%) of the predictive respiratory period. **The predictive algorithm uses historical peak data (i.e., begin-expiration data) to predict the time to the next peak**, which is equivalent to the predicted respiratory period." Ex. 1007, ¶94 (emphasis added).

In contrast to Petitioners' selective excerpt, Hoegh's full description establishes the teaching of including the 300 ms pre-inspiratory period pertains exclusively to synchronous stimulation based on actively sensed respiratory events.

Moreover, the 300 ms pre-inspiratory period fundamentally cannot be applied to asynchronous stimulation. Asynchronous stimulation delivers stimulation at predetermined intervals without using actively sensed respiratory events. In asynchronous operation, a system does not detect inspiration and, thus, does not know when the inspiratory phase begins or ends—therefore an asynchronous system simply cannot extend stimulation to cover the disclosed 300 ms "pre-inspiratory period" because the system is not detecting inspiration. *See* Ex. 1007, ¶92. Put simply, the disclosed 300 ms pre-inspiratory extension is

meaningless without the respiratory sensing that enables prediction of when inspiration will occur. A POSITA would recognize this fundamental incompatibility and would not attempt to apply the disclosed 300 ms pre-inspiratory period stimulation teachings to asynchronous operation as proposed by the Petitioners.

4. Hoegh's Variable Duty Cycle Teachings Are Also Tied to Synchronous Operation

Petitioners also cite Hoegh's variable duty cycle teaching in Hoegh ¶97 to argue Hoegh teaches longer stimulation periods. Pet. at 30. But again, Petitioners improperly extract this teaching from its synchronous context.

Hoegh's variable duty cycle teaching in ¶97 is in the context of synchronized stimulation, not asynchronous mode. Hoegh does not introduce any form of asynchronous mode until ¶113. The duty cycles in Hoegh vary as a function of the actively sensed respiratory signal. Hoegh states that "[i]n adaptive mode, the duty cycle may be allowed to vary as a function of a characteristic of respiration. Ex. 1007, ¶97. Indeed, the last sentence of the paragraph states that "when the prediction is highly accurate (stable respiration rate), the stimulation duty cycle may be reduced." *See also* Hoegh, ¶98 ("As mentioned above, the adaptive mode allows the duty cycle to decrease when respiratory period is stable and increase with respiratory period variability."). Therefore, the variable duty cycles are exclusively used for synchronized stimulation.

5. Hoegh's Asynchronous Disclosure Uses Only Equal Duration Periods

Notably, when Hoegh describes asynchronous stimulation (for daytime familiarization), it teaches equal stimulation and non-stimulation periods. Hoegh states: "Asynchronous mode (fixed mode) is when stimulation is delivered at regular programmable intervals (e.g., **2.5 seconds of stimulation, followed by 2.5 seconds off**)." Ex. 1007, ¶114 (emphasis added).

Hoegh continues: "Alternatively, **longer intervals (e.g. 8 seconds)** may decrease the probability of missing two consecutive inspirations, and increase the probability of providing the patient with stimulation during an entire respiratory cycle." Ex. 1007, ¶114 (emphasis added). This teaching by Hoegh addresses the asynchronous challenge (ensuring stimulation overlaps with inspiration without sensing), but Hoegh's solution is different than the solution claimed by the '526 Patent. Hoegh contemplates only longer intervals, not the claimed solution of creating unequal stimulation/non-stimulation periods with stimulation periods exceeding non-stimulation periods in length. Therefore, Petitioners cannot rely on Hoegh to teach or suggest the claimed inequality of stimulation and non-stimulation periods because Hoegh's limited asynchronous disclosure only ever shows using equal periods.

IX. GROUND 2 (HEADLEY-TRAN) FAILS TO DISCLOSE NERVE STIMULATION

Petitioners' combination of Headley and Tran-I/Tran-II fails at a basic level

because all three references fail to disclose stimulating a nerve as recited in the claims.

A. All Three References Disclose Intramuscular Stimulation, Not Nerve Stimulation

Claim 1 requires a "a non-cardiac stimulation means for **stimulating an upper airway patency-related nerve**," and claims 16 and 22 requires "a non-cardiac means for **stimulating an upper airway patency-related nerve**." (emphasis added). None of the three references Petitioners cited in Ground 2—Headley, Tran-I, or Tran-II—discloses nerve stimulation. All three disclose direct intramuscular stimulation.

1. Headley Discloses Direct Intramuscular Stimulation and, in Fact, Teaches Away from Nerve Stimulation

Headley's system is designed exclusively for direct intramuscular stimulation of the genioglossus muscle. Headley repeatedly describes stimulating a set of muscle fibers, not a nerve.

- Abstract:
    - "This method involves **the implantation of a muscle stimulation electrode directly into the muscle of the genioglossus** that advances the posterior aspect of the tongue anteriorly thus relieving the obstruction of the tongue in sleep apnea." Ex. 1008, Abstract (emphasis added).
- Brief Summary of the Invention:
    - "In preferred embodiments, there are provided method and

devices for treating obstructive sleep apnea by **direct wire stimulation to a specific set of muscle fibers**." Ex. 1008, ¶7 (emphasis added).

- "**applying direct intramuscular electrical stimulation to a specific set of muscle fibers** in a muscle of the patient's airway … wherein the **electrical current is delivered directly by wire to specific set of muscle fibers**." Ex. 1008, ¶8 (emphasis added).
- "wherein the implanted electrode assembly is in operative association with an external electromagnetic frequency transmitting antenna located on or near a patient's body, such that **electrical stimulation is directly provided by wire to a specific set of muscle fibers in a muscle** of the patient's airway when the antenna transmits an electromagnetic frequency to the implanted electrode assembly…. wherein **the electrical current is delivered directly by wire to the specific set of muscle fibers**." Ex. 1008, ¶11 (emphasis added).

- Detailed Description of the Invention:

  - "**The electrodes impart electrical pulses, generated by the pulse generator, directly by wire to the genioglossus muscle to stimulate the specific muscle fibers** to a point where the patient's tongue is moved anteriorly to maintain upper airway patency." Ex. 1008, ¶30 (emphasis added).
  - "The stimulator may be variably set to provide direct current pulses having an amplitude, a frequency, and a duration to provide a non-awakening **stimulation directly by wire to the**

specific muscle fibers." Ex. 1008, ¶30 (emphasis added).

Not only does Headley fail to disclose nerve stimulation, but Headley affirmatively teaches away from nerve stimulation. Headley's Background section explicitly identifies and disparages prior art nerve stimulation approaches:

> Others have also tried to address this problem. **Some have proposed implanting a cuff electrode around the hypoglossal nerve** (U.S. Patent 5,522,862, U.S. patent 5,549,655, U.S. patent 5,540,733, incorporated by reference herein in their entirety). **However, this requires a major surgical operation and there is great risk since there is a vital vein immediately adjacent the target nerve**.
> Ex. 1008, ¶006 (emphasis added).

Headley then presents its intramuscular electrode approach as the solution to the asserted nerve stimulation deficiencies of requiring "a major surgical operation" and posing "great risk" due to being close to a "vital vein."

Teaching away is established when a POSITA "upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009). Headley does precisely this: it criticizes hypoglossal nerve stimulation as dangerous and surgically burdensome, discouraging a POSITA from pursuing stimulation of the hypoglossal nerve. Put simply, a POSITA reading Headley

would be directed away from nerve stimulation.

2. Tran-I Also Discloses Direct Intramuscular Stimulation and Teaches Away from Nerve Stimulation

Like Headley, Tran-I describes intramuscular stimulation of the genioglossus muscle, not nerve stimulation. Tran-I describes hypothetically using "a single intralingual BION™ microstimulator" implanted directly into the posterior genioglossus muscle, with the stimulating electrode positioned within the muscle tissue itself. Ex. 1009 at 375–376.

While Tran-I references the hypoglossal nerve, it does so solely when identifying the optimal muscle fiber target site for intramuscular electrode placement—not to teach nerve stimulation. Specifically, Tran-I uses the anatomical reference to the hypoglossal nerve to explain that "[t]he hypoglossal nerve branches to the GG [genioglossus] muscle enter the tongue inferolaterally [sic] to innervate muscle fibers that are oriented transversely, longitudinally and radially in parasagittal fans," to identify where the motor endplates are placed within the muscle, concluding that "a single site of stimulation located in the midline (near these endplates as illustrated in FIG. 3) would recruit selectively those motor units that will produce symmetrical protrusion of the tongue." Ex. 1009 at 376.

Fig. 3. Implantation site of a single BION in posterior midline of the genioglossus muscle with tantalum electrode (effective cathode) near the endplates (toward the tongue base).

FIG. 3 of Tran-II

FIG. 3 depicts the "[i]mplantation site of a single BION in posterior midline of the genioglossus muscle." Ex. 1009 at 376. Notably, the hypoglossal nerve is not even identified in FIG. 3, further supporting Tran-I is directed to direct intramuscular stimulation, not nerve stimulation.

In fact, Tran-I expressly teaches away from placing the BION™ device near nerves. Tran-I discloses that its implantation site in the posterior midline of the genioglossus muscle "**minimizes the risk of damage to blood vessels and nerves** as well as reducing the risk of oral infection." Ex. 1009 at 376. (emphasis added).

3. Tran-II Discloses Only Direct Intramuscular Stimulation

Tran-II similarly discloses intramuscular stimulation, not nerve stimulation. Tran-II contains no disclosure of stimulating a nerve. Tellingly, the words "nerve" or "hypoglossal" or "HGN" do not appear a single time in the entire Tran-II paper. Ex. 1010. By contrast, the words "muscle" and "genioglossus"—referring to the target muscle tissue—appear repeatedly throughout the paper, consistently confirming that Tran-II's disclosure is directed to intramuscular stimulation of the genioglossus muscle, not nerve stimulation. Ex. 1010 at 4287–4289.

B. Petitioners' Chain of Inferences Does Not Bridge the Gap Between Intramuscular Stimulation and the Claimed Nerve Stimulation and Is Impermissible Hindsight

Recognizing that none of the cited references disclose nerve stimulation, Petitioners resort to a series of inferential leaps—repeatedly invoking "a POSITA understood" language—to argue that the claimed nerve stimulation would have been obvious. Pet. at 60–62. Petitioners' approach fails as a matter of law and fact. The inferential leaps in Petitioners' chain are unsupported, and the cumulative chain of inferences represents hindsight reconstruction.

Petitioners build their nerve stimulation argument through a series of inferences concluding with "[a] POSITA understood electrodes implanted in the GG [genioglossus] applied electrical stimulation to the HGN [hypoglossal nerve] to achieve the desired result of maintaining upper airway patency to treat OSA." Pet. at 61.

Petitioners' chain of inferences violates the requirement to give "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). It is fundamental that obviousness must be supported by actual teachings, not by what a POSITA could theoretically have understood, derived, or inferred. A chain of inferences about what a POSITA "understood" cannot substitute for actual prior art disclosure. *See In re NuVasive, Inc.*, 842 F.3d 1376, 1383 (Fed. Cir. 2016) (holding that conclusory statements that a POSITA "would have" done something, without adequate explanation and evidentiary support, cannot support an obviousness determination).

C. Petitioners' Obviousness Rationale Ignores Headley's and Tran-I's Express Teaching Away Disclosure

Petitioners assert that a POSITA would have understood that the Headly/Tran-I/Tran-II intramuscular stimulation electrode "implanted in the GG [genioglossus]" could be used to apply "electrical stimulation to the HGN [hypoglossal nerve] to achieve the desired result of maintaining upper away patency to treat OSA." Pet. at 61. Not only is this inference unsupported, but it is also directly contradicted by Headley's and Tran-I's express teachings.

First, applying electrical stimulation to the hypoglossal nerve would go against Headley's and Tran-I's express warnings. Headley warns that placing electrodes near or on the hypoglossal nerve poses "great risk since there is a vital

vein immediately adjacent the target nerve." Ex. 1008, ¶006. Likewise, Tran-I also cautions selecting an implantation site sufficiently away from the nerves to "minimize the risk of damage to blood vessels and nerves." Ex. 1009 at 376.

Second, transitioning from intramuscular stimulation to nerve stimulation is not a simple repositioning. The proposed modification would entail a number of additional modifications, such as different electrode placement, different surgical/implantation approach, and different stimulation parameters (e.g., nerve recruitment thresholds vs. muscle fiber activation thresholds). Moreover, changing to nerve stimulation may further require validation of nerve safety parameters to avoid nerve damage. Whatever the value of these theories, the Petition contains no such analysis.

X. GROUND 2 SHOULD BE REJECTED BECAUSE PETITIONERS MISCHARACTERIZE THE DISCLOSURES OF TRAN-I/II

A. Petitioners Improperly Intermingle the Disclosures of Tran-I and Tran-II

As an initial matter, Petitioners improperly treat Tran-I and Tran-II as a single unified reference (collectively called "Tran"), intermingling their disclosures throughout the Petition without clearly delineating which teachings come from which reference. Pet. at 19, 52–92. There is no collective Tran printed publication. Tran-I and Tran-II are separate, independent publications authored by different sets of authors, at different times, describing different experiments, and disclosing different subject matter. They must be treated as distinct prior art references, each

evaluated on its own merits for what it discloses. Petitioners' treatment of the Tran publications violates the requirements of 35 U.S.C. § 312(a)(3) and 37 C.F.R. § 42.104(b)(4)–(5), which demand that Petitioners specifically identify where each limitation is found in each reference, not merge multiple references into an undifferentiated body of alleged teachings from which claim limitations can be selectively drawn. By intermingling the disclosures of Tran-I and Tran-II, Petitioners obscure which reference purportedly teaches which claim limitation and the motivation to combine the teachings of each reference.

Tran-I is a preliminary feasibility paper presenting theoretical analysis—not a validated, enabling disclosure of a clinical therapeutic protocol. It presents data from control of a CPAP machine, and not from control by nerve stimulation. A POSITA would understand Tran-I as identifying an interesting research direction, not as providing the specific, reproducible design parameters.

Tran-II is an extremely preliminary single-subject feasibility paper describing a simulation—not a validation—of a BION™ device using temporary wire electrodes in one overnight session. As described below in Section X.C.1, it provides no validated stimulation parameters for an implantable system, no specific timing parameters for the asynchronous protocol depicted in FIG. 4, and no disclosure of the duration relationships required by the challenged claims.

B. Petitioners Materially Mischaracterize Tran-II's Core Disclosure

Petitioners' reliance on Tran-II is built upon a foundational mischaracterization of what that reference discloses. The Petition states:

> FIG. 4 of Tran-II, which is below, is a screen capture of polysomnogram of **the patient being treated using the BION™ device** providing asynchronous stimulation in the form of brief trains of electrical stimulus "in continuous cycles at approximately the natural respiratory rhythm of the sleeping participant, obviating the need for a sensor to synchronize stimulation with breathing. EX-1010, p. 4287. Pet. at 55 (emphasis added).

This statement is materially, factually incorrect: no BION™ device was used in the subject depicted in FIG. 4. Tran-II expressly states the opposite: "[w]e used **fine wire electrodes in place of the BION** as a study model to gather specific information to support a proposed clinical trial of BION treatment for OSA." Ex. 1010 at 4287 (emphasis added); *see also* Ex. 1010 at 4288 ("Bipolar hooked wires inserted at midline of posterior genioglossus."); *see also* Ex. 1010 at 4289 ("Bipolar wire electrodes were strategically placed at the optimal stimulation site in the genioglossus."). Indeed, Tran-II's title is "First Subject Evaluated with ***Simulated*** BION™ Treatment …." Ex. 1010.

Tran-II clearly states that bipolar wire electrodes were used to "simulate" a BION™ device, and no BION™ device was actually used on the single patient described in Tran-II. An implanted BION™ device and temporary percutaneous

hooked wire electrodes are categorically different.

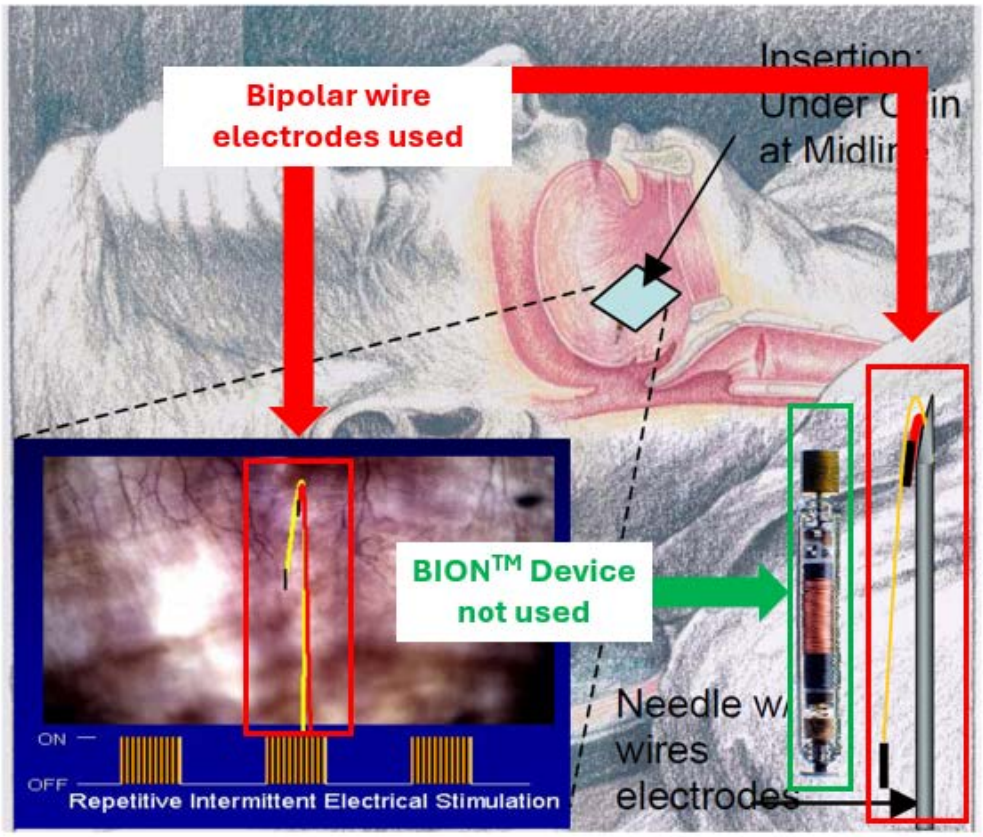


Fig. 2. Bipolar hooked wire electrodes inserted at midline of posterior genioglossus. *Right:* Bare tips of wire electrodes are separated at the same distance as the BION's electrodes. *Left:* Coronal/Horizonal section of wire electrodes in posterior genioglossus at midline. Repetitive intermittent electrical stimulation is used to activate motor endplates to produce the desired tongue movement.

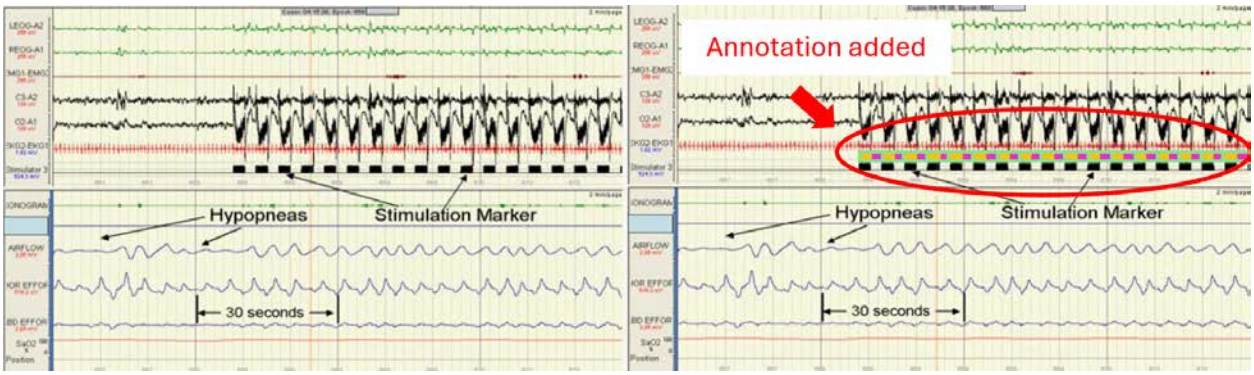
Annotated FIG. 2 of Tran-II.

Petitioners' mischaracterization transforms a preliminary simulation study into a clinical demonstration. A single-subject experiment using temporary wire electrodes to *simulate* what an implanted device *might* do provides fundamentally different—and far weaker—evidence than a study actually testing an implanted device. Petitioners' description of FIG. 4 as depicting "the patient being treated

using the BION™ device" misrepresents the evidentiary value of Tran-II and overstates what a POSITA would take from this reference.

C. Tran-II's FIG. 4 Is Ambiguous and Cannot Support the Weight Petitioners Place upon It

The Petition relies on Tran-II's FIG. 4 as a primary evidentiary basis for Ground 2's claimed timing parameters, citing this single figure throughout the Petition. Pet. at 6, 7, 55, 56, 64, 68, 71, 77, and 79. FIG. 4 is a low-resolution screenshot. Petitioners present both the original FIG. 4 and an annotated version of the same figure as alleged evidence of specific stimulation timing parameters. Pet. at 7, 56.



Tran-II FIG. 4 (left) and Petitioners' Annotated FIG. 4 (right) (Pet. at 7, 56)

1. Tran-II Does Not State Any Numerical Values for the Timing Parameters Petitioners Assert

The most fundamental problem with Petitioners' reliance on FIG. 4 is straightforward: Tran-II lacks the numerical timing parameter values that Petitioners assert, such as stimulation, non-stimulation, and inspiratory phase durations. The Petition and Dr. Loeb's Declaration state detailed numerical values

for FIG. 4's timing parameters in a conclusory manner, without providing any explanation of how these values were derived from the figure or the reference. *See* Ex. 1003, ¶271. Similarly, the annotations added to FIG. 4 in the Petition (Pet. at 7, 56) are not explained by any underlying facts, data, or methodology disclosed in Tran-II. In fact, annotated FIG. 4 in the instant Petition is not even found in the Declaration of Dr. Loeb submitted in this IPR Proceeding.

"Expert testimony that does not disclose the underlying facts or data on which the opinion is based is entitled to little or no weight." 37 C.F.R. § 42.65(a). The same is true for expert testimony asserting specific numerical values derived from a figure, without disclosing the underlying methodology or data supporting that derivation. Such testimony is entitled to little or no weight. Dr. Loeb's bare assertion of specific timing values from FIG. 4, without any explanation of the measurement technique, scaling assumptions, or analytical methodology employed to extract those values from a low-resolution polysomnogram screen capture, fails to satisfy the foundational requirements of 37 C.F.R. § 42.65(a). The Board should accord these unsupported numerical assertions no weight.

And to the extent they are information that Dr. Loeb, as co-author, may recall from his direct research, but which is not stated in Tran-II, such personal, subjective experience is improper fact testimony in IPRs, which rely on printed publication evidence. 35 U.S.C. § 311(b). The Board should accord this fact

testimony no weight.

2. The Petitions and Declaration Make Internally Inconsistent Assertions About FIG. 4's Timing Parameters

The unreliability of Petitioners' numerical assertions about FIG. 4 is further demonstrated by the internal inconsistencies. If the timing parameters were genuinely derivable from FIG. 4 through objective measurement or analysis, one would expect consistent numerical values across the Petition and Declaration. But that is not the case—Petitioners provide inconsistent values for the same parameters.

For example, the Petition first asserts that the stimulation period in FIG. 4 is "3 seconds" and later asserts that the same stimulation period is "approximately 2.5 seconds". *Compare* Pet. at 6 ("Annotated **FIG. 4 of Tran-II** below illustrates an asynchronous stimulation cycle with **a stimulation period (ON period) of 3 seconds** and a non-stimulation period (OFF period) of 2 seconds.") (emphasis added), *with* Pet. at 68 ("**FIG. 4 of Tran-II** … shows a two-second inspiratory phase and the stimulation markers indicating an **ON period [stimulation period] of approximately 2.5 seconds**.") (emphasis added).

As another example, the instant Petition states that the inspiratory phase in FIG. 4 is 2 seconds, but the petition for IPR2026-0092 states that the same inspiratory phase is approximately 2.5 seconds. *Compare* Pet. at 68 ("FIG. 4 of Tran-II … shows a **two-second inspiratory phase.**") (emphasis added), *with*

IPR2026-0092 Pet. at 71 ("with **the inspiratory phase** illustrated in FIG. 4 of Tran-II **lasting approximately 2.5 seconds**") (emphasis added).

These are not trivial rounding differences—they are substantively significant inconsistencies. The timing relationships at issue are on the order of a few seconds or even a fraction of a second. These inconsistencies are consequential because the specific timing values are central to Petitioners' argument that Tran-II discloses certain claimed duration relationships.

In summary, Tran-II's FIG. 4 is an unreliable and internally inconsistently characterized figure that cannot bear the evidentiary weight Petitioners place upon it. The Board should reject Petitioners' reliance on this figure and the unsupported, inconsistent numerical assertions derived from it. Without Petitioners' reliance on FIG. 4, Ground 2 undoubtedly fails.

XI. EVEN UNDER PETITIONERS' MISCHARACTERIZATIONS, GROUND 2 STILL FAILS TO DISCLOSE THE CLAIMED TIMING RELATIONSHIPS

As mentioned above in Section VIII, the claims require two concurrent timing relationships with respect to a stimulation cycle:

1. stimulation period > non-stimulation period

2. reference respiratory relationship where:

    a. stimulation period is based on a reference respiratory-related parameter (claim 1);

b. multiple stimulation periods within a reference respiratory cycle R (claim 16); or

c. stimulation cycle (stimulation period + non-stimulation period) > reference respiratory cycle R (claim 22)

The proposed combination would not practice both timing relationships concurrently. The Petition impermissibly cherry picks from each disclosure to try meet the claimed timing relationships.

A. Headley's Stimulation Ranges Are Incompatible with the Claimed Respiratory Reference Protocol

The Petition admits that Headley lacks the claimed inspiratory reference timing: "Headley does not expressly disclose using a reference respiratory-related parameter" Pet. at 6. Headley contains no discussion whatsoever of using a reference respiratory cycle (claim 1), let alone setting multiple stimulation periods within a reference respiratory cycle (claim 16), or setting the stimulation cycle (stimulation period + non-stimulation period) to be greater than a reference respiratory cycle R (claim 22).

The complete absence of respiratory-related reference from Headley reflects its fundamentally different design. Headley's approach is direct intramuscular stimulation focused on patient comfort and muscle fatigue management with no consideration of respiratory cycle. Headley discloses extraordinarily wide-ranging stimulation periods: "On periods may range, without limitations from 1 to **120**

seconds, and off periods similarly. On/off intermittent periods include from **5/5, 20/5, 10/10, 5/60, 60/5, 20/20, 30/30, 40/40, 50/50, 60/60, and so forth."** Ex. 1008, ¶48 (emphasis added).

Stimulation periods of up to 120 seconds (i.e., 2 minutes) cannot be related in any way to respiratory cycles, indicating that Headley considered respiratory phase entirely irrelevant to stimulation timing.

B. Even as Interpreted by the Petition, Tran-II Does Not Disclose Non-Stimulation Period Being Less Than Stimulation Period

As best understood, Dr. Loeb and the Petition seem to imply that Tran-II's FIG. 4 discloses a 5 second respiration period with stimulation period of 2.5 seconds on and non-stimulation period of 2.5 seconds off. Pet. at 67–68. Even based on this unsupported characterization, this stimulation cycle in Tran-II still would not satisfy the claimed requirement of "duration of each respective stimulation period is greater than a duration of each respective non-stimulation period."

C. The Combination's Resort to Headley's Broad Ranges Contradicts Tran-II's Respiratory-Rate Rationale

Recognizing that Tran-II's alleged respiratory-rhythm-matching approach fails to satisfy certain timing requirements (e.g., stimulation period > non-stimulation period), Petitioners abandon their own rationale for including Tran-II in Ground 2 and resort to Headley's broad stimulation ranges to try to encompass

the claim. *See*, *e.g.*:

- Pet. at 63: "Headley discloses stimulation/on period [*stimulation period*] duration that is greater than a rest/off period [*non-stimulation period*] duration (i.e., a duty cycle (on/off period) of 12/1)."
- Pet. at 68: "Thus, Tran discloses that each ON period [each respective stimulation period] has a duration greater than the inspiratory phase of the patient's respiratory cycle [reference respiratory cycle]. A POSITA understood that a period of stimulation [stimulation period] of 120 seconds, as disclosed by Headley, exceeded the duration of any patient's inspiratory phase, including the 2.5 second inspiratory phase disclosed by Tran."

This resort reveals an internal contradiction in Ground 2.

On one hand, Petitioners invoke Tran-II specifically for the teaching that stimulation should be timed at approximately the natural respiratory rhythm. The entire rationale for including Tran-I/II in Ground 2 is to provide a respiratory-rate-based timing approach to cure Headley's lack of respiratory reference.

On the other hand, when the respiratory-rate-based approach fails to satisfy certain timing requirements of the claim, Petitioners abandon Tran-I/II's respiratory-rate rationale and instead cite Headley's vastly broader stimulation ranges (up to 120 seconds, i.e., 2 minutes) that are incompatible with a respiratory-rate-based approach.

This is the definition of impermissible cherry-picking. *See Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1577–78 (Fed. Cir. 1987) (holding that selecting "bits and pieces from prior patents" instead of treating them "as a whole" was improper).

These approaches are fundamentally incompatible:

Tran-I/II's (alleged) approach: Constrain stimulation cycle to match respiratory rate (i.e., ~5-second total cycles with 2.5 seconds on/2.5 seconds off)

Headley's approach: Large stimulation periods up to 120 seconds (i.e., 2 minutes) bearing no relationship to respiratory rhythm.

A POSITA cannot simultaneously apply Tran-II's respiratory-rate-based timing and Headley's widely variable ranges without abandoning the entire rationale for including Tran-II in the combination. If Headley's "up to 120 seconds" ranges are the basis for the timing parameters, then Tran-II's respiratory-rate matching is irrelevant to the claim elements. If Tran-II's respiratory-rate matching is the basis, then Headley's broad ranges cannot be invoked to satisfy the same claim elements.

This internal inconsistency demonstrates that Ground 2's combination is purely hindsight driven.

XII. CONCLUSION

For the foregoing reasons, the Board should decline to institute a trial.

Date: March 31, 2026

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Counsel for Patent Owner

CERTIFICATE UNDER 37 C.F.R. § 42.24(d)

Under the provisions of 37 C.F.R. § 42.24(d), the undersigned hereby certifies that the word count for the forgoing Patent Owner's Preliminary Response to Petition totals 11,683, which is less than the 14,000 words allowed under 37 C.F.R. § 42.24(b)(1).

Date: March 31, 2026

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CERTIFICATE OF SERVICE

I hereby certify that on March 31, 2026, a true and correct copy of the Patent Owner's Preliminary Response was served on Petitioners via the electronic mail addresses identified in the Petition:

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