Protocol Title: Prospective Use of Awake Endoscopy to Direct Inspire Therapy for Obstructive Sleep Apnea

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Prospective Use of Awake Endoscopy to Direct Inspire Therapy for Obstructive Sleep Apnea

Principal Investigator Erica R. Thaler, MD
Department of Otorhinolaryngology – Head and Neck Surgery
3400 Spruce Street, 5 Silverstein Building
215-662-4533
erica.thaler@uphs.upenn.edu

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Study Product Inspire Upper Airway Stimulation Implant

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Study Summary

Title	Prospective Use of Awake Endoscopy to Direct Inspire Therapy for Obstructive Sleep Apnea
Short Title	Awake Endoscopy for Inspire
IRB Protocol Number	828956
Methodology	Validation cohort study
Study Duration	2 years
Study Center(s)	Single-center (University of Pennsylvania)
Objectives	Primary: • To determine the usefulness of awake endoscopy during activation of Inspire device Secondary: • To determine optimal configuration of the Inspire upper airway stimulator by quantifying changes in upper airway size for multiple implant configurations • To correlate changes in airway size on endoscopy with sleep study outcomes
Number of Subjects	30-40
Main Inclusion Criteria	• Patients with moderate to severe OSA • Recipient of Inspire Upper Airway Stimulation Implant surgery • Age 18 or above
Intervention	Awake endoscopic exam will be performed to measure airway size in the retropalatal and retroglossal upper airway regions using different Inspire implant configurations and voltages. The optimal test configuration determined on endoscopy will be tested during a sleep study and compared to the standard-of-care device configuration, with improvements in sleep study outcomes indicating that awake endoscopy is useful during Inspire implant activation.
Statistical Methodology	Paired t-tests will be used to compare differences in AHI and ODI using the test Inspire device configuration/voltage with the standard device configuration/voltage. Paired t-tests will also be used to analyze whether significant differences in airway size exist using different device configurations and voltages. A Pearson correlation test will be used to determine whether changes in airway size correlate with changes AHI and changes in ODI.
Data and Safety Monitoring Plan	PI will be responsible for monitoring the data quality and the ongoing safety of subjects.

Background and Study Rationale

1 Introduction

The Inspire Upper Airway Stimulation (UAS) system is an FDA-approved, commercially available, innovative surgical solution for patients with moderate-to-severe obstructive sleep apnea (OSA) that have failed continuous positive airway pressure (CPAP) therapy. It is a surgically-implanted device that is implanted in anesthetized patients using three incisions: a sensing lead that senses inspiration is placed in the lateral intercostal muscles in the low lateral chest, a pacemaker device is placed in the upper chest wall, and a stimulation lead is placed around the hypoglossal nerve in the neck for stimulation of tongue movement. This system is designed to push the tongue forward during inspiration to keep the upper airway open in patients who have tissue collapse causing obstructive sleep apnea. The Inspire device was FDA-approved for the treatment of moderate-to-severe OSA in 2014 and has been implanted in over 1,000 patients to date. Patients undergo outpatient surgery under general anesthesia for implantation then return to see their surgeon at 1 month postoperatively for device activation, which is performed in the awake patient. Current standard-of-care is to activate patients' devices using the "standard configuration" which is the +-+ electrode configuration. This "standard configuration" was determined by the Inspire Corporation, though there are many other possible configurations of the 3-electrode stimulation lead. These different configurations (e.g., +0+, -+-, etc) result in different stimulatory patterns of the hypoglossal nerve and different changes in upper airway architecture, however it is unknown how these changes differ among patients. In the current standard-of-care algorithm, after device activation, patients proceed to outpatient sleep study to titrate their device and assess their response to therapy. While most patients achieve therapeutic benefit from this initial standard setting, a subset of patients for which this is initial configuration is unsuccessful later undergoes awake endoscopy where the surgeon may examine the airway during stimulation with multiple other implant settings. Based on this exam, the surgeon then selects another setting to be tested during a repeat sleep study. **This subset of patients experiences a delay in delivery of effective therapy for OSA. Furthermore, it is unknown whether the patients who are successfully treated with the initial device setting are being optimally treated.** It is possible that these successfully treated patients could have an even greater response with reduction in OSA symptoms and burden of disease if they were to use a different implant setting. The goal of this study is to evaluate the efficacy of awake endoscopy during implant activation. We hypothesize that awake endoscopy can be used during the initial postoperative visit to identify an “optimal” implant configuration based on greatest change in airway size, and that changes in airway size will correlate with an improvement in in measures of obstructive sleep apnea on polysomnography.

1.1 Background and Relevant Literature

OSA is characterized by recurrent upper airway obstruction during sleep, resulting in oxygen desaturations, arousals, and sleep fragmentation. OSA affects a significant number of adults in the United States and results in excessive daytime sleepiness and reduced quality of life.[1] OSA is associated with the development of cardiovascular disease including hypertension and stroke, insulin resistance, obesity, cognitive dysfunction, and even death.[2-8] Continuous positive airway pressure (CPAP) is recommended for initial therapy for OSA, however its efficacy is limited by poor compliance in many patients. The Inspire system was developed to treat moderate-to-severe OSA (20 ≤ AHI ≤ 65) in adult patients who are not effectively treated by CPAP. Inspire therapy has been shown to be safe and efficacious, resulting in significantly decreased AHI and ODI as well as decreased symptom burden and improved quality of life.[9]

At present, one month after device implantation, patients are seen in follow up by the primary surgeon. A remote is used to activate the device in the awake patient using a standard configuration (+-+). The stimulator is then titrated to a comfortable voltage level. The patient uses their device at home for one month before undergoing a sleep study, when the voltage is titrated to achieve maximal reduction in

apnea-hypopnea index (AHI) while maintaining comfort. If a therapeutic AHI reduction is not achieved during the first post-operative sleep study, patients return to see the surgeon and undergo awake endoscopy in an attempt to determine an optimal configuration. The process of testing multiple different configurations during this visit is not standardized. Patients then undergo one or more additional sleep studies in an attempt to assess therapeutic benefit.

Measurements of airway size have been used to quantify changes in the airway during drug-induced sleep endoscopy, which is a procedure used to visualize the airway during drug-induced sleep to aid in the diagnosis and management for sleep apnea.[10] We hypothesize that airway measurements taken during awake endoscopy can be used to analyze changes in airway size with the Inspire UAS implant, and that this analysis will help guide Inspire therapy, potentially resulting in more efficient and effective therapy delivery.

2 Study Objectives

The aim of this study is to examine a new method of device configuration for the Inspire upper airway stimulator. First, we will attempt to determine optimal configuration by quantifying changes in upper airway size with different implant configurations using awake nasal endoscopy. The configuration/voltage that results in the greatest increase in upper airway size and is tolerated by the patient will be selected. Patients will then undergo a sleep study so that increased airway size may be correlated with changes in sleep study parameters including AHI and oxygen desaturation index (ODI). Airway size and sleep study parameters using the standard device configuration (+-+)/voltage will be compared to airway size and sleep study parameters using the test, or "optimal," configuration/voltage to determine the usefulness of awake endoscopy in activation of the Inspire device.

2.1 Primary Objective

- To determine the usefulness of awake endoscopy during activation of Inspire device

2.2 Secondary Objectives (if applicable)

- To determine optimal configuration/voltage of the Inspire upper airway stimulator by quantifying changes in upper airway size with multiple implant configurations
- To correlate change in airway size seen on awake endoscopy with outcomes of observed sleep study including AHI and ODI

3 Investigational Plan

Patients who are undergoing Inspire implantation by the principal investigator will be screened to determine whether they meet inclusion criteria and invited to participate in the study. All components of the study will be performed during visits that are scheduled as part of routine postoperative care; these visits will be modified to incorporate study activities. Written consent will be obtained at Visit 1. Subjects will present to clinic (Visit 1) for awake endoscopy during their regularly scheduled postoperative activation appointment. An aerosolized mixture of xylocaine and oxymetolazone (afrin) will be used as a numbing agent prior to awake endoscopy; this is routinely used for awake endoscopic exams in the ENT clinic. The surgeon will perform awake nasal endoscopy while a clinical assistant or nurse activates and configures the device using the Inspire remote control. Device voltage will be titrated to achieve tongue protrusion across the teeth, which is part of the standard method of activation. Endoscopic exam will be recorded and include visualization of baseline airway with device turned off and airway with multiple test configurations and voltages. At the end of this visit, devices will be set to the standard device configuration that is currently used in routine clinical practice (+-+). Patients then routinely use their device at home for the following month. The recorded exam will be used by a single blinded member of

the study team to formally measure and analyze airway size in the various conditions after this visit and the "optimal" test configuration will be determined based on airway measurements. Subjects subsequently will undergo an in-lab sleep study for titration of their device (Visit 2). Titration sleep study will ensue with the Inspire device in A) the standard (+-+) configuration and B) the "optimal" test configuration. Voltage used with each implant configuration may be increased to achieve effective reduction in AHI at the discretion of the sleep physician; this is routinely performed during titration polysomnography in our current clinical practice. At the end of the sleep study, the device will be returned to the standard setting until further follow up with their sleep medicine physician. This concludes the subject's participation in the study. Subjects will obtain the results of the sleep study and discuss further device management with their sleep medicine physician during routine follow up.

3.1 General Design

This is a cohort study that will evaluate the use of awake endoscopy as a diagnostic tool used to determine optimal configuration of the Inspire UAS device.

3.2 Allocation to Interventional Group

All patients will receive the same intervention.

3.3 Study Measures

Awake endoscopy will be performed during Visit 1 during which airway size will be video recorded at rest with implant off and with a standardized sequence of implant configurations that were determined by Inspire Corporation during pre-market testing including +-+, ---, o-o, -o-, and -+-. These settings will be tested to determine the voltage at which patients sense tongue movement (sensation threshold) and the voltage at which the tongue is visualized protruding from rest past the teeth (functional threshold). The different electrode configurations will then be tested at various voltages above the subject's measured functional thresholds.

Measurements of cross-sectional, anterior-to-posterior, and lateral airway size in the retropalatal and retroglossal regions will be taken from recorded endoscopic exams using the image analysis program Amira by Visage Imaging (Richmond, Victoria, Australia). Measurements will take place between Visits 1 and 2. Standard AHI and ODI measurements will take place during in-lab sleep study (Visit 2). Efficacy of awake endoscopy to determine optimal device configuration will be assessed by comparing cross-sectional airway size (retropalatal and retroglossal), AHI and ODI with the standard device configuration compared to airway size, AHI and ODI with the test configuration. In patients for whom the standard configuration (+-+) results in greatest airway size, this will be the sole configuration tested during sleep study, and identical values for airway size, AHI, and ODI will be used in analysis comparing the standard configuration with the "test" configuration.

3.4 Study Endpoints

3.4.1 Primary Study Endpoint

The primary endpoint is to assess the efficacy of awake endoscopy in determining optimal implant configuration during implant activation. A decrease in in AHI and ODI with test configuration compared to standard configuration will indicate that awake endoscopy is useful for identifying optimal implant configuration compared to the current method of activation without endoscopy.

3.4.2 Secondary Study Endpoints

The secondary endpoints will be to determine absolute and percent changes in airway size using different decide configuration settings and to determine the degree to which changes in airway size correlate with changes in sleep study parameters including AHI and ODI.

4 Study Population and Duration of Participation

The study population includes male and female patients over the age of 18 who have undergone Inspire UAS implantation to treat moderate to severe OSA.

4.1 Duration of Study Participation

Participation is estimated to last 4-6 weeks and will occur during routine clinical follow up appointments.

4.2 Total Number of Subjects and Sites

All eligible patients undergoing Inspire implantation by the primary investigator during a 2-year period will be recruited. This is estimated to amount to up to 50 eligible patients at the University of Pennsylvania.

4.3 Inclusion Criteria

- Patients with moderate to severe OSA who have undergone Inspire UAS implantation by the principal investigator
  - Must have symptoms of OSA prior to Inspire implantation
- AHI between 15 and 65, where central and mixed apnea is 25% or more, and the level of collapse is in the soft palate area BMI less than 32
- Age 18 or above

4.4 Exclusion Criteria

- Significant central sleep apnea
- Presence of other sleep disorders
- History of neurologic or neuromuscular disease
- Historical or present substance abuse
- Bleeding disorders
- Autoimmune diseases that increase risk of nasal trauma such as Wegener's, Sarcoidosis, etc.
- Pregnancy

4.5 Subject Recruitment

Subjects will be identified using the surgical log of the principal investigator. All patients who have recently undergone device implantation by the principal investigator and are presenting for device activation will be recruited to the study.

4.6 Vulnerable Populations:

Children, pregnant women, fetuses, neonates, or prisoners are not included in this research study. Pregnancy status will be determined based on patient report; and that if a patient becomes pregnant during the study, the subject will be removed from the study and will resume receiving standard care for sleep apnea. Students or employees of Penn will be informed that their decision to participate will not affect their standing with the University in any way.

5 Study Procedures

See below and Table 1.

5.1 Screening

- Medical records review to determine that patients meet inclusion criteria and do not meet exclusion criteria
    - Includes: medical history, age, allergies, BMI, prior sleep studies, and Inspire device usage report from last Sleep Clinic visit

5.2 Study Intervention

5.2.1 Visit 1: Otolaryngology Clinic for Awake Endoscopy

- Informed consent
- Vital signs: HR, RR, BP, SpO2, BMI
- Targeted Head and Neck Physical Exam
    - Tongue size, lateral peritonsilar narrowing, palate shape, Modified Mallampati score
- Recorded exam of awake endoscopy at rest and with standardized configurations detailed in section 3.3 (Attachment 1)
    - Measurement and analysis of airway size to be completed by single co-investigator between Visits 1 and 2. Configuration resulting in greatest airway size will be used as test configuration during Visit 2 sleep study.

5.2.2 Visit 2: In-lab Sleep Study

- Polysomnography
    - Half of study using standard implant configuration, half of study using test configuration determined by awake endoscopy.

5.3 Unscheduled Visits

Patients will be given information to contact the research team in case there are any concerns that arise. They will also be allowed to schedule appointments with the research team to discuss any issues in person.

5.4 Subject Withdrawal

Patients may withdraw from the study for any reason with no explanation or excuse required. They may do this without impact to their care. They may also be removed from the study at the discretion of the PI for lack of adherence to intervention, to visit schedules, adverse events, or due to changes that may result in alteration of sleep architecture. This includes significant weight loss or weight gain, ablative or orthognathic upper airway surgery, trauma, neoplasm of head and neck, autoimmune disease affecting airway, substance abuse, or initiation of medication that may alter sleep architecture prior to completion of the study.

5.4.1 Data Collection and Follow-up for Withdrawn Subjects

Subjects who withdraw from the study may withdraw at any time. Follow up visits are not necessary as there will be no study material to be collected.

5.5 Efficacy Evaluations

Efficacy of the intervention being tested (awake endoscopy to determine optimal Inspire device configuration) will be assessed by comparing AHI and ODI using the standard device configuration compared to AHI and ODI with the test configuration. The intervention will be deemed efficacious if a statistically significant reduction in AHI and/or ODI is achieved with the test configuration determined using awake endoscopy compared to the standard device setting.

6 Statistical Plan

6.1 Sample Size and Power Determination

We estimate enrollment of roughly 30-40 patients. This is a pilot study since there has been no similar attempt at using and validating awake endoscopy for implant activation. Sample size and power calculations for paired t-test indicate that ~30 subjects would yield a study that is powered to detect a 50% effect size (using a standard α=0.05, β=0.2). Additional subjects would enable detection of a smaller effect size.

6.2 Statistical Methods

Analysis of all outcomes will be performed at the completion of the study. In the analysis of the primary outcome of interest, paired t-tests will be used to compare differences in AHI and ODI using the test Inspire device configuration and the standard device configuration. Paired t-tests will also be used to analyze whether significant differences in airway size exist using different device configurations: namely, the “test” configuration that has the largest airway size compared to the standard device configuration. A Pearson correlation test will be used to determine whether changes in airway size using standard and test configurations correlate with changes AHI and changes in ODI.

6.3 Control of Bias and Confounding

The following measures for randomization and blinding will be employed to reduce bias:

- All subjects that have undergone implantation during the study period and meet criteria will be recruited to the study
- Measurements and analysis of airway size will be performed in a blinded fashion, without knowledge of subject history

6.3.1 Baseline Data

Baseline and demographic characteristics will be summarized by standard descriptive statistics (including mean and standard deviation for continuous variables such as age and standard percentages for categorical variables such as gender). Additionally, pertinent information relating to patients’ OSA and history of present illness will be summarized.

6.3.2 Analysis of Primary Outcome of Interest

A paired t-test will be used to compare differences in AHI and ODI using the test configuration compared to the standard device configuration.

7 Safety and Adverse Events

All subjects entered into the study will have detailed information collected on adverse events for the overall study safety analysis.

7.1 Definitions

7.1.1 Adverse Event

An adverse event (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries should be regarded as adverse events. Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms

- leads to additional treatment or to further diagnostic tests
- is considered by the investigator to be of clinical significance

7.1.2 Serious Adverse Event

Adverse events are classified as serious or non-serious. A serious adverse event is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- required intervention to prevent permanent impairment or damage
- a congenital anomaly or birth defect
- an important medical event

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in in-patient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as non-serious adverse events.

7.2 Recording of Adverse Events

At each contact with the subject, the investigator will seek information on adverse events by specific questioning and, as appropriate, by examination. Information on all adverse events will be recorded immediately in the source document, and also in the appropriate adverse event module of the case report form (CRF). All clearly related signs, symptoms, and abnormal diagnostic procedures results should recorded in the source document, though should be grouped under one diagnosis.

All adverse events occurring during the study period will be recorded. The clinical course of each event will be followed until resolution, stabilization, or until it has been determined that the study intervention or participation is not the cause. Serious adverse events that are still ongoing at the end of the study period will be followed up to determine the final outcome. Any serious adverse event that occurs after the study period and is considered to be possibly related to the study intervention or study participation will be recorded and reported.

7.3 Relationship of AE to Study

The relationship of each adverse event to the study procedures will be assessed by the PI.

7.4 Reporting of Adverse Events and Unanticipated Problems

The Investigator will promptly notify the Penn IRB of all on-site unanticipated, Adverse Events that are related to the research activity. Other unanticipated problems related to the research involving risk to subjects or others will also be reported promptly. Written reports will be filed using the HS-ERA and in accordance with the Penn IRB timeline of 10 working days.

7.4.1 Follow-up Report

If an AE has not resolved at the time of the initial report and new information arises that changes the investigator's assessment of the event, a follow-up report including all relevant new or reassessed

information (e.g., concomitant medication, medical history) should be submitted to the IRB. The investigator is responsible for ensuring that all SAEs are followed until either resolved or stable.

7.4.2 Investigator reporting: notifying the study sponsor

Within six months after completion of study conduct or termination of the applicable study, whichever occurs first, PI will provide Inspire with a written report of the study results. Unless otherwise agreed in writing by the parties, the study report may take the form of a manuscript for publication. The study report will include the study results of the study as a whole. If the study is terminated early, the study report must include, at minimum, the results of the study up until the date of termination.

7.4.3 Data and Safety Monitoring Plan

The study PI will be responsible for monitoring the safety of research subjects throughout the trial.

8 Study Administration, Data Handling and Record Keeping

8.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

PHI will be stored on an institutionally secured and managed drive and/or device, accessible only to study personnel.

8.2 Data Collection and Management

Data collected from each phase of the study will be stored on the Otorhinolaryngology – Head and Neck Surgery shared, institutionally secured and managed departmental drive. This drive is only accessible through the UPHS Intranet, has HIPAA compliant security, and is routinely used for other clinical and research purposes of the department. Access will be given only to members of the research team. Data will be stored in encrypted folders and files. Data will be deidentified prior to analyses, and will be made anonymous prior to publication of any studies. Data will be stored for 10 years; this will allow for revisiting data in the event that a full-scale study is performed.

8.3 Records Retention

Records will be retained during the duration of the study and for up to 10 years following conclusion of the study. This is in order to allow for further validation analyses that may be relevant to the disease process.

9 Study Monitoring, Auditing, and Inspecting

9.1 Study Monitoring Plan

The study PI will be responsible for ensuring the ongoing quality and integrity of the research study.

9.2 Auditing and Inspecting

The investigator will permit study-related monitoring, audits, and inspections by the EC/IRB, the sponsor, government regulatory bodies, and University compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable University compliance and quality assurance offices.

10 Ethical Considerations

This study is to be conducted in accordance with applicable US government regulations, standards of Good Clinical Practice, and applicable institutional research policies and procedures. This protocol and any amendments will be submitted to a properly constituted Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study.

10.1 Risks

Overall, this study is designed to pose minimal risk to patients. Flexible laryngoscopy is a standard part of otolaryngology exams, and the associated risks are minor. Risks associated with flexible laryngoscopy include bleeding from the nasal cavity related to passage of the scope, which is typically limited and minor. Extremely rarely patients will have anxiety reaction which results in a sensation of fainting and lightheadedness known as a vasovagal reaction or fainting. There is also the risk of a reaction to the medications in the anesthetic and nasal decongestant spray. Sleep studies are noninvasive and carry minimal risk. Subjects may experience mild skin irritation from electrode adhesive. Risks associated with gathering of medical information include physical, emotional, economic, psychological effects of having information inadvertently discovered in the public domain. This will be mitigated through the use of exclusive HIPAA compliant systems and through deidentification of patient data.

10.2 Benefits

This study has the potential to increase effectiveness of Inspire therapy and to decrease latency from time of implantation to time of effective therapy for the individuals enrolled in the study. If awake endoscopy is deemed a useful adjunctive procedure during implant activation, future patients may also benefit from this new protocol and experience improved sleep outcomes and decreased latency to effective therapy. Improving OSA has the potential to benefit associated comorbidities and overall health for all patients. Decreased latency time to effective therapy has the potential to decrease health system use and costs.

10.3 Risk Benefit Assessment

The risks of participating in this study are outweighed by the benefits. The risks of nasal endoscopy and routine sleep study are minimal. The benefit will be significant in improving our understanding of upper airway anatomy and physiology for OSA patients using the Inspire UAS device, and potentially in improving our ability to deliver maximally efficient, effective care for such patients.

10.4 Informed Consent Process / HIPAA Authorization

Informed consent will be obtained by an investigator. Consent process will take place in the clinic during Visit 1. All subjects for this study will be provided a consent form describing this study providing sufficient information for subjects to make an informed decision about their participation in this study. See attached Informed Consent Form. The formal consent of a subject, using the IRB-approved consent form, must be obtained before that subject undergoes any study procedure. Potential subjects will review the consent form in detail with the person designated to consent and they may be given a copy of the consent form for further review. Privacy will be ensured by discussing the study and the patient's disease in private within a private room in the clinic, where they are unlikely to be overheard. Investigators will ensure that patients understand the nature and risks of the study by having an informed discussion; this will include having patient relay their understanding. Patients will be reminded and reassured that participation or lack of participation in the study will have absolutely no effect on their care. A combined consent/HIPPA authorization will be used.

11 Study Finances

11.1 Funding Source

No funding is required.

11.2 Conflict of Interest

All University of Pennsylvania Investigators will follow the University of Pennsylvania Policy on Conflicts of Interest Related to Research

Dr. Thaler has received honorara by Inspire Medical Systems, Inc. (Maple Grove, MN) for presentations at conferences.

11.3 Subject Stipends or Payments

Subjects will not be offered compensation, as there will be no additional time or travel required for study procedures beyond routine follow up.

12 Publication Plan

Findings will be published in the appropriate medical literature; all data will be anonymized for publication purposes.

13 References

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14 Attachments

1. Study consent form

15 Appendices

Study Visit	1	2
Duration	30 minutes	12 hours (overnight)
Review inclusion/exclusion criteria	X	
Informed consent	X	
Vital Signs: HR, RR, BP, SpO2, BMI	X	
Targeted head and neck exam	X	
Recorded awake endoscopy with testing of device configurations and determination of test configuration	X	
Review of Inspire data		X
Sleep study with standard and test device configurations		X
Adverse Event / Unanticipated Problems Assessment	X	X

Penn IRB Definition of Unanticipated Problems Involving Risk to Subjects or Others
Any incident, experience, or outcome that meets all of the following criteria:

- *Unexpected in nature, severity, or frequency (i.e. not described in study-related documents such as the IRB-approved protocol or consent form, the investigators brochure, etc.)*
- *Related or possibly related to participation in the research (i.e. possibly related means there is a reasonable possibility that the incident experience, or outcome may have been caused by the procedures involved in the research)*
- *Suggests that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm).*

15.8 Source Documents

Source data is all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents. Examples of these original documents, and data records include: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions

certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial.

15.9 Case Report Forms (CRFs)

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write “N/D”. If the item is not applicable to the individual case, write “N/A”. All entries should be printed legibly in black ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.