Protocol Title: *The Effect of Head Pitch and Roll Rotation Independent of Torso Position on the AHI in Positional Obstructive Sleep Apnea*

Protocol Number: Apnea Guard-1400

Version: 1.0

Principle Investigator: Dr. Stacia Sailer

Mass Lung & Allergy, PC

85 Prescott Street, Worcester, MA.

774-420-2611

Sponsor: Sleep Systems, LLC

12 Curtis Road, Tyngsboro, MA. 01879

978-835-7036

ifo@sleepsystems-lls.com

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PROTOCOL APPROVAL

INVESTIGATOR STATEMENT

As Investigator of the study titled "*The Effect of Head Pitch and Roll Rotation Independent of Torso Position on the AHI in Positional Obstructive Sleep Apnea*" (the study), I agree to:

(1) Conduct the Study with: a) this Investigator Agreement b) the Study's Protocol as approved by the IRB (the "Protocol"); all applicable laws and regulations; and any IRB or FDA conditions of approval;
(2) Await IRB approval for the Protocol before obtaining informed consent.
(3) Ensure that all requirements for informed consent are met and not let any subject participate in the Study before obtaining that subject's informed consent and Protected Health Information consent.
(4) Not make modifications to the Protocol as supplied by Sleep Systems, LLC (the "Sponsor") without first obtaining the written approval of the Sponsor.
(5) Provide the Sponsor with accurate financial information as required by appropriate regulations.
(6) Supervise all testing of investigational devices that involve any Study subject.
(7) Maintain Study documentation for the period of time as required by appropriate regulations.

PRINCIPLE INVESTIGATOR

Signature: Stacia Sailer

Printed Name: Stacia Sailer, MD

Date: 6/8/2016

DOCUMENT CONTROL PAGE

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PROTOCOL NUMBER: Apnea guard-1400

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AUTHOR (S): Michael S. Lawee

SPONSOR: Sleep Systems, LLC

12 Curtis Road

Tyngsborro, MA 01879

STUDY MONITORS: Michael S. Lawee

mlawee@masslung.com

GLOSSARY OF DEFINITIONS AND TERMS

Obstructive Sleep Apnea: Obstructive sleep apnea (OSA) is a disorder in which a person frequently stops breathing during his or her sleep. It results from an obstruction of the upper airway during sleep that occurs because of inadequate motor tone of the tongue and/or airway dilator muscles.

Positional Obstructive Sleep Apnea (POSA): Defined as a total apnea-hypopnea index (AHI) > or = 5 with a 50% reduction in the AHI between the supine and non supine postures, and an AHI that normalizes (AHI <5) in the non-supine position.

Apnea: Cessation of breathing for 10 seconds or more

Hypopnea: A decrease in airflow associated with subsequent desaturation

Head Pitch: The movement of the head as determined by chin position, up or down

Head Roll: The movement of the head as determined by head rotation from right to left or left to right.

Independent of Torso position: In the context of this protocol, "Independent of Torso position" means sleeping supine while maneuvering the head from left to right or right to left to potentially alleviate collapse of the upper airway.

Polysomnogram: The overnight measurement of 6 or more physiological variables that includes a minimum number of EEG measurements, cardio-respiratory data, EKG data and data pertaining to movement during the sleep period.

Montages: Refers to a specific sequences of collection of physiological data in a sleep study (polysomnogram). The montage specifically details how and what electrodes are placed on the patient.

Participant Clinical Data (PCD): Individual assignable bonded clinical forms that contain research data pertaining to overnight sleep study and screening data. PCD shall only contain the assigned study number with no identifying information and is the property of the Sponsor.

AHI (Apnea-Hypopnea Index): The number of abnormal respiratory events (including cessation of breathing of decreased airflow) divided by the Total Sleep Time (TST). The final number is used to diagnose and determine the severity of patient symptoms.

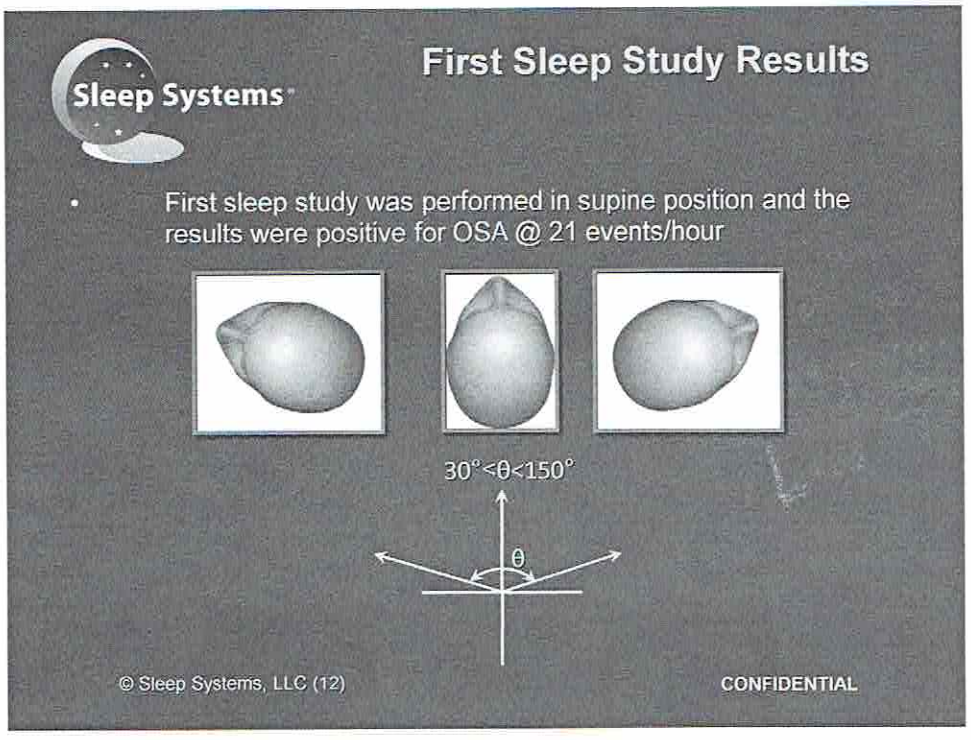
The Effect of Head Pitch and Roll Rotation Independent of Torso Position on the AHI in Positional Obstructive Sleep Apnea

1. Background and Study Aim

The prevalence of Obstructive Sleep Apnea (OSA) can be as high as 9% within the general population. A subset of OSA, described as Positional Obstructive Sleep Apnea (POSA), defined operationally as apneas occurring during specific positions while asleep, occurs predominantly in the supine position. Approximately 30% of obstructive sleep apnea (OSA) patients have supine-predominant OSA.(2) The patients diagnosed with obstructive sleep apnea that position dependent are at least twice as severe when sleeping supine. . In one study, the prevalence of POSA was as high as 50% in patients diagnosed with mild sleep apnea (AHI, 5-15/h) and as low as 7% in patients diagnosed with severe sleep apnea (AHI > 30/hr) (1) . Results from another study of 1170 adults Asian patients conducted over a span of four years, from 2004 through 2008, demonstrated that the presence of POSA is almost three-fourths of the patients and that the AHI is the most dominant factor for determining positional dependency, followed by BMI. (3)

It has been hypothesized that POSA may also occur independent of torso position but is affected solely by head position, independent of supine. A review of drug-induced endoscopy in OSA which is predominantly performed in the supine position concluded that head rotation improves upper airway collapse during this procedure in supine position. (4). Thus while the treatment of POSA has generally been directed at limiting sleeping in the supine position without regards to effects of head position, rotating the head away from the 90 degree position might alleviate the "crush force" seeking to close the upper airway. This study seeks to verify whether rotation of the head while sleeping in the supine position during polysomnography affects the calculated AHI. Head rotation will be defined in terms of degree rotation from a 90 degree starting position (head position aligned with supine position) and rotating the head from right to left defining the movement in terms of a widening angle from 0 degrees to 90 degrees through 180 degrees, thus reducing the AHI. A secondary aim is to develop an algorithm that can predict whether a specific degree of head rotation can be assigned to a percentage reduction in AHI.

The diagram below, provided by the sponsor, illustrates this maneuver:



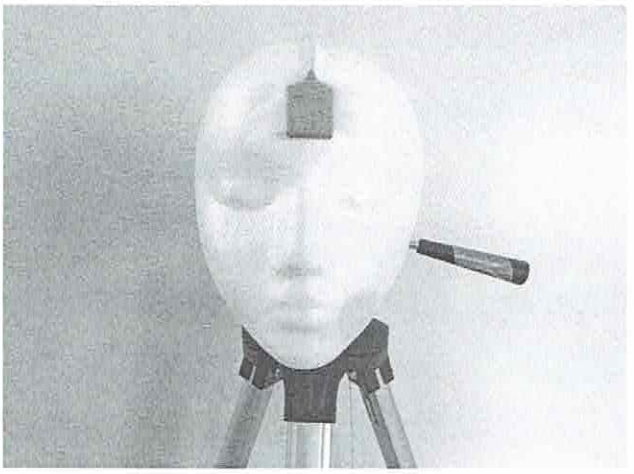
2. Study Design

This is a non-randomized study with the intent of enrolling up to 10 participants to collect up to ten completed polysomnograms. The polysomnogram montages have specifically been altered to include the investigational channels for head pitch and roll. Head pitch and roll recorded data have been added with recorded data tagged as degrees of change from the vertical (head aligned with supine torso) as 90 degrees. Eligible participants, those meeting the inclusion criteria, will provide written informed consent. We will recruit stable, previously diagnosed POSA patients who self-report persistent apnea and who are currently on treatment by PAP.

Eligible participants will come into the Sleep Center for a screening visit. Following the screening visit, qualified participants will be asked to complete one overnight sleep study (polysomnogram) monitored by staff technologists. The sensor patch will be placed on the forehead as illustrated below and calibrated along with other calibrations that are required to complete a standard polysomnogram.

POSA will be determined as per standard collection procedures and when the threshold AHI is calculated, the research technologist shall initiate the head roll from right to left at specific degree changes to eliminate apneas and hypopneas. The changes in head roll shall be accomplished by the placement of pillow wedges to keep the head stable at the particular degree settings. The pillow wedges are selected for the predetermined angle of roll. Additionally, during these maneuvers, the torso shall be maintained in the supine position for a

specific amount of time to assess the effects of head roll independent of torso position in addition to sleeping positions that are comfortable for the participant. The data will be recorded and analyzed as such utilizing standard polysomnography body position sensors.



(Illustration of head pitch and neck roll sensor)

Following collection of overnight data, data will be scored as per standard polysomnography scoring including specific scoring of head pitch and roll in correlation with other polysomnographic data. The sleep study will be reviewed by the principle investigator to determine whether the maneuvering of head pitch and roll had normalized the AHI (See Appendix A).

Subject Selection:

Subject selection will be based upon the following inclusion, exclusion criteria:

Inclusion criteria:

1. Participant has provided written informed consent.
2. Participant is diagnosed with P~~ositional~~ Obstructive Sleep Apnea.
3. Participant age is between 21 and 60 years
4. If currently on PAP therapy, is able to produce compliance data within the last week before screening visit
5. Is able to follow directions during the overnight sleep study.
6. If currently on PAP therapy participant self-report that excessive daytime sleepiness persists when PAP therapy is not in use.
7. Able to be "off" PAP therapy for 4 nights

Exclusion criteria:

1. Documented diagnosis of Insomnia
2. Chronic ear infections

3. Persistent neck "pains".
4. Previous C-Spine fusion
5. History of Cardiac arrhythmias
6. History of seizures
7. Allergic to standard tape used in Sleep Centers
8. Persistent chronic posture physical issues, including shoulder issues.
9. Non-English speaking.
10. Hospitalization within the previous 4 weeks.
11. Use of antibiotics or steroids within the previous 4 weeks.
12. Any major uncontrolled disease or condition, such as congestive heart failure, malignancy, end-stage heart disease, end-stage heart disease. ALS, or sever stroke, or other condition as deemed appropriate by investigator as determined by review of medical history and/or participant reported medical history.
13. History of severe osteoporosis.
14. Excessive alcohol intake (> 6oz hard liquor, 48 oz beer or 20 oz wine daily), or illicit drug use by review of medical history and/or participant reported medical history.
15. Daily use of prescribed narcotics (greater than 30 mg morphine equivalent)

Study Procedures:

1. Subject (participant) how are eligible will be scheduled for a daytime screening session at the Sleep Center located at 85 Prescott Street, Worcester, MA with either the Study Coordinator or Staff Research Technologist. Following the screening visit and signed consent, qualified participants shall be asked to complete an overnight sleep study (polysomnogram).
2. Following the screening visit, participant will be scheduled for an overnight sleep study and participant will arrive at scheduled time, generally between the hours of 7:00 PM and 8:30 PM.
3. Research Technologist greets patient, verified individual personal information and matches the assigned Participant Clinical Data Binder (PCD) including the assigned study number.
4. Research Technologist shall complete the demographic section of the PCD and explain the sleep study to the participant.
5. Research Technologist shall attach electrodes as per Sleep Systems Research Montage and escort participant to assigned sleep room and will further explain to the participant the "process" of gathering sleep study data (i.e. calibrations, use of call button and the system that will be utilized to rotate the head as per protocol.)

6. Research Technologist will attach forehead sensor to the most level surface of forehead without getting too close to the eyes with medical tape. Small foam wedges may be necessary under the sensor to adjust for calibration. Research Technologist will confirm the pitch and roll angles to be 90 degrees +/- 5 degrees.
7. Participant is allowed to watch Television or read until "Lights Out" as determined by the Research Technologist.
8. Once recording has commenced the Research Technologist shall complete the scoring forms as per protocol. Once the baseline AHI for POSA is verified (generally about 2 hours following sleep) Research Technologist shall enter the Sleep room and initiate neck roll maneuvers, utilizing wedge pillows as follows:
   a) 30 degrees on right for 45 minutes.
   b) 60 degrees on right for 45 minutes
   c) 90 degree (head and neck aligned with supine torso) for 45 minutes
   d) 120 degrees to left for 45 minutes
   e) 150 degree to left for 45 minutes.

   The goal is to normalize AHI (<5).

9. If no calculated AHI indicative of POSA (>5) is achieved the participant will be awakened at 7:00 AM and discharged from Sleep Center.

Risks and Discomforts:

Potential adverse effects of monitoring sleep studies are minimal. Allergic reaction to electrode placement has been reported but the frequency of these reports is not known. If the participant does experience an allergic reaction to either the placement of electrodes or the sensor patch to the forehead the Research Technologist, shall terminate the study and recording will be terminated.

Data Analysis, Safety, Confidentiality and Compensation:

Demographic data will be presented with descriptive analysis. Sleep Study data will be scored as per AASM (American Academy of Sleep Medicine) standards and will be tested for normal distribution with respect to prediction of neck and head roll angles normalizing the AHI (Apnea Hypopnea Index). Normalizing AHI or reducing to sufficient levels to decrease the symptoms of untreated POSA will be documented for each subject. The results of this pilot study may be used to power a larger trial.

With respect to confidentiality, a unique identification number designed to protect the identity of participant will be used to identify the participant on report forms, recruitment logs, data forms or other report containing information. Each participant will sign a HIPAA authorization

permitting the release of protected health information to the sponsor, the investigative team, and regulatory authorities.

Safety maintenance at the Sleep Center during the overnight visit shall be maintained in accordance Policies and Procedures currently in place at the Sleep Center located at 85 Prescott Street, Worcester, MA.

Participants will be compensated for travel expenses and time commitment. Participants will be compensated $50.00 for the screening visit and up to $400.00 for each overnight sleep study they complete.

Monitoring and Quality Assurance:

This clinical trial will be monitored by Mass Lung & Allery, Sleep Center, New England IRB (NEIRB) located in Newton, Massachusetts, and Sleep Systems-LLC (Sponsor) in compliance with the Code of Federal Regulations (CFR) for clinical research. The purpose of such monitoring is to assure that the study remains in compliance with the approved protocol, investigator agreement and regulatory requirements, and resolve any issues that arise during the conduct of the study. The monitoring process includes initial site qualification by NEIRB, and ongoing monitoring throughout the study to assure compliance with the investigational plan, and to verify the completeness and accuracy of study data. Monitoring also aids in identifying any research related problems for the sponsor and/or investigator to correct.

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(1) Prevalence of positional sleep apnea in patients undergoing Polysomnography ; Mador MJ, Kutel T.J., Magalang UJ, Rajesh SK, Watwe V., Grant BJ. *Chest 2005, Oct; 128 (4) 2130-7*

(2) Accurate position monitoring and improved supine-dependent obstructive sleep apnea with a new position recording and supine avoidance device; Bignold JJ, Mercer JD, Antic NA, McEvoy RD, Catcheside PG *J Clin Sleep Med, 2011 Aug 15; 7(4): 376-83. Doi: 10.5664/JCSM 1194*

(3) The impact of body posture and sleep stages on sleep apnea severity in adults. Eiseman NA; Westover MB; Ellenbogen JM; Bianchi MT; *J Clin Sleep Medicine, 2012 Dec 15; 8(6); 655-66A, doi: 10.5664/jcsm. 2258*

(4) Analysis of the influence of head rotation during drug-induced sleep endoscopy in obstructive sleep apnea. Safiruddin, F.; Koutsourelakis I; de Vries, N; *Laryngoscope, 2014,Sep, 124(9):2195-9 doi:10.1002/lary.24598. Epub 2014 Mar 1*

APPENDIX A

Sleep Study Score Sheet

This score sheet represents the ideal baseline information that Sleep Systems would like to see for the sleep study. All numbers in the table should be replaced with actual values

Measured Head Pitch Angle(°)	Measured Head Roll Angle(°)	Pillow Angle (°) or Style Used	Torso Position	Start Time	Stop Time	Measured Duration (Min.)	Measured AHI Events /Hour	Measu Oxyg Satura (%
70-90	90	Flat	Supine	10:00P	11:00P	60	25	90
70-90	90	Flat+Towell	Side	11:00P	12:00P	60	25	90
70-90	15 or 165	15	Side	12:00A	1:00A	60	5	10
70-90	15 or 165	15+Towell	Supine	1:00A	2:00A	60	5	10
70-90	0 or 180	Flat	Side	2:00A	3:00A	60	17.5	96
70-90	45 or 135	45	Side or Supine	2:00A	3:00A	60	17.5	96

Apnea Severity Calculator

STEP 1

Enter the subjects peak measured AHI in the yellow box below, at a head pitch and roll angle near 90 degrees

Measured Peak AHI (events/hour)
25

STEP 2

Enter the pitch and roll angle in the yellow boxes below to see the calculated AHI index in green

Measured Head Pitch Angle (°)	Measured Head Roll Angle (°)	Calculated AHI (events/Hour)
90	90	**25.0**

1)HAVE YOU BEEN TOLD THAT YOUR SLEEP APNEA IS POSITIONAL (IT HAPPENS MOSTLY WHEN YOU SLEEP ON YOUR BACK)?

2)HAVE YOU HAD A SLEEP STUDY WITHIN THE PAST 2 YEARS?

3)ARE YOU NOW ON CPAP THERAPY?

4) ARE YOU BETWEEN THE AGES OF 21 AND 60 YEARS?

IF YOU ANSWERED YES TO THE ABOVE, YOU MIGHT BE ELIGIBLE AND COMPENSATED TO PARTICIPATE IN A CLINICAL TRIAL. ASK YOUR PHYSICIAN FOR MORE DETAILS