PROTOCOL TITLE:

Treatment of eustachian tube dysfunction (ETD) and facial pain with combined acoustic vibration and oscillating expiratory pressure

The study will be conducted in compliance with the clinical study protocol, international good clinical practice principles (International Conference on Harmonization [ICH]-Good Clinical Practice [GCP]), and regulatory authority requirements.

PRINCIPAL INVESTIGATOR:

Dr. McRackan

NCT04404036

1.0 Objectives / Specific Aims

Aim 1: To determine if combined acoustic vibration and oscillating expiratory pressure impacts exhaled nasal Nitric Oxide (NO) in healthy controls as a potential mechanism

Aim 2: To determine the safety and efficacy of combined acoustic vibration and oscillating expiratory pressure for treatment of eustachian tube dysfunction (ETD).

Aim 3: To determine the safety and efficacy of combined acoustic vibration and oscillating expiratory pressure for treatment of sinus pain/pressure

2.0 Background

Eustachian tube dysfunction (Meyer TA, etal) and sinus pain/pressure impact the quality of life of millions of Americans (Falco JJ, etal). It is thought that these disorders may be due to positive or negative pressure differential between the middle ear or paranasal sinuses. Current treatment options for ETD and sinus pressure/pain are typically Valsalva (positive expiratory pressure) with the hopes of equalizing pressures between the middle ear space or paranasal sinuses and the nasal cavity/external environment. Pharmacologically, nasal steroid sprays can be used to try to open the ET and sinus drainage pathways. If this fails, then procedures to include pressure equalization tubes (PETs) or balloon eustachian tube/paranasal sinus dilation are offered.

Future treatment options: This study aims to test the safety, efficacy and potential mechanism of action of the SinuSonic device on adults with ETD or facial pain/pressure. SinuSonic is a medical device that utilizes sound and pressure combined with normal breathing. It has been shown to be safe and relieve nasal congestion (Soler ZM, etal). The study will have 3 aims. Aim 1 will examine healthy controls with no signs of upper respiratory infection, inflammation, or ETD to determine if exhaled nasal NO is increased. Acoustic energy (humming) has been shown to increase nasal NO dramatically, thus equalization of gas pressures between the middle ear, the paranasal sinuses and the nasal cavity may very well explain any efficacy noted. Aim 2 will be performed to examine therapeutic efficacy for ETD. Aim 3 will be performed to examine therapeutic efficacy for sinus pain/pressure.

3.0 Intervention to be studied

Aim 1: Exhaled NO in healthy controls (N=10)

- Initial intervention: Baseline exhaled nasal NO will be measured using a clinically available nasal airflow sampling device at rest. Then using SinuSonic devices for 2 exhalations followed by the 30 second NO sampling period. We will use 4 SinuSonic devices with frequencies between 64Hz and 2,000Hz in random order. Five minutes rest will be allowed between trials. The final trial will use 128 Hz for 1 minute.

Aim 2: Clinical efficacy in subjects with ETD (N=30)

- Baseline: Subjects will complete ETD questionnaire to confirm eligibility. Tympanogram will be completed. After confirming eligibility, subjects will use the SinuSonic device for 3 minutes in the clinic setting. Immediate treatment effect will be assessed with questionnaires.
- Primary timepoint: Subjects will use SinuSonic device twice daily for 3 minutes in the home setting for 6 weeks. Tympanogram and ET questionnaires will be completed.

Aim 3: Clinical efficacy in subjects with sinus pain/pressure (N=30)

- Baseline: Subjects will complete VAS to confirm eligibility. After confirming eligibility, subjects will use the SinuSonic device for 3 minutes in the clinic setting. Immediate treatment effect will be assessed with questionnaires.
- Primary timepoint: Subjects will use SinuSonic device twice daily for 3 minutes in the home setting for 4 weeks. Questionnaires will be completed at 2 weeks and 4 weeks.

3.1 Device Instructions

Instructions for use:

1. Hold the SinuSonic device at a 45-degree angle
2. Deep breathe

3. Hold the SinuSonic to your nose and blow out into the mask of the SinuSonic. The goal here is to hear the "target flutter" sound that is desired during treatment with the SinuSonic
4. Put the device over the nose using the nasal mask
5. Breathe in and out thru the nose if possible. If nasal breathing is not possible it is ok to open mouth to breathe in and try and hear the "target flutter" sound when you breathe out
6. You will feel a little resistance to breathe out and a vibration sensation from a speaker in the device
7. Remove the device to "blow the nose" if nasal drainage occurs
8. Return the device to the nose then breathe in and out thru the nose to try and hear the "target flutter" sound
9. Time of use is 3 minutes of nasal breathing with the device - as tolerated

3.2 Device Usage and Safety

The SinuSonic consists of a fully-disposable medical grade silicone nosepiece mounted to a resin body. The device is equipped with a flutter valve located at the top of the device which creates gentle, self-guided oscillating expiratory resistance.

4.0 Inclusion and Exclusion Criteria/ Study Population

Aim 1 exhaled NO: For the exhaled NO portion of the study, we will examine 10 healthy control patients with no symptoms of upper airway infection, inflammation or ETD to determine impact of SinuSonic upon NO release.

Inclusion Criteria

- -Adults 18 years or older with no symptoms of URI, ETD or other ENT conditions

Exclusion Criteria

-Sinonasal or ear surgery within last 3 months (including balloon ET dilation)
-Any ENT condition that may impact upper airway to include sinusitis, otitis, or allergies
-Upper respiratory illness within last 2 weeks
-Topical decongestant use in last week
-Current nasal crusting or ulceration on rhinoscopy
-History of severe nose bleeding within last 3 months
-Known pregnancy
-Allergic sensitivity to silicone or any other component of device
-Inability to read and understand English
-Inability to perform treatment due to underlying medical condition

Aim 2 ETD efficacy: The ETD study population will consist of individuals presenting for care at the Otolaryngology clinics at the Medical University of South Carolina with ETD, or from the community at large.

Inclusion Criteria

- -Adults 18 years or older with diagnosis of ETD by an otolaryngologist

- ≥6 months of symptoms duration
- ≥3 ETD symptoms (ear pressure, feeling that ears are clogged, cracking/popping of ears, muffled hearing, tinnitus)
- ETDQ-7 score ≥ 3
- Audiogram within the last year

Exclusion Criteria

-Sinonasal or ear surgery within last 3 months (including balloon ET dilation)
-Indwelling ear tubes
-Tympanic membrane perforation
-Hx of cholesteatoma, mastoidectomy, tympanoplasty, or ossicular chain reconstruction
-Patulous ET
-Hx of Meniere's disease
-Moderate or severe nasal valve collapse
-Grade 3-4 polyps
-Upper respiratory illness within last 2 weeks
-Topical decongestant use in last week
-Current nasal crusting or ulceration on rhinoscopy
-History of severe nose bleeding within last 3 months
-Known pregnancy
-Allergic sensitivity to silicone or any other component of device
-Inability to read and understand English
-Inability to perform treatment due to underlying medical condition

Aim 3 Facial pain/pressure efficacy: The facial pain/pressure study population will consist of individuals presenting for care at the Otolaryngology clinics or community at large with self-reported sinus pain/pressure.

Inclusion Criteria

- -Adults 18 years or older who complain of facial pain or pressure
- ≥3 months of symptoms duration (can be intermittent)
- Pain/pressure VAS score ≥ 5

Exclusion Criteria

-Sinonasal surgery within the last 3 months
-Grade 3-4 polyps
-Upper respiratory illness within last 2 weeks
-Topical decongestant use in last week
-Current nasal crusting or ulceration on rhinoscopy
-History of severe nose bleeding within last 3 months
-Known pregnancy
-Allergic sensitivity to silicone or any other component of device
-Inability to read and understand English
-Inability to perform treatment due to underlying medical condition

5.0 Number of Subjects

Aim 1, exhaled NO: We anticipate 10 healthy control subjects for the exhaled NO portion of the study.

Aim 2, ETD: This is a pilot study. The anticipated ETD study population is 30 subjects.

Aim 3, Facial pain/pressure: This is a pilot study. The anticipated facial pain/pressure study population is 30 subjects.

6.0 Setting

Research will be conducted at the Medical University of South Carolina. Potential participant screening for all subjects across all aims, as well as baseline evaluations, will occur in the outpatient ENT clinics. For AIM 2, the 6-week post treatment assessment will take place in the outpatient ENT clinics. For AIM 3, follow-up measures will be collected remotely using REDCap at 2 and 4 weeks.

7.0 Recruitment Methods

MUSC Otolaryngologists will notify the study coordinator (SC) of potential participants through the ENT Clinic. If the patient is interested, the coordinator will approach them and explain the study in further detail and begin the informed consent process.

8.0 Consent Process

Patients who are deemed eligible for this study will be approached by the Principal Investigator or Co-Investigator in the ENT Clinic at the Medical University of South Carolina about the study. A member of the study team will describe in full detail the study and the informed consent form to the potential subject. The prospective participant will be given adequate time to review the informed consent form and ask any questions that they have before the consent is obtained. Participants will be given a signed copy of the ICF.

8.1 Withdrawal

At any point during the study, a subject may withdraw from the study.

9.0 Study Design / Methods

This study is designed as a pilot study.

Data will be collected by the study investigators as well as the subjects themselves throughout the entirety of the study. The data will consist of answers from subjects for questionnaires asked by the clinicians as well as self-reported answers from the subjects.

Safety will be monitored throughout the study based on monitoring of adverse events, performing nasal, measuring vital signs (i.e. blood pressure, pulse) and weight, and through collection of concomitant medication information.

The period of observation for collection of non-serious adverse events extends from the time the subject gives informed consent until completion of the End-of-study visit or Early Termination Visit. Serious adverse events (SAE) will be reported from the time of informed consent through 30 days after the last use of the SinuSonic. Adverse event data listings will be reviewed by SinuSonic at regular intervals throughout the study. In

addition, SinuSonic will be alerted of Adverse Events of interest via automated emails programmed in the EDC system. Patient compliance will be assessed via weekly phone calls from study coordinator.

9.1 Schedule of Events

Aim 1: NO in N=10 controls	**Screening and baseline assessment**
Day	0
Informed consent	X
Inclusion/exclusion criteria	X
Medical history	X
Rhinology, otoscopy	X
Vital signs	X
Exhaled nasalNO at 30 seconds and 5 min	X

Aim 2: ETD efficacy in N=30 patients	**Screening and baseline assessment**	**Primary timepoint for outcomes**
Week	0	6 + 1
Informed consent	X	
Inclusion/exclusion criteria	X	
Medical history	X	
Rhinology, otoscopy	X	X
Vital signs	X	
Distribution of Sinusonic	X	X
ETDQ-7	X	X
ETD VAS questionnaire	X	X
Tympanogram	X	X

Aim 3: Facial pain/pressure in N=30 patients	**Screening and baseline assessment**	**Primary timepoint for outcomes**	**Secondary timepoint for outcomes**
Week	0	2	4
Informed consent	X		
Inclusion/exclusion criteria	X		
Medical history	X		
Rhinology, otoscopy	X		

Vital signs	X		
Distribution of Sinusonic	X		
Pain/pressure VAS	X	X	X
BPI-SF	X	X	X
MPQ-SF	X	X	X

10.0 Data Management

All analyses and graphs will be performed with SPSS 24.0, Sample Power 3.0, and Sigma Plot 10.0 (SPSS, Chicago, IL.). Disease information and demographic variables, such as age, gender, race, quality of life (QOL) scores, and VAS scores will be summarized using frequencies, means, and standard deviation as appropriate. Aim 1 nasal NO metrics will be compared between baseline vs 10 seconds and baseline vs 3 minutes. Aim 2 metrics (ETDQ-7, ETD VAS and tympanogram) will be compared between baseline and 6 weeks. Aim 3 metrics (VAS, BPI-SF, MCQ-SF) will be compared between baseline vs 2 weeks and baseline vs 4 weeks. Categorical variables will be compared using Chi Square or McNemar's test. Continuous variables will be compared using One-Way ANOVA with repeated measures follow by post-hoc analysis. Data regarding safety and patient satisfaction will be summarized for each time point. A p-value ≤ 0.05 will be considered statistically significant. Due to the exploratory nature of this study, no p-value correction (ie Bonferroni) will be applied.

11.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Safety will be monitored throughout the study based on the monitoring of adverse events, performing nasal exams, measuring vital signs (i.e. blood pressure, pulse) and weight, and through the collection of concomitant medication information.

The period of observation for collection of non-serious adverse events extends from the time the subject gives informed consent until the completion of the End-of-Study visit or Early Termination Visit. Serious adverse events (SAE) will be reported to the MUSC IRB and to the sponsor from the time of informed consent through 30 days after the last use of the SinuSonic. Adverse event data listings will be reviewed by Principal Investigator and the research team at regular intervals throughout the study.

12.0 Risks to Subjects

There is a risk of a loss of confidentiality of your personal information as a result of participation in this study.

There are risks to subjects using the SinuSonic device. Subjects may experience a degree of pain due to use of the device. This degree of pain is unknown. There may also be risk of nose bleeds or crusting around the nasal cavity.

The Rhinoscopy may activate the gag reflex. Additionally, nasal discomfort, nose bleeds, spasms, and coughing may also occur.

13.0 Potential Benefits to Subjects or Others

This study is for research purposes only. There is no direct benefit to you from your participation in the study. Information learned from the study may help other people in the future.

14.0 Sharing of Results with Subjects

Information about the subjects (including your identifiable private information) may have all of their identifiers removed and used for future research studies.

Records of the subjects' participation in this study will be held confidential except as disclosure is required by law or as described in the ICF.

15.0 Payment

For participating in this study, participants will be compensated with a $50 Visa gift card per visit for a maximum of $50 for the Control group, $100 for the ETD groups and $150 for the Facial Pain/Pressure groups.

18.0 Devices

Dispensing and storage of SinuSonic devices will be done by the study team. All SinuSonic devices will be stored on the 11th floor of Rutledge Tower in Room 1126 and locked in a cabinet for ambient storage. The device will be dispensed in the Outpatient Sinus Clinic. Only study participants will receive the SinuSonic for use.

19.0 DATA SAFETY MONITORING AND REPORTING

Safety data listings will be reviewed by Principal Investigator, Co-Investigators, and the research team at regular intervals throughout the study.

Safety will be monitored throughout the study based on monitoring of adverse events, performing nasal exams, measuring vital signs (ie blood pressure, pulse) and weight, and through collection of concomitant medication information.

The period of observation for collection of non-serious adverse events extends from the time the subject gives informed consent until completion of the End-of-study visit or Early Termination Visit. Serious adverse events (SAE) will be reported to the MUSC IRB and to the sponsor from the time of informed consent through 30 days after the last use of the SinuSonic. Adverse event data listings will be reviewed by the principal investigator, co-investigators, and the research team at regular intervals throughout the study.

All AEs, regardless of seriousness or relationship to SinuSonic use, spanning from the signature of the informed consent form until the end of the study as defined by the protocol for that patient, are to be reported to the Healthy Humming, LLC. All AEs which follow the MUSC IRB qualifications will also be reported to the MUSC IRB within 24 hours of site knowledge of the event.

The Investigator will take appropriate measures to follow all AEs until clinical recovery is complete and laboratory results have returned to normal, or until progression has been stabilized, or until death, in order to ensure the safety of the patients. This may imply that observations will continue beyond the last planned visit per protocol, and that additional investigations may be requested by the monitoring team up to as noticed by Healthy Humming, LLC.

In the case of occurrence of an SAE, the Investigator will immediately (within 24 hours) report the event to Healthy Humming, LLC and to the MUSC IRB, as applicable.

References

Meyer TA, O'Malley EM, Schlosser RJ, Soler ZM, Cai J, Hoy MJ, Slater PW, Cutler JL, Simpson RJ, Clark MJ, Rizk HG, McRackan TR, D'Esposito CF, Nguyen SA. A Randomized Controlled Trial of Balloon Dilation as a Treatment for Persistent Eustachian Tube Dysfunction With 1-Year Follow-Up. Otol Neurotol. 2018 Aug;39(7):894-902

Falco JJ, Thomas AJ, Quin X, Ashby S, Mace JC, Deconde AS, Smith TL, Alt JA. Lack of correlation between patient reported location and severity of facial pain and radiographic burden of disease in chronic rhinosinusitis. Int Forum Allergy Rhinol. 2016 Nov;6(11):1173-1181.

Soler ZM, Nguyen SA, Salvador C, Lackland T, Desiato VM, Storck K, Schlosser RJ. Safety and efficacy of a novel device combining acoustic vibration with oscillating expiratory pressure for the treatment of nasal congestion. Int Forum Allergy Rhinol (in press).

APPENDICES

AIM 1, CONTROL PATIENTS, EXHALED NO:

Baseline medical history and exam

SinuSonic Study

PI: McRackan

Subject ID#: _____ Subjects Initials: _____

DEMOGRAPHIC AND CLINICAL VARIABLES (If not previously collected):

Age at enrollment (years): | | |

Gender: Male Female

What is/was your profession (current/retired)?_____

LANGUAGE, ETHNICITY, RACE, MARITAL STATUS

Please mark one of the following categories which describes your native language:

- ☐ American English
- ☐ Other: please specify _____

Please mark one of the following categories which describes your ethnicity:

- ☐ Not Hispanic or Latino
- ☐ Hispanic or Latino

Please mark one or more of the following categories which describes your race:

- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White
- ☐ Other

SMOKING HISTORY

1. Do you **currently** smoke tobacco products? **Yes** **No** **(If No please go to question 2)**

How many tobacco products do you use in a day?_____ Singles Packs

CURRENT MEDICATION USAGE

- ☐ Nasal steroid sprays (Flonase, Nasonex, etc) ☐Yes ☐No
- ☐ Nasal antihistamine spray (Astelin, etc) ☐Yes ☐No
- ☐ Oral antihistamines (Allegra, Claritin, Benedryl, etc) ☐Yes ☐No
- ☐ Oral decongestant (Sudafed, etc) ☐Yes ☐No
- ☐ Mucolytic (Mucinex, etc) ☐Yes ☐No
- ☐ Luekotriene (Singulair, etc) ☐Yes ☐No

COMORBID MEDICAL CONDITIONS: Check box and provide details if present

- ☐ Depression history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated
- ☐ Anxiety history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated
- ☐ Obstructive Sleep Apnea: ☐Currently being treated ☐History / No current treatment
- ☐ Allergic rhinitis:_____
- ☐ Previous allergy testing (blood test or skin prick): ☐Yes ☐No
- ☐ Immunotherapy shots for allergies: ☐Yes ☐No ☐Currently
- ☐ Non-allergic rhinitis ☐Yes ☐No
- ☐ Asthma ☐Yes ☐No
- ☐ Chronic rhinosinusitis ☐Yes ☐No
- ☐ Nasal polyps ☐Yes ☐No
- ☐ Viral upper respiratory infection ☐Yes ☐No
- ☐ Prior ear/sinus surgery ☐Yes ☐No
- ☐ Migraine headache history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated

_____

- ☐ Height (ft/in):_____
- ☐ Weight (lbs):_____

Rhinoscopy:

Septal Deviation: None Mild Moderate Severe Nasal valve collapse: None Mild Moderate Severe Bleeding: None Yes
Crusting: None Yes

Otoscopy: Normal Abnormal findings:_____

Baseline exhaled NO measurements

Resting peak: _____

10 second peak: _____

3 minute peak:_____

AIM 1: DAY 1 REPEAT EXAMINATION

Rhinoscopy:

Septal Deviation: None Mild Moderate Severe Nasal valve collapse: None Mild Moderate Severe Bleeding: None Yes
Crusting: None Yes

Otoscopy: Normal Abnormal findings:_____

Day 1 exhaled NO measurements

Resting peak: _____

10 second peak: _____

3 minute peak:_____

Day 1 patient satisfaction/safety

How much pain did you experience using device? None Mild Moderate Severe

Would you use device again? Yes No

Would you recommend device to others? Yes No

AIM 2, ETD: Patient Medical History and exam

SinuSonic Study

PI: McRackan

Subject ID#: _____ Subjects Initials: _____

DEMOGRAPHIC AND CLINICAL VARIABLES (If not previously collected):

Age at enrollment (years): | | |

Gender: Male Female

What is/was your profession (current/retired)?_____

LANGUAGE, ETHNICITY, RACE, MARITAL STATUS

Please mark one of the following categories which describes your native language:

- ☐ American English
- ☐ Other: please specify _____

Please mark one of the following categories which describes your ethnicity:

- ☐ Not Hispanic or Latino
- ☐ Hispanic or Latino

Please mark one or more of the following categories which describes your race:

- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White
- ☐ Other

SMOKING HISTORY

1. Do you **currently** smoke tobacco products? **Yes** **No** **(If No please go to question 2)**

How many tobacco products do you use in a day?_____ Singles Packs

CURRENT MEDICATION USAGE

☐ Nasal steroid sprays (Flonase, Nasonex, etc)	☐Yes	☐No
☐ Nasal antihistamine spray (Astelin, etc)	☐Yes	☐No
☐ Oral antihistamines (Allegra, Claritin, Benedryl, etc)	☐Yes	☐No
☐ Oral decongestant (Sudafed, etc)	☐Yes	☐No
☐ Mucolytic (Mucinex, etc)	☐Yes	☐No
☐ Luekotriene (Singulair, etc)	☐Yes	☐No

COMORBID MEDICAL CONDITIONS: Check box and provide details if present

☐ Depression history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated

☐ Anxiety history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated

☐ Obstructive Sleep Apnea: ☐Currently being treated ☐History / No current treatment

☐ Allergic rhinitis:_____

☐ Previous allergy testing (blood test or skin prick): ☐Yes ☐No

☐ Immunotherapy shots for allergies: ☐Yes ☐No ☐Currently

☐ Non-allergic rhinitis ☐Yes ☐No

☐ Asthma ☐Yes ☐No

☐ Chronic rhinosinusitis ☐Yes ☐No

☐ Nasal polyps ☐Yes ☐No

☐ Viral respiratory infection ☐Yes ☐No

☐ Prior ear/sinus surgery ☐Yes ☐No

☐ Migraine headache history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated

_____

☐ Height (ft/in):_____

☐ Weight (lbs):_____

Rhinoscopy:

Septal Deviation: None Mild Moderate Severe Nasal valve collapse: None Mild Moderate Severe Bleeding: None Yes
Crusting: None Yes

Otoscopy: ☐Normal ☐Retracted no effusion ☐Effusion

Valsalva: ☐Successful ☐Not successful

Tympanogram type: A B C

AIM 2, ETD: Baseline Questionnaires

PATIENT QUESTIONS	
How long have you had eustachian tube problems? <3 months 3-6 months 6-12 months 1-3 year >3 years	
OVER THE LAST FEW MINUTES, HOW TROUBLESOME HAVE THE FOLLOWING SYMPTOMS BEEN? PLEASE PLACE A MARK ON THE LINE.	
	Not troublesome **Worst thinkable/troublesome**
Ear pressure	
Feeling that ears are clogged	
Cracking/popping of ears	
Muffled hearing	
Tinnitus (noise in ears)	
OVERALL ASSESSMENT OF EAR and EUSTACHIAN TUBE PROBLEMS	

BASELINE ETDQ-7

Next to each question, circle the number that best describes how you feel.

During the past 1 month, how much of a problem was each of the following?	**No problem**		**Moderate Problem**			**Severe Problem**	
Pressure in the ears?	1	2	3	4	5	6	7
Pain in the ears?	1	2	3	4	5	6	7
A feeling that your ears are clogged or "under water"?	1	2	3	4	5	6	7
Ear problems when you have a cold or sinusitis?	1	2	3	4	5	6	7
Crackling or popping sounds in the ears?	1	2	3	4	5	6	7
Ringing in the ears?	1	2	3	4	5	6	7
A feeling that your hearing is muffled?	1	2	3	4	5	6	7

Do you get these symptoms in one ear only or both ears?

Left ear only Right ear only Both ears

INCLUSION CRITERIA (all must be yes):

Does patient have ETD sx for ≥6mos? Yes No

Is ETDQ-7 score ≥ 3? Yes No

Does patient have ≥ 3 ETD symptoms above? Yes No

AIM 2, ETD: Follow Up Questionnaire 5 minutes

FOLLOW UP ETD VAS 5 MINUTES

OVER THE LAST FEW MINUTES, HOW TROUBLESOME HAVE THE FOLLOWING SYMPTOMS BEEN? PLEASE PLACE A MARK ON THE LINE.	
	Not troublesome — **Worst thinkable/troublesome**
Ear pressure	
Feeling that ears are clogged	
Cracking/popping of ears	
Muffled hearing	
Tinnitus (noise in ears)	
OVERALL ASSESSMENT OF EAR and EUSTACHIAN TUBE PROBLEMS	

AIM 2, ETD: 6-Week Follow Up Questionnaires

Objective Evaluation
Rhinoscopy: Bleeding: None Yes Crusting: None Yes Otoscopy: ☐Normal ☐Retracted no effusion ☐Effusion Valsalva: ☐Successful ☐Not successful Tympanogram type: A B C

OVER THE LAST FEW MINUTES, HOW TROUBLESOME HAVE THE FOLLOWING SYMPTOMS BEEN? PLEASE PLACE A MARK ON THE LINE.		
	Not troublesome	**Worst thinkable/troublesome**
Ear pressure	◆———	———◆
Feeling that ears are clogged	◆———	———◆
Cracking/popping of ears	◆———	———◆
Muffled hearing	◆———	———◆
Tinnitus (noise in ears)	◆———	———◆
OVERALL ASSESSMENT OF EAR and EUSTACHIAN TUBE PROBLEMS	◆———	———◆

6 WEEK ETDQ-7

Next to each question, circle the number that best describes how you feel.

During the past 1 month, how much of a problem was each of the following?	**No problem**		**Moderate Problem**			**Severe Problem**	
Pressure in the ears?	1	2	3	4	5	6	7
Pain in the ears?	1	2	3	4	5	6	7
A feeling that your ears are clogged or "under water"?	1	2	3	4	5	6	7
Ear problems when you have a cold or sinusitis?	1	2	3	4	5	6	7
Crackling or popping sounds in the ears?	1	2	3	4	5	6	7
Ringing in the ears?	1	2	3	4	5	6	7
A feeling that your hearing is muffled?	1	2	3	4	5	6	7

Do you get these symptoms in one ear only or both ears?

Left ear only Right ear only Both ears

Change in eustachian tube symptoms and use of device

Please rate changes in your nasal symptoms and use of device.

Symptom	None	Mild	Moderate	High
Improvement in ear pressure	0	1	2	3
Improvement in ear clogging	0	1	2	3
Improvement in cracking/popping of ears	0	1	2	3
Improvement in muffled hearing	0	1	2	3
Improvement in tinnitus (noise in ears)	0	1	2	3
Improvement in ear pain	0	1	2	3
Improvement in ear problems with cold or sinus infection	0	1	2	3
Overall improvement in ear symptoms	0	1	2	3
Tolerability				
Pain with use of device	None	Mild	Moderate	Severe
Comfort and ease of use	Poor	Low	Moderate	High
Bleeding:	Yes	No		

Week 6 patient satisfaction

Would you use device again? Yes No

Would you recommend device to others? Yes No

AIM 3, SINUS PAIN/PRESSURE: Baseline Medical History and exam

SinuSonic Study

PI: McRackan

Subject ID#: _____ Subjects Initials: _____

DEMOGRAPHIC AND CLINICAL VARIABLES (If not previously collected):

Age at enrollment (years): | | |

Gender: Male Female

What is/was your profession (current/retired)?_____

LANGUAGE, ETHNICITY, RACE, MARITAL STATUS

Please mark one of the following categories which describes your native language:

- ☐ American English
- ☐ Other: please specify _____

Please mark one of the following categories which describes your ethnicity:

- ☐ Not Hispanic or Latino
- ☐ Hispanic or Latino

Please mark one or more of the following categories which describes your race:

- ☐ American Indian or Alaska Native
- ☐ Asian
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ White
- ☐ Other

SMOKING HISTORY

1. Do you **currently** smoke tobacco products? **Yes** **No** **(If No please go to question 2)**

How many tobacco products do you use in a day?_____ Singles Packs

CURRENT MEDICATION USAGE

- ☐ Nasal steroid sprays (Flonase, Nasonex, etc) ☐Yes ☐No
- ☐ Nasal antihistamine spray (Astelin, etc) ☐Yes ☐No
- ☐ Oral antihistamines (Allegra, Claritin, Benedryl, etc) ☐Yes ☐No
- ☐ Oral decongestant (Sudafed, etc) ☐Yes ☐No
- ☐ Mucolytic (Mucinex, etc) ☐Yes ☐No
- ☐ Luekotriene (Singulair, etc) ☐Yes ☐No

COMORBID MEDICAL CONDITIONS: Check box and provide details if present

- ☐ Depression history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated
- ☐ Anxiety history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated
- ☐ Obstructive Sleep Apnea: ☐Currently being treated ☐History / No current treatment

- ☐ Allergic rhinitis:_____
- ☐ Previous allergy testing (blood test or skin prick): ☐Yes ☐No
- ☐ Immunotherapy shots for allergies: ☐Yes ☐No ☐Currently
- ☐ Non-allergic rhinitis ☐Yes ☐No
- ☐ Asthma ☐Yes ☐No
- ☐ Chronic rhinosinusitis ☐Yes ☐No
- ☐ Nasal polyps ☐Yes ☐No
- ☐ Viral respiratory infection ☐Yes ☐No
- ☐ Prior ear/sinus surgery ☐Yes ☐No
- ☐ Migraine headache history: ☐Resolved/past diagnosis ☐Present/medicated ☐Present/not medicated

_____

- ☐ Height (ft/in):_____
- ☐ Weight (lbs):_____

Rhinoscopy:

Septal Deviation: None Mild Moderate Severe Nasal valve collapse: None Mild Moderate Severe Bleeding: None Yes
Crusting: None Yes

Otoscopy: Normal Abnormal findings:_____

AIM 3, SINUS PAIN/PRESSURE: Baseline questionnaires

PATIENT QUESTIONS	
How long have you had sinus or facial pain/pressure? <3 months 3-6 months 6-12 months 1-3 year >3 years	
OVER THE LAST WEEK, HOW WOULD YOU RATE YOUR AVERAGE SINUS OR FACIAL PAIN/PRESSURE?	
	None possible **Worst**
Sinus or facial pain/pressure	

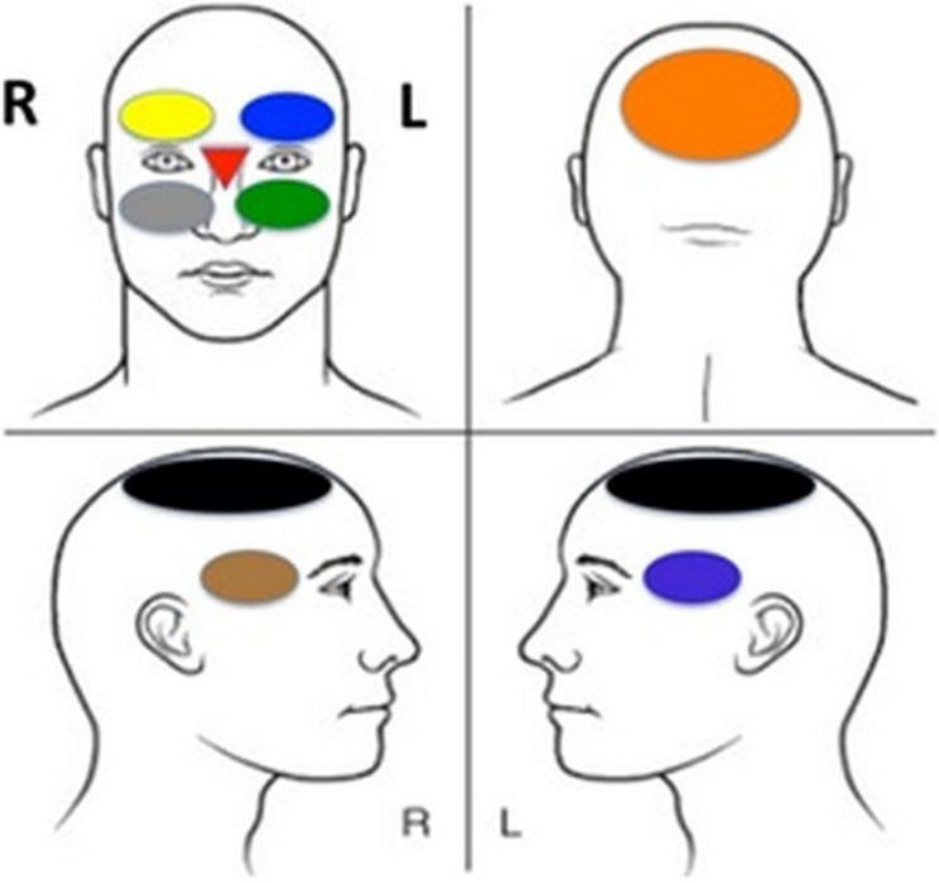
INCLUSION CRITERIA (all must be yes):

Does patient have sinus pain/pressure for ≥ 3mos? Yes No

Is VAS score ≥ 5? Yes No

AT THIS EXACT MOMENT, HOW WOULD YOU RATE YOUR SINUS OR FACIAL PAIN/PRESSURE?	
	None possible — **Worst**
Sinus or facial pain/pressure	◆——————————◆

Place an X over an area where you typically experience sinus or facial pain/pressure (mark all that apply)



BASELINE Brief Pain Inventory-Short Form (BPI-SF)

2. Please rate your pain by circling the one number that best describes your pain at its worst in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

3. Please rate your pain by circling the one number that best describes your pain at its least in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain on average.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

8. Circle the one number that describes how, during the past week, pain has interfered with your:

a. General activity

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

b. Mood

0	1	2	3	4	5	6	7	8	9	10

c. Walking ability

0	1	2	3	4	5	6	7	8	9	10

d. Normal work (includes both outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10

e. Relations with other people

0	1	2	3	4	5	6	7	8	9	10

f. Sleep

0	1	2	3	4	5	6	7	8	9	10

g. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

BASELINE McGill Pain Questionnaire – Short Form (MPQ-SF)

1) The words below describe average pain. Circle the one number that represents the degree to which you feel that type of pain. Please limit yourself to a description of your pain in the **Sinuses or Face**

A. Throbbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
B. Shooting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
C. Stabbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
D. Sharp:	None (0)	Mild (1)	Moderate (2)	Severe (3)
E. Cramping:	None (0)	Mild (1)	Moderate (2)	Severe (3)
F. Gnawing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
G. Hot-Burning:	None (0)	Mild (1)	Moderate (2)	Severe (3)
H. Aching:	None (0)	Mild (1)	Moderate (2)	Severe (3)
I. Heavy:	None (0)	Mild (1)	Moderate (2)	Severe (3)
J. Tender:	None (0)	Mild (1)	Moderate (2)	Severe (3)
K. Splitting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
L. Tiring-Exhausting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
M. Sickening:	None (0)	Mild (1)	Moderate (2)	Severe (3)
N. Fearful:	None (0)	Mild (1)	Moderate (2)	Severe (3)
O. Punishing-Cruel:	None (0)	Mild (1)	Moderate (2)	Severe (3)

2) Please rate your **SINUS or facial** pain by circling the one number that tells how much pain you have **RIGHT NOW**.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

3) Evaluate overall intensity of total pain experience. Please limit yourself to a description of the pain in your **SINUS area or face** only. Place a check mark (✓) in the appropriate column:

Evaluate		
0	No pain	
1	Mild	
2	Discomforting	
3	Distressing	
4	Horrible	
5	Excruciating	

AIM 3, SINUS PAIN/PRESSURE: Immediate (5 minute) Questionnaire

PATIENT QUESTIONS	
AFTER USING THE DEVICE, HOW WOULD YOU RATE YOUR SINUS OR FACIAL PAIN/PRESSURE?	
	None **Worst possible**
Sinus or facial pain/pressure	◆——————————————————◆

AIM 3, SINUS PAIN/PRESSURE: 2 week Questionnaire

PATIENT QUESTIONS	
<u>OVER THE LAST WEEK</u>, HOW WOULD YOU RATE YOUR AVERAGE SINUS OR FACIAL PAIN/PRESSURE?	
	<u>None possible</u> **<u>Worst</u>**
Sinus or facial pain/pressure	◆——————————◆

<u>IMMEDIATELY AFTER USING THE DEVICE</u>, HOW WOULD YOU RATE YOUR SINUS OR FACIAL PAIN/PRESSURE?	
	<u>None possible</u> **<u>Worst</u>**
Sinus or facial pain/pressure	◆——————————◆

2 WEEK: Brief Pain Inventory-Short Form (BPI-SF)

2. Please rate your pain by circling the one number that best describes your pain at its worst in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

3. Please rate your pain by circling the one number that best describes your pain at its least in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain on average.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

8. Circle the one number that describes how, during the past week, pain has interfered with your:

a. General activity

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

b. Mood

0	1	2	3	4	5	6	7	8	9	10

c. Walking ability

0	1	2	3	4	5	6	7	8	9	10

d. Normal work (includes both outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10

e. Relations with other people

0	1	2	3	4	5	6	7	8	9	10

f. Sleep

0	1	2	3	4	5	6	7	8	9	10

g. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

2 WEEK: McGill Pain Questionnaire – Short Form (MPQ-SF)

2) The words below describe average pain. Circle the one number that represents the degree to which you feel that type of pain. Please limit yourself to a description of your pain in the **Sinuses or Face**

A. Throbbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
B. Shooting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
C. Stabbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
D. Sharp:	None (0)	Mild (1)	Moderate (2)	Severe (3)
E. Cramping:	None (0)	Mild (1)	Moderate (2)	Severe (3)
F. Gnawing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
G. Hot-Burning:	None (0)	Mild (1)	Moderate (2)	Severe (3)
H. Aching:	None (0)	Mild (1)	Moderate (2)	Severe (3)
I. Heavy:	None (0)	Mild (1)	Moderate (2)	Severe (3)
J. Tender:	None (0)	Mild (1)	Moderate (2)	Severe (3)
K. Splitting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
L. Tiring-Exhausting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
M. Sickening:	None (0)	Mild (1)	Moderate (2)	Severe (3)
N. Fearful:	None (0)	Mild (1)	Moderate (2)	Severe (3)
O. Punishing-Cruel:	None (0)	Mild (1)	Moderate (2)	Severe (3)

2) Please rate your **SINUS or facial** pain by circling the one number that tells how much pain you have **RIGHT NOW**.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

3) Evaluate overall intensity of total pain experience. Please limit yourself to a description of the pain in your **SINUS area or face** only. Place a check mark (✓) in the appropriate column:

Evaluate		
0	No pain	
1	Mild	
2	Discomforting	
3	Distressing	
4	Horrible	
5	Excruciating	

Week 2 patient satisfaction/safety

How much pain did you experience using device? None Mild Moderate Severe

Bleeding after using device? None Mild Moderate Severe

Would you use device again? Yes No

Would you recommend device to others? Yes No

AIM 3, SINUS PAIN/PRESSURE: 4 week Questionnaire

PATIENT QUESTIONS	
<u>OVER THE LAST WEEK</u>, HOW WOULD YOU RATE YOUR AVERAGE SINUS OR FACIAL PAIN/PRESSURE?	
	<u>None possible</u> **<u>Worst</u>**
Sinus or facial pain/pressure	◆——————————◆

<u>IMMEDIATELY AFTER USING THE DEVICE</u>, HOW WOULD YOU RATE YOUR SINUS OR FACIAL PAIN/PRESSURE?	
	<u>None possible</u> **<u>Worst</u>**
Sinus or facial pain/pressure	◆——————————◆

4 WEEK: Brief Pain Inventory-Short Form (BPI-SF)

2. Please rate your pain by circling the one number that best describes your pain at its worst in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

3. Please rate your pain by circling the one number that best describes your pain at its least in the last week.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain on average.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

5. Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No pain										Pain as bad as you can imagine

8. Circle the one number that describes how, during the past week, pain has interfered with your:

a. General activity

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

b. Mood

0	1	2	3	4	5	6	7	8	9	10

c. Walking ability

0	1	2	3	4	5	6	7	8	9	10

d. Normal work (includes both outside the home and housework)

0	1	2	3	4	5	6	7	8	9	10

e. Relations with other people

0	1	2	3	4	5	6	7	8	9	10

f. Sleep

0	1	2	3	4	5	6	7	8	9	10

g. Enjoyment of life

0	1	2	3	4	5	6	7	8	9	10
Does not interfere										*Completely interferes*

4 WEEK: McGill Pain Questionnaire – Short Form (MPQ-SF)

3) The words below describe average pain. Circle the one number that represents the degree to which you feel that type of pain. Please limit yourself to a description of your pain in the **Sinuses or Face**

A. Throbbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
B. Shooting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
C. Stabbing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
D. Sharp:	None (0)	Mild (1)	Moderate (2)	Severe (3)
E. Cramping:	None (0)	Mild (1)	Moderate (2)	Severe (3)
F. Gnawing:	None (0)	Mild (1)	Moderate (2)	Severe (3)
G. Hot-Burning:	None (0)	Mild (1)	Moderate (2)	Severe (3)
H. Aching:	None (0)	Mild (1)	Moderate (2)	Severe (3)
I. Heavy:	None (0)	Mild (1)	Moderate (2)	Severe (3)
J. Tender:	None (0)	Mild (1)	Moderate (2)	Severe (3)
K. Splitting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
L. Tiring-Exhausting:	None (0)	Mild (1)	Moderate (2)	Severe (3)
M. Sickening:	None (0)	Mild (1)	Moderate (2)	Severe (3)
N. Fearful:	None (0)	Mild (1)	Moderate (2)	Severe (3)
O. Punishing-Cruel:	None (0)	Mild (1)	Moderate (2)	Severe (3)

2) Please rate your **SINUS or facial** pain by circling the one number that tells how much pain you have **RIGHT NOW**.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

3) Evaluate overall intensity of total pain experience. Please limit yourself to a description of the pain in your **SINUS area or face** only. Place a check mark (✓) in the appropriate column:

Evaluate		
0	No pain	
1	Mild	
2	Discomforting	
3	Distressing	
4	Horrible	
5	Excruciating	

Week 4 patient satisfaction/safety

How much pain did you experience using device? None Mild Moderate Severe

Bleeding after using device? None Mild Moderate Severe

Would you use device again? Yes No

Would you recommend device to others? Yes No