Utilization of a Microcurrent Device for Postoperative Pain Following Functional Endoscopic Sinus Surgery: a Randomized Controlled Trial
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Protocol Title:	Utilization of a microcurrent device for postoperative pain following functional endoscopic sinus surgery: a randomized controlled trial
Principal Investigator:	Alfred Iloreta, MD
Sponsor:	Icahn School of Medicine at Mount Sinai
Study ID:	21-01392
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Revision Date:	16-Feb-2023

Revision	Date	Description of Change
V0.1		Initial release
V0.2	8.27.2021	Draft Finalized protocol for IRB submission
V0.3	9.16.2021	Updated with ISMMS/Sponsor language
V0.4	9.20.2021	Updated with Data Ownership and Publication Agreement
V0.5	10.27.2021	Updated inclusion/exclusion criteria
V0.6	11.5.2021	Updated inclusion/exclusion criteria
V0.7	1.10.2022	Updated inclusion/exclusion criteria
V0.8	3.29.2022	Added incentive for study completion
V0.9	4.5.2022	Updated consent section to allow for e-consenting
V1.0	2.3.2023	The rationale for the study Modification: to Expand and capture other patients seen by providers at the same FPA who qualify for functional nasal and endoscopic sinus surgery, in an effort to accelerate recruitment and enrollment to meet study end date in 10/31/2023. 1) Changing final inclusion criteria to VAS >0 postop (instead of Postop pain VAS ≥ 5 in PACU).

		Justification: We are aiming to include participants who can benefit from the treatment to reduce postoperative pain at home and have seen that there is a time lag in pain which potentially increases after discharge. Therefore, we are amending the final inclusion criteria from Postop pain VAS ≥ 5 in PACU, where analgesia can still be in effect, to VAS >0 postop which will better capture the population of interest. 2) Revising the subject demographics questionnaire Justification: We have added 'Procedure to be Performed, Physician performing procedure, Tissue to be Operated On and Additional procedure details (such as splints, etc.)' to the demographic form to capture additional information that will allow us to segment results of the primary endpoint of acute change in peak postoperative pain 3) Updated Post-op timelines day 7 and day 14 to allow follow-up up to 21 post-surgeries to accommodate change in patient and clinic scheduling that occur for varying reasons 4) Updated Study Population to expand scope to include patients electing for functional nasal surgery, common among patients requiring functional rhinoplasty or reconstructive surgery 5) Rephrasing Compensation language
V1.1	1.17.2024	Increased recruitment numbers from 100 to 130. Justification: due to high drop-out rate post randomization; there is the need to increase the recruitment numbers to reach the target of 60 completed participants.

STUDY SUMMARY:

Title	Utilization of a microcurrent device for postoperative pain following functional endoscopic sinus surgery: a randomized controlled trial
Purpose	The purpose of this study is to investigate whether daily use of a microcurrent neuromodulation device will decrease the pain experienced by patients in the days following functional nasal andsinus surgery , including pain during postoperative debridement following Endoscopic sinus surgery
Study Design and Duration	A prospective randomized controlled study of 60 recruited subjects undergoing functional nasal or sinus surgery. Enrolled subjects will be randomized (1:1) to receive either an active neuromodulation study device or a sham device that appears identical to the active device while emitting no therapeutic microcurrent. Subjects will self-treat with the device at home and will be followed for a minimum of 2 weeks after surgery up to 21 days post-surgery.
Target Subject Population	60 subjects undergoing functional nasal or sinus surgery
Subject Inclusion Criteria	• Scheduled for FESS or Functional Rhinoplasty • Possessing an American Society of Anesthesiologists physical status classification of I or II • Age ≥ 18 • Possess the capacity to give informed consent • Able to read write and understand English or Spanish • Able to attend follow up visits at postop Visit 1 (within 0 – day 14) and post-op Visit 2 (within 10 – 21 days) • Postop pain VAS > 0 in PACU phase II
Subject Exclusion Criteria	• Does not meet inclusion criteria • History of chronic pain • Experiencing chronic pain requiring opioids at baseline and/or who are under the care of pain management specialists • Seizure disorders • Undergoing planned or unplanned additional procedures at the time of surgery • Planned procedure involves nerve cryoablation • In custody of the state • Prisoners • Known to be pregnant • Implanted cranial metallic components or devices including deep brain stimulators or cochlear implants • Has an implanted or external worn cardiac device including pacemakers, automated implantable cardioverter defribrillator (AICD), or any other cardiac electric devices (including non-implanted devices, e.g. defibrillator vest)

Study Endpoints	• Analgesic Efficacy • Safety
Investigator	Alfred-Marc Iloreta, Jr. MD 234 East 85th Street 4th Floor New York, NY 10028
Industry Collaborator	Tivic Health Systems 750 Menlo Ave, #200 Menlo Park, CA 94025 Contact: Blake.gurfein@tivichealth.com 5615737652

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1. BACKGROUND AND RATIONALE

The opioid epidemic is driven by opioid misuse, addiction, and overdose. 10.3 million people misused prescription opioids in 2018[1]. There are over 1 million sinus surgeries in US every year and the majority of sinus surgery patients are given opioid medications to treat postoperative pain. Otolaryngologists have become more vigilant in their prescription practices, however, non-opioid pain management solutions are needed to further reduce dependence on opioid drugs. Strategies to avoid or minimize opioid consumption while effectively managing patient pain are of the utmost importance. Furthermore, patient apprehension over the pain experienced during postoperative debridements often negatively impacts patient adherence to postoperative visits. Several non-opioid alternative medications have proven efficacious in postoperative pain management following a variety of otolaryngology surgeries. Non-medication alternatives, such as pain management devices, remain uncharted territory. Tivic Health previously developed and received FDA clearance for ClearUP Sinus Pain Relief, a non-invasive microcurrent emitting device applied to the face. ClearUP was found to be safe and highly effective at reducing facial pain. In the current study, we use the same form factor for ClearUP with minor modifications to the waveform emitted by the device to assess its feasibility for use at home in treating post-operative pain after sinus surgery. The microcurrent study device has yielded auspicious results in a pilot studies examining its ability to reduce postoperative pain following functional endoscopic sinus surgery (FESS). We hypothesize that daily use of the self-administered, handheld, microcurrent study device will reduce patients' pain levels following functional nasal or sinus surgery, thereby lowering the need for analgesic medications.

1. https://www.cdc.gov/drugoverdose/featured-topics/abuse-prevention-awareness.html

2. DESCRIPTION OF THE STUDY DEVICE

The study device is a handheld micro-current TENS emitter intended to be used for the relief of postoperative pain after functional nasal or sinus surgery. The device uses an average current that is several orders of magnitude smaller than that of TENS devices used in the facial area. The design of the study device was optimized to provide transcutaneous nerve stimulation to the regional areas associated with the sinuses.

The pear-shaped device is held in the hand, with the rounded tip of the device applied to the facial skin in the region of skin overlying the sinus passages for 5 minutes per treatment. The tip is the active electrode of a monopolar design. The housing of the device serves as the return electrode. The hand holding the device completes the electrical path.

When the user turns the device on and presses the tip to the skin, the device lights up and initiates a low-frequency, pulsed AC circuit that is maintained at a constant current. The device uses the current to calculate the impedance in the path between the tissue at the tip and the hand in contact with the device. If the calculated impedance is above an impedance threshold, the device is in "Detection" mode. Conversely, when the impedance falls below the impedance threshold, the device enters a "Treatment"

mode. The impedance threshold is calculated dynamically by an adaptive algorithm that incorporates the measured parameters of the individual user.

The user is instructed to glide the tip of the device along the skin along the cheek, nose and under brow bone. When a low-impedance point is detected, the device signals the user via a slight haptic (vibration) feedback. The user is instructed to hold the device in place until the Treatment period has passed as indicated by cessation of the haptic indicator.

Once the Treatment period ends, the device resets to Detection mode. The user is instructed to glide the device along an indicated path until reaching the next low-impedance area.

The user may adjust the current setting of the device (low, medium, high) if they prefer more or less current intensity. The default setting for the device is low.

The study device emits a 14.7 Hz frequency and has previously shown to be safe and well-tolerated in an IRB-approved 4 person pilot feasibility study. The study device is configured to emit alternating current in the microampere range, significantly less energy than has been safely used in TENS treatment of the face for pain [1-3].

1. Hansson, P., & Ekblom, A. (1983). Transcutaneous electrical nerve stimulation (TENS) as compared to placebo TENS for the relief of acute oro-facial pain. *Pain*, *15*(1-4), 157-165.

2. Hansson, P., Ekblom, A., Thomsson, M., & Fjellner, B. (1986). Influence of naloxone on relief of acute oro-facial pain by transcutaneous electrical nerve stimulation (TENS) or vibration. *Pain*, *24*(3), 323-329.

3. Bremerich, Andreas, et al. "Transcutaneous electric nerve stimulation (TENS) in the therapy of chronic facial pain: Preliminary report." *Journal of Cranio-Maxillofacial Surgery* 16 (1988): 379-381.

The sham device appears and operates identically to the active device, including indicator lights and haptic vibration, however it emits a weak direct current that is non-therapeutic.

- **INDICATIONS FOR USE**

The study device is being evaluated for use in the treatment of postoperative pain after functional nasal or sinus surgery.

- **STUDY OBJECTIVES**

The purpose of this study is to investigate whether daily use of a microcurrent study device will decrease the pain experienced by patients in the days following functional nasal or sinus surgery, including during postoperative debridements.

- **STUDY DESIGN**

A prospective randomized controlled study of 60 recruited subjects undergoing functional nasal or sinus surgery. Enrolled subjects will be randomized (1:1) to receive either an active neuromodulation study device or a sham device that appears identical to the active device while emitting no therapeutic microcurrent. Subjects will self-treat with the device after surgery while in the PACU Phase II and at home for a minimum of two weeks. Study visits will include enrollment, the day of the surgical procedure, and two postoperative debridement visits both to be completed at the end of day 21 post-op. Subjects will record data on pain, medication use, and congestion symptoms at home. At the second postop study visit, the study device will be returned and subjects will complete questionnaires related to sinonasal symptoms and user experience.

Study Flow & Data Collection

Study Participant Timeline

T = Enrollment Visit	• Confirm eligibility and obtain informed consent • Patient demographics • SNOT22 and NOSE scores • Instruct patient in use of device
T = 0 days	• Date of Surgery. • Participant screened for study inclusion based on post-operative pain score. • Participant instructed in use of study device. • Use of device and measurement of pre and post pain level
T = 1-14 days	• Participant uses study device and records pain before and after usage in pain diary • Participant records medication usage in medication diary
T = 6-14 days	• Participant seen for their regularly scheduled post-operative visit #1 • Device usage before and after debridement (applicable to FESS patients)
T = 0 -21 days	• Participant continues to use study device and record pain diary and medication diary
T = 12 – 21 days	• Participant seen for their regularly scheduled post-operative visit #2 • Device usage before and after debridement (applicable to FESS patients) • Termination of participation in study protocol. Collection of study device • Patient completes user experience survey

Enrollment Visit (Clinic)

- Confirm eligibility & consent
- Subject Demographics
- Nasal Obstruction Symptom Evaluation
- Sino-Nasal Outcome Test 22
- Device and study protocol training

Postop Day 0 Visit (PACU Phase II)

- Confirm postoperative pain VAS > 0

- Collect VAS before and after first study device use

Postop Day 0-21 (At Home)

- Record VAS before and after study device use (before, 10 mins, 2 hours, 4 hours)
- Record medication use daily

Postop Visit 1 (V1) (Clinic)

- Complete Nasal Obstruction Symptom Evaluation
- Record VAS before and after study device use, during debridement, after debridement (applicable to FESS patients)

Postop - Visit 2 (V2) (Clinic)

- Complete Nasal Obstruction Symptom Evaluation
- Complete Sino-Nasal Outcome Test 22
- Record VAS before and after study device use, during debridement, after debridement (applicable to FESS patients)
- Return device
- User Experience Questionnaire

- **SUBJECT POPULATION**

It is anticipated that 130 subjects will be recruited to achieve a sample size of 60 participants, accounting for potential drop-outs and/or screen failures. Any subject that meets all the inclusion and none of the exclusion criteria may be eligible to participate in the study.

- **INCLUSION/EXCLUSION CRITERIA**

All subjects meeting the following inclusion criteria will be eligible to participate in this study.

Inclusion Criteria

- Scheduled for functional nasal or sinus surgery
- Possessing an American Society of Anesthesiologists physical status classification of I or II
- Age ≥ 18
- Possess the capacity to give informed consent
- Able to read write and understand English or Spanish
- Able to attend follow up visits at postop Visits 1 and 2
- Postop pain VAS >0 in PACU phase II

Exclusion Criteria

- Does not meet inclusion criteria
- History of chronic pain
- Experiencing chronic pain requiring opioids at baseline and/or who are under the care of pain management specialists
- Seizure disorders
- Undergoing planned or unplanned additional procedures at the time of surgery

- Planned procedure involved nerve cryoablation
- In custody of the state
- Prisoners
- Known to be pregnant
- Implanted cranial metallic components or devices including deep brain stimulators or cochlear implants
- Has an implanted or external worn cardiac device including pacemakers, automated implantable cardioverter defribrillator (AICD), or any other cardiac electric devices (including non-implanted devices, e.g. defibrillator vest)

- **STUDY PROCEDURES**

All study procedures involving subject participation will be conducted according to good clinical practices (GCP) and in compliance with the principles enunciated in the Declaration of Helsinki. All study procedures will be performed at an Investigational Site, under the direction of an Investigator or designee, and at which this protocol will be approved by:

Icahn School of Medicine IRB
1 Gustave L. Levy Place
New York, NY 10029

- **Subject Screening**

Subjects with a planned functional nasal or sinus surgery will be recruited with the recommendation of the attending physician during their preoperative office visit. The attending physician or research personnel will determine if the subject meets inclusion criteria and does not meet exclusion criteria during their routine preoperative visit (with the exception of postop pain).

- **Randomization**

Eligible subjects that elect to enroll will be randomized via block randomization and assigned to either active or sham study device groups.

- **Blinding**

The study will be double-blind – neither the investigators nor the study subjects will know which group is receiving active or sham treatment. Unblinding will occur after all data has been collected for all study subjects.

- **Study procedure**

Patients undergoing standard functional nasal or sinus surgery will be recruited with the recommendation of the attending physician during their preoperative office visit. The attending physician or research personnel will determine if the subject meets inclusion criteria and does not meet exclusion criteria during their routine preoperative visit (with the exception of postop pain). If the patient elects to enroll in the study, the following data will be collected from their medical record:

- Basic demographic information: age, sex, insurance status, race and ethnicity
- Medical history: history of opioid use or chronic pain, medication list, allergies, preoperative pain level, other past medical history

In their final preoperative visit, subjects will complete the Sinonasal Outcome Test 22 (SNOT22) and a modified version of the Nasal Obstruction Symptom Evaluation (NOSE). Patients will be instructed by study staff on how to correctly self-administer the device to the periorbital skin. Subjects will be randomized in a 1:1 fashion to one of two groups and given either an active study device or a sham device that appears identical to the active device while emitting no therapeutic microcurrent. These devices will be labeled “A” or “B” depending on the group randomization. Both groups will be instructed to use the device on postoperative days 0-21 and sent home with instructions.

On the day of surgery, standard total intravenous anesthesia (TIVA) will be administered for each enrolled subject. Standard TIVA is as follows: anesthetic induction will be performed using propofol 1.5-2.5 mg/kg and remifentanil 2-5 mcg/kg, with neuromuscular blockade used to facilitate endotracheal intubation only if deemed necessary by the anesthesiologist placing the endotracheal tube (ETT). Anesthesia will be maintained using propofol 30-50 mcg/kg/min, remifentanil 0.05-0.5 mcg/kg/min and nitrous oxide 50-70% titrated based on hemodynamics to maintain a mean arterial pressure of 60-70 mmHg. Each subject will receive the standard dose of 10 mg intravenous dexamethasone prior to the start of surgery, and 4 mg ondansetron prior to emergence. Vital signs, anesthetic technique (i.e., bolus and infusion drug totals, end tidal gas concentrations, narrative comments), and inputs and outputs for the case will be recorded to control hemodynamic differences between subjects. No new imaging will be obtained as part of the study. In PACU phase II, subjects will report their visual analog scale (VAS) for pain to confirm eligibility for the study. Subjects will complete their first study device treatment in the PACU phase II and study staff will record their VAS for pain before treatment and 10 minutes and 1 hour after treatment. Subjects will be instructed to record their VAS for pain at 2 hours and 4 hours after treatment at home.

The day after surgery, subjects will be reminded by staff members via phone to self-administer the treatment with the device. Subjects will glide the device over the periorbital skin for 2.5 minutes per side of the face (five minutes total) three times every 24 hours for up to V2 or 21 days post-op, whichever comes sooner with additional administrations as needed. When in pain, subjects will be instructed to use the device and wait ten minutes before using oxycodone 5 mg or acetaminophen 325 mg as rescue pain medication if needed. Subjects will complete a daily pain diary (either paper or online via REDCap) documenting their pain on a visual analog scale of 0-10 before and 10 minutes, 1 hour, 2 hour, 4 hours after treatment. Subjects will also record the time and dose of all medications used (either paper or online via REDCap). The questions asked are as follows:

- How many times did you administer the device today?
- How many acetaminophen 325 mg have you taken in the last 24 hours?
- How many oxycodone 5 mg have you taken in the last 24 hours?

- Were you able to complete your daily work activities?
- Were you able to complete your daily non-work activities?

Subjects will return to clinic for their first two postoperative visits o . On postoperative V1 and V2 subjects will complete a modified version of the NOSE questionnaire to quantify changes in congestion and nasal obstruction. Post-op V2 subjects will complete the SNOT-22 to capture other sinonasal symptoms. For patients undergoing debridement, upon arriving in clinic, subjects will be instructed to record their current pain level via VAS in their pain diary before and after they self-administer treatment with the study device. They will subsequently record their pain levels during and after the debridement. During the second postop visit, subjects will be asked to complete a user experience questionnaire assessing their satisfaction with the study device and safety/tolerability.

- **Data analysis**

All data will be tabulated. The difference between the symptom scores before and after treatment will be computed for each individual in the study. Differences in change scores will be compared across treatment groups.

An appropriate two-sided statistical test (paired t-test or repeated measure ANOVA) will be used to assess the pre and post differences in symptom severity.

- **STUDY ENDPOINTS**

This study is intended to assess the analgesic efficacy and safety of the study device after functional nasal or sinus surgery. The primary endpoint is the acute change in peak postoperative pain score 10 minutes after treatment.

Auxiliary outcomes include:

- Pain at 1 hour, 2 hours, 4 hours after device treatment
- Pain before, during, and after debridement (applicable to FESS patients)
- Postoperative debridement compliance (applicable to FESS patients)
- Self-report of congestion and nasal obstruction severity
- Total opioid and/or acetaminophen consumption (the former calculated in oral morphine equivalents)
- Patient satisfaction
- Safety and tolerability
- Direct and indirect cost of pain management as calculated by total medications used and number of days missed from usual daily activity
- Utilization of additional healthcare resources (including telephone encounters and visits to any healthcare provider regarding postoperative pain)

- **INDUSTRY COLLABORATOR AND INVESTIGATOR OBLIGATIONS**

  - **IRB Review/Approval/Reporting**

The final protocol and Informed Consent for this study will be reviewed and approved by the appropriate duly constituted Institutional Review Board (IRB) prior to the enrollment of subjects into the study. It is the responsibility of the Investigator to assure that all aspects of the institutional review are conducted in accordance with current United States Food and Drug Administration (FDA) regulations. The Industry Collaborator must receive a letter documenting the IRB approval that specifically identifies the protocol by title, prior to initiation of the study.

After the completion or termination of the study, the Investigator will submit a final report to the IRB and to the Industry Collaborator.

  - **Informed Consent**

It is the responsibility of the Investigator to assure that Informed Consent is obtained from each subject in accordance with current regulations. The content of the Informed Consent should conform to current ICH and FDA guidelines for the protection of human subjects, and/or to the specific IRB requirements.

The Informed Consent form must be in English, signed and dated by the subject and Investigator or designee.

Each subject will be given verbal and written information describing the nature and duration of the study. This shall take place under conditions where the subject has adequate time to consider the risks associated with his/her participation in the study. All subjects' questions must be answered adequately to ensure that they have the information they require to make an informed decision about participation in the study. Informed consent may be obtained from patients either in-person or via the eConsent framework provided by RedCAP. In the case of eConsent, study staff will set-up a phone call with the potential subject in order to explain the study, elicit feedback and understanding from the patient, and answer any outstanding questions. The signed Informed Consent form will be filed in a study file along with all study forms.

Subjects must not be tested until they sign an Informed Consent form.

  - **Study Discontinuation and Closure**

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants and the investigators. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

- **Confidentiality and Privacy**

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

Authorized representatives of the Institutional Review Board (IRB) may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at the clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB or Institutional policies.

- **Data Retention**

The Investigator will maintain adequate records for the study including the Subject Demographics log, Data Collection sheets, Informed Consent forms, information regarding discontinued subjects, and other pertinent data.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored on the password protected, encrypted Mount Sinai network, and/or HIPAA compliant REDCap database. Hard copies of study records will be maintained in a locked cabinet within the Department of Otolaryngology, accessible only to the PI and study team members. Participant's

identifiable information will be stored separately and linked to the research data through the use of a unique study identification number. At the end of the study, all study databases will be de-identified and stored for up to 6 years following the completion of the study.

The original study record will consist of:

- Subject Demographics Questionnaire
- Pain Data Sheet(s)
- Debridement Pain Data Sheet
- Medication Data Sheet(s)
- NOSE Data Sheet (Enrollment, Postop V1, Postop V2)
- SNOT22 Data Sheet (Enrollment, Postop V2)
- User Experience Questionnaire

Original study records will be filled out manually by study staff and the study patient, where applicable. If an entry requires change, the correction will be made as follows:

- Draw a single line through the incorrect entry.
- Enter data, date, and initial the change ("white-out", erasure, or any form of obliteration of data is not permitted under any circumstances).

All fields must be completed in study records. Blank responses will not be interpreted as "none" or "N/A". If data are not available, a straight line should be drawn through all applicable fields and unused pages, dated and initialed to indicate there was no omission.

After completion of the study, the Investigator will provide the Industry Collaborator with deidentified digital copies of study databases and the original study record.

- **Protocol Deviations/Amendments**

The Investigator shall not deviate from the protocol without documented approval from the Industry Collaborator. Any significant changes or deviations in the protocol will be made as an amendment to the protocol and must be approved in writing by the IRB and by the Industry Collaborator prior to being implemented. Unless the Industry Collaborator has consented to any such deviation or change in writing, the Industry Collaborator will not assume any resulting responsibility or liability.

Amendments to the protocol will be subject to the same requirements as the original protocol, with the exception of administrative amendments. The Industry Collaborator will submit a protocol amendment via the Investigator to the IRB for any change in the protocol that significantly affects the safety of subjects or scope of the investigation.

Administrative amendments may be made by mutual agreement between the Investigator and the Industry Collaborator and will be documented in writing with copies to both the Investigator and the Industry Collaborator.

- **Study Monitoring**

The individual(s) at the Icahn School of Medicine at Mount Sinai (ISMMS) who will be responsible for data and safety monitoring of this study.

ISMMS Principal Monitor:

Principal Investigator

Last Name: Iloreta

First Name: Alfred-Marc

Academic Title: Assistant Professor

Department: Otolaryngology

Mailing Address: 1 Gustave L Levy Place

10th Floor

New York, NY 10020

Phone: Office 212-241-9410

E-mail: Alfred-Marc.Iloreta@mountsinai.org

Dr. Iloreta will be the principal monitor for this study. The majority of study patients will be under his care. He will be best positioned to assess and respond to any adverse events that are reported.

Safety and data information will be reviewed by the monitors every 6 months.

Data will be recorded in patient binders and secure Mount Sinai network drive folder and REDCap database, ensuring completeness and accuracy through redundancy. Data will also be checked at set intervals by the study team.

If temporary or permanent suspension of the study occurs, the occurrence will be reported to the IRB.

- **Adherence to the Protocol**

Except for an emergency situation in which proper care for the protection, safety, and well-being of the study patient requires alternative treatment, the study shall be conducted exactly as described in the approved protocol.

- **Emergency Modifications**

Investigators may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard(s) to trial subjects without prior IRB approval.

- **Other Reportable New Information and Protocol Deviations/Violations**

In accordance with local IRB requirements, the following information must be reported within five (5) business days.

- Non-compliance with federal regulations governing human research or with the requirements or determinations of the IRB, or an allegation of such non-compliance
- Failure to follow the protocol due to the action or inaction of the investigator or research staff.
- Breach of confidentiality
- Premature suspension or termination of the research by the sponsor or investigator.

- **Adverse Event Reporting**

A significant adverse event (SAE) is one that has a serious adverse effect on the health or safety of a subject or causes any life-threatening problem or death of the study subject.

All SAEs should be recorded by the Investigator and reported by the Investigator to the Industry Collaborator and to the IRB the next business day after the Investigator becomes aware of the SAE.

The Investigator will collect adverse effects information and will report serious and unanticipated adverse effects to the Industry Collaborator and IRB. The Investigator will terminate the study within five working days if the Investigator and Industry Collaborator determine that the adverse system effects present an unreasonable risk to subjects (21 CFR 812.46(b) (2)).

An adverse event (AE) during a clinical evaluation is “any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.” It is not dependent on whether the event is considered to be related to the investigational product or the study. An adverse event includes events not seen at the beginning of the study or worsened if present at the beginning.

All AEs observed by the Investigator or reported by the subject will be documented (including all symptoms) and included in the study file.

- **Potential Benefits**

There is no guaranteed benefit to a subject for participation in this study.

- **COST**

There will be no additional charge to subjects for any study procedures.

- **COMPENSATION**

Subjects will be given compensation for participation.in the form of an electronic -gift card sent via their email upon successful completion of the study procedures and return of the device

- **STUDY QUALITY CONTROL AND QUALITY ASSURANCE**

- **Site Training**

The Investigator is required to attend an Industry Collaborator's training session which will be conducted at a site initiation visit or other appropriate training sessions. Training will include, but not be limited to the procedures with which to address subjects, the protocol plan, the completion of the various forms and the responsibilities of study staff. All Investigators or study staff that are trained must sign a Staff Training log. No Investigator or study staff will perform any study-related procedures prior to being trained and prior to signing a Staff Training log.

At the initiation of the study, the Industry Collaborator or designee will visit the site where the study is conducted. The Industry Collaborator will ensure that clinical study staff are informed and understand the clinical study requirements.

- **Compliance to Standards and Regulations**

The Principal Investigator is responsible for obtaining and reviewing copies of IRB approvals, and ensuring that the study is conducted in compliance with the protocol, Code of Federal Regulations, the Declaration of Helsinki and applicable local regulatory requirements, ensuring proper clinical site monitoring and ensuring subject informed consent is obtained.

The Investigator shall ensure that all work and services described herein shall be conducted in accordance with the highest standards of medical and clinical research practice. The Investigator will provide copies of the protocol to all co-Investigators or other staff responsible for study conduct.

The Investigator shall ensure that all serious adverse events will be reported to the Institutional Review Board and Industry Collaborator within 24 hours.

Regulatory documentation includes those documents that must be submitted, reviewed and approved by the Institutional Review Board before subject enrollment can begin at the clinical site. These documents function to demonstrate compliance of the Investigator and Industry Collaborator with regulatory requirements.

- **Quality Assurance Audit**

In the event that an Investigator is contacted by a Regulatory Agency in relation to this study, the Investigator will notify the Industry Collaborator immediately. The Investigator or his designee must be available to respond to reasonable requests and audit queries made during an audit process. The Investigator must provide the Industry Collaborator with copies of all correspondence that may affect the review of the current study (e.g., Form FDA 483, Inspectional Observations, and warning letters).

- **PUBLICATION POLICY**

The data and results from this study will be co-owned by the Investigator and the Industry Collaborator. The Investigator is free to communicate and/or publish with respect to the Study being conducted hereunder with prior approval of Industry Collaborator. The Investigator agrees to submit to Industry Collaborator the proposed publication at least thirty (30) days prior to the submission thereof for publication. The purpose for such prior submission is to identify any Confidential Information to be deleted from the proposed publication and to solicit collaborative feedback on the manuscript. At the end of the thirty (30) day period, the Investigator shall be free to proceed with publication if consent from the Industry Collaborator has been granted. The Investigator and Industry Collaborator are bound by the terms outlined within the Investigator-Initiated Clinical Trial Agreement.

- **ClinicalTrials.org Registration**

The Investigator will register **st**udy with the https://www.Clinicaltrials.gov website, a public clinical trials **registry**, in accordance with applicable laws and regulations**.** A description of this study and summary of the results of this study will be included on this website. This Web site will not include patient identifiable information.

- **CONFIDENTIALITY**

Neither the Investigator nor the Industry Collaborator will release the subject's private and personal information.

This study protocol, documentation data, and all other information generated, will be held in strict confidence by the Investigator and their representatives. No information concerning the study or the data will be released to any unauthorized third party without prior written approval by the Industry Collaborator.

No subject names, medical record numbers, or other personally identifying information will be used as part of the study. Data Collection forms will not contain confidential information linking the outcome result to a subject. Only the study site will have the information that links a subject to his/her identifying information. Subjects will only be referred to by using their unique Subject ID number.