# Cochlear Promontory Stimulation for Treatment of Tinnitus: Towards Developing an Implantable Device

NCT03759834

13September2022

# COCHLEAR PROMONTORY STIMULATION FOR TREATMENT OF TINNITUS: TOWARDS DEVELOPING AN IMPLANTABLE DEVICE


Principal Investigators:

*Matthew L. Carlson[1], MD*

Co – Investigators:

*E. Matthew Hoffman[3], DO, PhD; Nicole M. Tombers[1], RN, CCRP; Jeffrey P. Staab[4], MD; Amy M. Tuchscherer[1], CCRC; Ashlee P Kirtz[1]; Melissa D. DeJong[2], AuD; Jill M. Gruenwald[2], AuD; Corey A. Stoelb[2], AuD; Kaitlyn E. Caceres[2], AuD; John P. Marinelli[1], MD*

Institutional affiliations:

[1]Department of Otorhinolaryngology, Mayo Clinic, Rochester, MN, U.S.A..; [2]Division of Audiology, Mayo Clinic, Rochester, MN, U.S.A.; [3]Department of Neurology, Mayo Clinic, Rochester, MN, U.S.A; [4]Department of Psychiatry, Mayo Clinic, Rochester, MN, U.S.A.





Version 23
September 13, 2022

**TABLE OF CONTENTS**

# STUDY SUMMARY

Title: Cochlear Promontory Stimulation for Treatment of Tinnitus: Towards Developing an Implantable Device

IRB Protocol Number: 17-004832

Methodology: Prospective, investigational

Target subject accrual: 100

Expected duration of study: 10 years

Subject participation duration: 4 days [3 sequential clinic visits scheduled 7 days (+14/- 2 days) apart with a 3 month follow up visit]

Primary Objective: Use of a cochlear promontory stimulation electrode to provide safe, short term relief of tinnitus.

Secondary Objective: Map the optimum regions of the cochlear promontory in planning for an implantable electrical device for long term tinnitus suppression.

Principal Investigator: Matthew L. Carlson, MD

# 1 BACKGROUND

Tinnitus is the perception of sound when no external noise is present. The exact mechanism(s) underlying the development and maintenance of tinnitus remains largely unknown. The Center for Disease Control (CDC) estimates over 50 million — nearly 15% of the general public — experience some form of tinnitus [9]. Roughly 20 million people struggle with burdensome chronic tinnitus, with 2 million experiencing extreme and debilitating symptoms [9].

Currently, there are no Food and Drug Administration (FDA) approved pharmacological therapies or surgical devices available for the treatment of tinnitus. The 2014 Clinical Practice Guideline on tinnitus from the American Academy of Otolaryngology – Head and Neck Surgery summarized the existing state of tinnitus management by stating “A cure for primary tinnitus does not yet exist, and despite claims to the contrary, no method has been proven to provide long-term suppression of tinnitus.” Existing treatment methods largely focus on counseling, cognitive behavioral therapy, masking, and sound therapy for habituation – strategies that may render tinnitus more tolerable, but do not abolish the symptom.

To date, the preponderance of research evaluating the feasibility of electrical stimulation for suppression of tinnitus comes from studies examining cochlear implantation and promontory stimulation [7]. Cochlear implantation is currently the gold standard for rehabilitation of severe to profound sensorineural hearing loss and a demonstrated byproduct of cochlear implant electrical stimulation is tinnitus suppression. A recent review of the literature evaluating the efficacy of cochlear implantation for treatment of tinnitus in patients with single-sided deafness reveals that tinnitus is improved in 82% to 100% of implantees, abolished in 14% to 100% of implantees and none of the studies reported worsening of tinnitus during device use [10]. Despite these promising findings, cochlear implantation cannot be feasibly applied to patients with normal to moderate hearing loss, which comprises the majority of the population with tinnitus, since placement of an *intracochlear* electrode commonly results in significant hearing loss or deafness.

Promontory stimulation is an established otologic procedure that was initially developed as a diagnostic tool to assess patient candidacy for cochlear implantation. Promontory stimulation is most commonly performed in the outpatient setting on an awake patient by placing a single insulated probe through a topically anesthetized tympanic membrane and applying monopolar current for several seconds to minutes. The safety and efficacy of *transtympanic* promontory stimulation for the temporary relief of tinnitus in patients with normal hearing and varying degrees of hearing loss has recently been evaluated [3]. Overall, the literature supports that 45% to 86% of subjects gain significant or complete suppression of tinnitus according to different measures and varying stimulation parameters. Furthermore, in most cases, electrical stimulation can be successfully administered with either no perception or only transient and minimal perception [4]. When evaluating the efficacy of tinnitus suppression according to underlying etiology, it has been found that patients with acoustic trauma or noise-induced hearing loss had the highest success rates of tinnitus suppression compared to other etiologies such as presbycusis or Ménière's disease [5]. However, most patients only experience tinnitus suppression during and shortly after active electrical stimulation, with a smaller subset enjoying

residual inhibition for hours to days after treatment [5-6]. Thus, while successful at providing temporary reprieve, the method of *transtympanic* promontory stimulation utilizing an external system does not provide a solution to manage chronic tinnitus. To suppress tinnitus long-term, patients must have access to continuous or repetitive electrical stimulation.

From these data, the investigators hypothesize that a partially- or totally-implantable device, capable of administering electrical stimulation via cochlear surface (i.e., promontory), will provide safe and effective long-term suppression of tinnitus in patients with normal to moderate sensorineural hearing loss. Paramount to the development of an implantable device, the optimum region(s) of device placement in relation to the cochlear turns (i.e., basal, mid, apical or multiple levels) must be evaluated. Placement of the electrode in the region of the posteroinferior promontory or at the round window can effectively stimulate the basal turn of the cochlea, which corresponds to high-frequency regions of the tonotopic map. In contrast, placement in the region of the anterosuperior cochlear surface, inferior to the cochleaform process for example, can stimulate the mid- and apical turns of the cochlea, which correspond to mid- and low-frequency regions of the cochlear tonotopic map. Several studies have demonstrated successful electrical suppression of tinnitus through promontory stimulation in the region of the round window, while other studies have suggested that the region of optimal stimulation varies across subjects and more complete “cochlear coverage” is beneficial [11].

# 3 STUDY OBJECTIVES

**Primary Objective**: To characterize the safety and efficacy of cochlear promontory stimulation in the short-term relief of tinnitus.
**Hypothesis**: Cochlear promontory stimulation is a safe procedure that provides short term tinnitus relief to a select subset of patients with chronic tinnitus.

**Secondary Objective**: To determine the optimum region(s) of the cochlear promontory in planning for an implantable electrical device for long term tinnitus suppression.
**Hypothesis**: Electrical suppression of tinnitus is dependent on the cochlear tonotopic map, with an optimum region for tinnitus suppression individualized to each patient.

# 4 STUDY DESIGN

## 4.1 General Design

1. Experimental approach: adult patients with normal to moderate hearing loss and disruptive intractable asymmetric tonal tinnitus will be recruited for electrical promontory stimulation testing.

2. Candidate subjects will undergo a temporal bone Computed Tomography (CT) scan, contrast enhanced head Magnetic Resonance Imaging (MRI), audiogram with immittance testing, pitch and level matching of tinnitus, Distortion Product Otoacoustic Emissions (DPOAE) and Auditory Brainstem Response (ABR) testing prior to promontory stimulation. Head MRI, DPOAE, audiogram and immittance testing are considered clinically routine for assessment of asymmetric tinnitus. Temporal bone CT, ABR, tinnitus pitch, level matching, masking levels and residual inhibition testing are not standard clinical assessments for asymmetric tinnitus. In addition, subjects will complete the Tinnitus Handicap Inventory (THI), Tinnitus Functional Index (TFI) and Tinnitus Visual Analog Scale (VAS)-L (loudness) and Tinnitus VAS-A (annoyance) questionnaires three separate times within the 10 days prior to promontory stimulation testing. Additional testing for comorbid anxiety and depressive conditions will be a screening Generalized Anxiety Disorder (GAD7), Patient Health Questionnaire (PHQ8), and short Health Anxiety Inventory (HAI-S). The NEO Personality Inventory (NEO PI) will be administered to provide baseline information. The initial session of promontory stimulation will define safety stimulation parameters, with a continual treatment after defining these parameters. After treatment is completed, the patient will complete the THI, TFI, and Tinnitus VAS-A and Tinnitus VAS-L immediately prior to stimulation, during stimulation, and following completion of stimulation at 10-minutes, 1-hour, 24-hours, 48-hours, and 1-week (or prior to the next scheduled stimulation treatment, whichever occurs first) following completion of stimulation. There will also be a “recall survey” in which patients will recall the time and feeling that their tinnitus felt in the week after the stimulation procedure. In addition, pitch and level matching of tinnitus will be completed prior to the first promontory stimulation session and after the last session. Each patient

will undergo three successive treatments separated by 7 days (+14/- 2 days). Prior to each treatment, the patient will receive an audiogram and DPOAE testing to document interval safety. At the conclusion of the study, subjects will be asked about their willingness to undergo surgical implantation of a device capable of long-term scheduled or on-demand electrical stimulation for tinnitus suppression.

### 4.2 Primary Study Endpoints

The primary study endpoints include tinnitus relief based upon questionnaires and tinnitus matching, tactile and auditory feedback, and the perception of discomfort during stimulation.

### 4.3 Secondary Study Endpoints

The secondary study endpoints include determining treatment parameters of the cochlear promontory for maximum tinnitus suppression.

### 4.4 Early termination

If during the pilot study the placement or use of the cochlear promontory stimulation electrode is documented or suspected by the surgeon to cause sensorineural hearing loss or undue discomfort, the study protocol will be revisited and re-written or the study will be terminated.

### 4.5 Risk / Benefits

**Benefit**: We propose a study evaluating short term suppression of tinnitus with the information accumulated to aid in the development of a future implantable device capable of providing long term tinnitus suppression.
**Risk**: There is a 1.6% risk of persistent tympanic membrane perforation; the risk of perforation requiring intervention is 0.5% [13]. The risk of electrical current spread on the surface of the promontory could theoretically cause facial nerve stimulation, discomfort through stimulation of the tympanic plexus, or hearing loss. CT scans involve exposure to radiation. The amount of radiation from these studies has a low risk of harmful effects.

# 5 SUBJECT ENROLLMENT AND WITHDRAWAL

## 5.1 Inclusion Criteria

- Age: 18 years of age or older
- Normal to moderate sensorineural hearing loss (based on PTA of 500, 1000 and 2000 Hz) and a word recognition score equal to or greater than 60%
- Asymmetric or unilateral subjective tonal tinnitus
- Tinnitus that is disruptive by at least two of the three criteria:
    - Determined by THI score (in the severe range i.e. ≥56/100)
    - TFI (in the severe range i.e. ≥52/100)
    - Tinnitus VAS (≥ 5/10 )
- Tinnitus that is intractable, and has not been ameliorated by conventional measures such as a hearing aid or masking, when such interventions are potentially clinically indicated (e.g., it is not expected that people with minimal or no hearing loss would trial a conventional hearing aid)
- MRI of the head that does not reveal any anatomical or structural abnormalities of the inner ear, cochlear nerve, or brainstem that would negatively impact response to study intervention (e.g., vestibular schwannoma)

## 5.2 Exclusion Criteria

- Age: less than 18 years of age
- Subjectively severe tinnitus present less than 6 months or longer than 12 years; it is permissible to include people who have had intermittent or constant tinnitus longer than 12 years as long as it was not perceived as severe longer than 12 years
- History of brain or major ear surgery
- Prior major head trauma, defined for the purposes of this study as head trauma that results in sudden injury that causes damage to the brain and results in lasting cognitive impairment
- Ongoing clinical diagnosis of depression or anxiety; for the purposes of this study, it is permissible to include people who: 1. have a past history of clinically diagnosed depression or anxiety that is no longer currently active; or 2. people who have depressive or anxious symptoms that are thought to primarily result from severe tinnitus
    - Determined by screening using the GAD 7, PHQ8, and HAI-S
        - GAD7 > 9 (indicates clinically significant anxiety)
        - PHQ > 9 (indicates clinically significant depression)
        - HAI-S > 25 (hypochondriacal level illness anxiety)
- Inability to assess, continue or complete trial
- Currently on regularly scheduled antidepressants, anxiolytics, or antipsychotics; for this study, it is permissible to include people who use such medications at lower doses as a sleep aid or for people who intermittently use such medications for situational anxiety (e.g., Ativan before airplane travel)
- Active use of other tinnitus treatments; for the purposes of this study it is permissible to include people who prefer to use a hearing aid to amplify ipsilateral hearing loss
- Known pregnancy

## 5.3 Subject Recruitment

There will be three available recruitment sources for the study. The first will be existing tinnitus patients cared for by Otorhinolaryngology providers. The second will be patients being referred for tinnitus to the Department of Otorhinolaryngology. These patients will be identified by the appointment coordinators, consulting team, investigator, or study coordinator. The third group are people who have contacted the study team to participate in a tinnitus related research study at Mayo Clinic, after having seen a posting on ClinicalTrials.gov or the Mayo Clinic website. The study team may then contact the subject with a letter mentioning the prospective trial and will provide study team contact number to obtain more information. All members of the clinic team, including consultants, residents, audiologists, and nurses will be made aware of this study's inclusion and exclusion criteria and will identify appropriate patients. Consent to participate in the study will be obtained at the time of consultation. Alternatively, subjects may be contacted by phone or video to review the inclusion and exclusion criteria, with the potential of being consented by phone or video and either signing the consent form electronically or by mail, if the subject can't or doesn't want to sign electronically.

### 5.4 Withdrawal of Subjects

Patients who are not able to be evaluated on the date of appointment or those who should choose to withdraw for any reason will have the option to withdraw at any time.

# 6 STUDY PROCEDURES

### 6.1 Pre Visit Evaluation

Eligible subjects will be identified for inclusion at the time of referral. The study coordinator or departmental research staff will confirm compliance with initial inclusion and exclusion criteria. Informed consent will then be obtained. Then initial screening documentation, including THI, TFI, Tinnitus VAS-A and VAS-L, GAD7, GHQ, PHQ8, NEO-PI, and patient history will be reviewed.

If the patient is being seen in the Otolaryngology clinic for an alternative chief complaint, but a screening review of systems identified significant tinnitus, one of the members of the research team will be available for screening consultation and may provide informed consent at that time. A copy of the consent form will be provided to the patient to keep, and a copy will be filed and stored. Once enrolled, the THI, TFI, Tinnitus VAS-A and VAS-L, GAD7, GHQ, PHQ8 and NEO-PI scores of the subject will be recorded by the research staff.

If the patient is unable to schedule a Pre Visit Evaluation, consent may then be mailed (either via the postal service or electronically through PTRAX) to the patient. The consenting provider will meet with the patient by phone or video visit and read through the consent form with the potential participant. If desire to proceed, signed consent form will be returned either electronically or by mail and screening documentation will be provided to the patient. The THI, TFI, Tinnitus VAS-A and VAS-L, and Pain VAS, GAD-7, PHQ-8, and/or the NEO-PI may be mailed or sent electronically to the subject after consent so they may do these eligibility screening surveys at home without making a trip to Mayo Clinic. They will return these screening surveys which will be scored, and if the scores qualify, the subject will come in person for a clinical visit and the rest of the initial screening surveys, if they did not do the whole set at home.

After eligibility is determined, subject will complete study questionnaires (THI, TFI, and Tinnitus VAS-A and VAS-L) at three separate time periods in conjunction with the first clinical visit.

### 6.2 First Clinical Visit

1. Patients enrolled in the study will proceed to Mayo Clinic Otorhinolaryngology Department for additional evaluation. Candidate subjects will undergo a temporal bone CT, contrast enhanced head MRI, audiogram with immittance testing, pitch and level matching of tinnitus, and DPOAE and ABR testing prior to promontory stimulation. If during the course of the patient's visit, any of the exclusion criteria are met, the patient will be withdrawn from the study, and will be notified of this as soon as possible. If the patient has already had a temporal bone CT and/or a head MRI, they do not need to get another for this study.
    a. The number and estimated length of each study visit

i. 5 visits in total. The first visit would include a ~30 minute overview. The next visit would require ~2 min temporal bone CT, ~45 min MRI with contrast, ~45 min ABR, ~45 min audiogram and DPOAE, ~30-60 min of stimulation. The next 2 visits would require ~30-60 min stimulation. The last visit would require ~20 min for tympanic membrane evaluation for residual perforation and ~45 min for audiogram.

### 6.2.1 Transtympanic Cochlear Promontory Stimulation

a. At the first, second and third clinical appointment, the promontory stimulation equipment (Cochlear Corporation Nucleus Promontory Stimulator Z10012®; Cochlear Corporation, Melbourne, Australia) will be used. The initial session of promontory stimulation will define optimal stimulation parameters (i.e., current level, and frequency), where maximal tinnitus suppression occurs with minimal or no auditory percept. Stimulus amplitude will be increased slowly to establish threshold and maximum acceptable loudness. As an internal control function, testing will include a run of "on-off" simulations blinded to the subject, with patient blinded status to the "off" or "on" position of the stimulation machine. After these parameters are established, the patient will complete the THI, TFI, and VAS immediately prior to stimulation, during stimulation, and following completion of stimulation at 10-minutes, 1-hour, 24-hours, 48-hours, and 1-week following completion of stimulation (or prior to the next scheduled session of promontory stimulation, whichever occurs sooner), in addition to the recall survey, which is completed after a time period of one week (or prior to the next scheduled session of promontory stimulation, whichever occurs sooner). In addition, pitch and level matching of tinnitus will be completed immediately prior to the first promontory stimulation session and after the last session. Each patient will undergo three successive treatments separated by 7 days (+14/- 2 days). Prior to each treatment, the patient will receive an audiogram and DPOAE testing to document interval safety. At the conclusion of the study, subjects will be asked about their willingness to undergo surgical implantation of a device capable of long-term scheduled or on-demand electrical stimulation for tinnitus suppression.

b. The Cochlear Corporation Nucleus Promontory Stimulator Z10012 (Cochlear Corporation, Melbourne, Australia) will deliver stimulatory electric pulses. The stimulation will be delivered to the target sites using a transtympanic electrode kit, which contains a monopolar transtympanic needle electrode referenced to a surface electrode to be placed on the patient's forehead. The tympanic membrane will be visualized with otomicroscopy with the patient in the supine position. Phenol will be applied to the tympanic membrane for local anesthesia. If residual irritation is perceived, EMLA cream will be used in the external auditory canal. The transtympanic electrode needle will be guided through the external canal aiming for the posteroinferior quadrant of the tympanic membrane. The needle will be stabilized in the ear canal using cotton packing or hearing aid mold putty and adhesive tape. Initially, an electrode impedance test will be performed

to validate proper placement and electrical contact of the electrodes. An indicator light will denote when impedances are not acceptable. If impedance values are not acceptable, a gentle repositioning of the proximal end of the needle electrode may be employed to ensure proper placement on the promontory. Otherwise, the needle electrode will be removed and reintroduced. Once proper electrical contact is validated, a calibration session to assess optimal stimulation parameters for the therapeutic session will be carried out using a ranged of 0 to 1 mA for pulse frequencies 100 Hz, 800 Hz and 1600 Hz. For each stimulus frequency, current level will be gradually increased to determine the following perceptual parameters: 1) Detection threshold or minimum threshold: first detection of the electrical stimulus (tactile or audible) as reported by the patient. 2. Maximum acceptable loudness level or discomfort level: when the applied current is perceived as loud but not uncomfortable. 3. The effective stimulation level will be determined to be 80% of the discomfort level or at minimum the minimum threshold level. The total duration of the electrical stimulation (at the optimal level) in each session will be ~30-60 minutes.

#### 6.2.2 ABR

a. A threshold ABR using a 37.7 rate click stimulus will be used for auditory brainstem response testing.

#### 6.2.3 DPOAEs

a. DPOAEs will be tested 1-10 kHz. Presence of DPOAEs will be determined using the following criteria: 6 dB SNR; absolute level of >=-10 dB.

### 6.3 Postprocedural appointment

The primary investigator will visit with each patient one month after the three sequential electrical stimulation visits. The tympanic membrane will be evaluated for evidence of persistent perforation.

### 6.4 Study Coordination

When a prospective subject is identified by the appointment schedulers, consultants, audiologists or research team, the research team will be notified. A member of the study team will provide information about the study to the subject and will serve as the point of contact for the subject. A member of the study team will help organize the administration and receipt of surveys, as well as coordinate appointment visits. They will allot for breaks in between separate tests for patient comfort.

# 7 DATA COLLECTION AND ANALYSIS

### 7.1 Data to Be Collected

Demographic data to be collected will include patient's age, sex, medical comorbidities, current medications and medications taken within the last year, preoperative THI, TFI, Tinnitus VAS-A and VAS-L, GAD7, PHQ8, GHQ and NEO PI-R.

The patient will complete the THI, TFI and Tinnitus VAS-A and VAS-L immediately prior to stimulation, during stimulation, and following completion of stimulation at 10-minutes, 1-hour, 24-hours, 48-hours, and 1-week (or prior to the next scheduled session of promontory stimulation, whichever occurs sooner) following completion of stimulation.

### 7.2 Data Analysis

a Power Analysis

Assuming the power was 80% and a **one** sided alpha of .05; we sought to determine a power analysis to detect a clinically significant decrease in tinnitus symptoms [3,12].

| True Change in THI | SD of Change of THI | Sample Size | | |
|---|---|---|---|---|
| | | Equality | Superiority using 7 as bottom threshold | Superiority using 5 as bottom threshold |
| 7 | 10 | 11 | | 156 |
| 7 | 15 | 22 | | 350 |
| 7 | 20 | 38 | | 619 |
| 10 | 10 | 6 | 71 | 27 |
| **10** | **15** | 12 | 156 | **58** |
| 10 | 20 | 19 | 277 | 101 |
| 15 | 10 | 4 | 12 | 8 |
| **15** | **15** | 4 | **24** | **16** |
| 15 | 20 | 6 | 41 | 27 |

There are three different types of analysis used above to calculate sample size.

The first analysis shown is an equality test which assesses whether the mean change in THI level is different from zero. This is the simplest power calculation and is usually associated with a t-test. In our research question, we would like to consider the procedure a success if the scores improve significantly by a certain amount. This test only examines that, if the true change is 7 (10), it is different from zero.

The second two analyses seek to quantify the amount of change in THI we would like to consider clinically relevant. If we believe a clinically relevant change is 7 points on the THI scale we want to ensure that we have sufficient sample size to detect a mean change at or higher than 7. The final sample size column is less stringent in the mean we have to detect to consider the treatment a success, with requiring only a 5 point change to be clinically relevant (the threshold for not improving in the paper above).

The power calculation suggests that if we believe our true mean change to be a 15 THI points with a SD of 15, a difference greater than or equal to 5 can be detected using 16 subjects, while if we want to **detect a mean change greater than 7 we would need 24 subjects.**

b Data Analysis

THI, TFI and Tinnitus VAS scores will be analyzed based on numeric change over time after each promontory stimulation procedure. Data from the Audiograms / DPOAE will be assessed to ensure no baseline change in hearing has occurred as safety precautionary measures.

The NEO PI will be evaluated to determine correlation between tinnitus improvement scores and baseline personality assessment. Results of the NEO PI will not be used to screen for enrollment.

# 8 DATA HANDLING

Data will be collected and handled in a manner to protect patient health information.

Data extracted from the cochlear promontory stimulation monitoring system will be collected by the investigator. The data will then be extracted to a secure database on the Mayo Clinic server. Once the data has been transferred, the data will be deleted from the flash drive. Only the principal and co-investigators will have access to this data. Visit data will also be entered into this secure database. Access to the database will be restricted to research staff and will be unavailable to any third party.

The Head Study Coordinator will be responsible for handling of protected health information according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In accordance to this, a signed consent form by patient will be obtained that informs the subject of the following:

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

# 9 STUDY FUNDING

Part of the funding for this study will be obtained via internal research funds within the Department of Otorhinolaryngology, Mayo Clinic, Rochester, Minnesota.

Part of the funding for this study will be financed by the Peer Reviewed Medical Research Program (PRMRP) Clinical Trial Award through the Department of Defense.

# 10 REFERENCES


1. Tunkel DE, Bauer CA, Sun GH, Rosenfeld RM, Chandrasekhar SS, Cunningham ER Jr,Archer SM, Blakley BW, Carter JM, Granieri EC, Henry JA, Hollingsworth D, Khan FA, Mitchell S, Monfared A, Newman CW, Omole FS, Phillips CD, Robinson SK, Taw MB, Tyler RS, Waguespack R, Whamond EJ. Clinical practice guideline: tinnitus. Otolaryngol Head Neck Surg. 2014 Oct;151(2 Suppl):S1-S40.
2. Tsai BS, Sweetow RW, Cheung SW. Audiometric asymmetry and tinnitus laterality. Laryngoscope. 2012 May;122(5):1148-53.
3. Perez R, Shaul C, Vardi M, Muhanna N, Kileny PR, Sichel JY. Multiple electrostimulation treatments to the promontory for tinnitus. Otol Neurotol. 2015 Feb;36(2):366-72.
4. Rubinstein JT, Tyler RS, Johnson A, Brown CJ. Electrical suppression of tinnitus with high-rate pulse trains. Otol Neurotol. 2003 May;24(3):478-85.
5. Watanabe K, Okawara D, Baba S, Yagi T. Electrocochleographic analysis of the suppression of tinnitus by electrical promontory stimulation. Audiology. 1997 May-Jun;36(3):147-54.
6. Steenerson RL, Cronin GW. Treatment of tinnitus with electrical stimulation. Otolaryngol Head Neck Surg. 1999 Nov;121(5):511-3.
7. Mertens G, De Bodt M, Van de Heyning P. Cochlear implantation as a long-termvtreatment for ipsilateral incapacitating tinnitus in subjects with unilateral hearing loss up to 10 years. Hear Res. 2016 Jan;331:1-6.
8. Tyler RS. Patient preferences and willingness to pay for tinnitus treatments. J Am Acad Audiol. 2012 Feb;23(2):115-25.
9. https://wwwn.cdc.gov/Nchs/Nhanes/2011-2012/AUQ_G.htm
10. Arts RA, George EL, Stokroos RJ, Vermeire K. Review: cochlear implants as a treatment of tinnitus in single-sided deafness. *Curr Opin Otolaryngol Head Neck Surg.* 2012;20(5):398-403.
11. Arts RA, George EL, Chenault MN, Stokroos RJ. Optimizing intracochlear electrical stimulation to suppress tinnitus. *Ear Hear.* 2015;36(1):125-135.
12. Zeman F, Koller M, Figueiredo R, Aazevedo A, Rates M, Coelho C, Kleinjung T,de Ridder D, Langguth B, Landgrebe M. Tinnitus handicap inventory for evaluating treatment effects: which changes are clinically relevant? Otolaryngol Head Neck Surg. 2011 Aug;145(2):282-7.
13. Topf MC, Hsu DW, Adams DR, Zhan T, Pelosi S, Willcox TO, McGettigan B, Fisher KW. Rate of tympanic membrane perforation after intratympanic steroid injection. Am J Otolaryngol. 2017 Jan - Feb;38(1):21-25.

# APPENDIX A. COCHLEAR PROMONTORY STIMULATION