

Cochlear Implantation after Labyrinthectomy or a Translabyrinthine Surgical Approach

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**Cochlear Implantation After Labyrinthectomy or a Translabyrinthine
Surgical Approach**

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II. Introduction

The treatment for cases of vestibular schwannoma or Meniere's disease may require a translabyrinthine surgical approach. This surgical approach results in a complete loss of hearing in the surgical ear, leaving the patient with a unilateral hearing loss. Though assistive hearing technologies exist to route signals from the poorer hearing ear to the better hearing ear, affected patients continue to have limitations with localization and speech perception in noise. An alternative hearing device is a cochlear implant, which would provide the signal to the affected ear. This could potentially offer binaural cues, thus improving localization and speech perception in noise. Since the surgical procedures for a translabyrinthine approach parallel those for cochlear implantation, insertion of the cochlear implant could occur within the same surgery.

A vestibular schwannoma is a benign tumor on cranial nerve VIII that affects the vestibular and auditory systems. Hearing loss on the side of the vestibular schwannoma may result from degeneration of hair cells and spiral ganglia (Roosli et al, 2012) or growth of the schwannoma into the cochlear space (Falcioni et al, 2003). Treatment options include observation from routine imaging, radiation therapy, or surgical removal of the tumor. Despite treatment for the vestibular schwannoma, auditory sensitivity may be further reduced on the affected side as a result of the radiation therapy or compromises to the inner ear or cranial nerve VIII from surgical removal. Thus, in cases of unilateral vestibular schwannoma the patient is often left with a unilateral profound hearing loss.

Patients who are scheduled to undergo labyrinthectomy for intractable Meniere's disease are a second population with resulting unilateral profound hearing loss. These patients typically have non-functional hearing on the affected ear prior to the procedure. The main indication for the surgery is intractable vertigo and thus the loss of already non-functional hearing is typically well accepted.

Though hearing on the contralateral ear may be within normal limits, unilateral hearing loss is known to result in reduced speech perception in noise (Welsh et al, 2004; Rothpletz, Wightman & Kistler, 2012), variable abilities on localization tasks (Slattery & Middlebrooks, 1994), increased report of hearing handicap (Iwasaki et al, 2013), and reduced quality of life (Wie, Pripp & Tvette, 2010). Due to the severity of the hearing loss, these patient populations cannot utilize conventional amplification that would offer auditory input to the affected ear. The current hearing device options for this patient population include CROS hearing aids and bone-conduction devices. With a CROS hearing aid, a microphone positioned near the affected ear picks up the signal and sends it to a hearing aid placed on the contralateral ear to present the signal to the unaffected side. Bone-conduction devices transmit the signal from the affected ear to the contralateral ear via transcutaneous vibrations. Though CROS hearing aids and

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bone-conduction devices provide the patient with auditory information from both sides, the ability to use binaural cues for localization and speech perception in noise is variable (Kunst et al, 2007).

It is of interest as to the potential benefit of cochlear implantation in these populations considering the profound hearing loss resulting from surgical intervention. A cochlear implant is a two-part system, including the internal electrode array and external speech processor. The internal electrode array is surgically implanted into the affected cochlea. The external speech processor receives sounds and transmits this signal to the internal portion. The electrode array presents the signal via electrical pulses within the cochlear space, which is interpreted by the brain as sound.

Cochlear implantation has been reported as a viable treatment option in other cases of unilateral hearing loss, including sudden sensorineural hearing loss (Firszt et al, 2012), and severe tinnitus (Vermiere & Van de Heyning, 2009; Van de Heyning et al, 2008). Further, cochlear implantation has been shown to offer superior speech perception in noise, localization abilities, and subjective report in cases of unilateral sensorineural hearing loss as compared to CROS hearing aids and bone-conduction devices (Arndt et al, 2011).

There is limited evidence as to the success of cochlear implantation in patients with unilateral profound hearing loss resulting from vestibular schwannoma. Pai et al (2013) reported variable speech perception outcomes in five cochlear implant recipients with a history of vestibular schwannoma due to NF2 or sporadic growth. Limitations of this study are the subjects underwent a range of treatments prior to cochlear implantation and the cases reviewed had profound hearing loss in both ears. Zanetti et al (2008) reported on a case study of unilateral vestibular schwannoma removal and simultaneous cochlear implantation. This subject reportedly experienced an improvement in speech perception abilities and quality of life postoperatively. Determining the preferred treatment option for patients suffering from unilateral vestibular schwannoma is still needed.

Further, there is limited evidence of the preferred treatment option for patients suffering from unilateral profound hearing loss after undergoing a labyrinthectomy for intractable Meniere's disease. Osborn, Yeung and Lin (2012) reported on a patient who underwent bilateral labyrinthectomies for Meniere's disease. They reported an improvement in speech perception abilities and subjective benefit; however, there was a delay between the two surgeries. Allowing for a waiting period between the two surgeries is not ideal as cochlear ossification may occur (Wareing & O'Connor, 1997), limiting the ability to successfully insert the electrode array. Lustig et al (2003) also reported successful outcomes from cochlear implantation in subjects with bilateral Meniere's disease. However, there is no published report investigating whether

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cochlear implantation improves speech perception and/or localization abilities in unilateral cases of Meniere's disease.

The goal of this project is to determine whether subjects who have undergone labyrinthectomy or a translabyrinthine surgical approach as the treatment for vestibular schwannoma or Meniere's disease with intractable vertigo benefit from cochlear implantation on speech perception and localization tasks. If the auditory nerve is able to transmit this signal effectively, then these two populations may be able to utilize the combination of electric (in the affected ear) and acoustic (in the non-affected ear) information for improved speech perception in noise and localization as reportedly experienced in other unilateral sensorineural hearing loss populations.

III. Objectives

- A. The purpose of this study is to demonstrate the safety and effectiveness of cochlear implantation in subjects with unilateral deafness resulting from either a labyrinthectomy or a translabyrinthine surgical approach. Postoperative results will be evaluated with speech perception measures, localization tasks, and subjective reports.

IV. Investigational Device

- A. Subjects will be implanted with the commercially available MED-EL SYNCHRONY cochlear implant with either the standard or Flex²⁸ electrode array (MED-EL Corporation, Innsbruck, Austria). The device consists of a stimulator, a coil with a magnet within its center, a reference electrode, an EAP reference electrode and an active electrode permanently attached to the stimulator. The electrode is made of medical grade silicone, platinum (electrode contacts) and platinum/iridium (90/10) wires and nitinol.

The purpose of the device is perception of environmental sound and potential for improvement in communication abilities.

For the adult population, the MED-EL SYNCHRONY cochlear implant is indicated for those 18 years of age or older, who have bilateral sensorineural hearing impairment and obtain limited benefit from appropriately fitted binaural hearing aids. Additional information regarding this device is provided in **Appendix A**.

The standard electrode array is 31.5 mm long, with 12 pairs of contacts spaced over 26.4 mm with 2.4 mm spacing between each contact pair. The electrode's length allows insertion into the scala tympani and stimulation of the cochlear canal to the fullest extent possible. The array features a marker ring 31.5 mm from the apex that is used to seal the cochleostomy and to

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indicate maximum electrode insertion. The diameter of the array increases to 1.3 mm at the proximal thicker part of array just before the marker ring.

The Flex28 electrode array is 28 mm long featuring FLEX tip technology. The contacts for the 12 channels are arranged as 5 single contacts at the apical array end and 7 contact pairs at the base with 2.1 mm spacing between each channel. The specially designed electrode tip offers increased mechanical flexibility for reduced insertion force. The marker ring is located 28 mm from the electrode tip and indicates the deepest insertion. Near the marker ring, the electrode lead features an additional marker on the same side of the array as the single apical contacts. The marker allows the surgeon to ensure appropriate alignment of the single contacts toward the modiolus.

Subjects will be fit with the SONNET speech processor. The SONNET speech processor is an external component of the MAESTRO Cochlear Implant System and is indicated for use on patients who have been implanted with a MED-EL cochlear implant. The SONNET audio processor consists of the control unit with the earhook attached, the battery pack frame and cover, the connecting piece, the coil and the coil cable. The audio processor uses batteries that provide sufficient power for both the external and the implanted electronics.

The MAESTRO Fitting Software will be used to program the SONNET speech processor. The MAESTRO software is used for different intraoperative and postoperative purposes for the MED-EL Cochlear Implant System. Currently, it contains the implant Telemetry and Fitting of the SONNET, OPUS 2, RONDO, OPUS 1, or TEMPO+ processors, EABR (Electrical Auditory Brainstem Response), ART (Auditory nerve Response Telemetry) and ESRT (Electrically Evoked Stapedius Reflex Threshold), and Audiogram functions. The MAESTRO software is an external component of the MED-EL Cochlear Implant System and is intended to be used in a clinical or office environment by persons adequately skilled and trained to perform all intended tasks and with patients who received one of the intended MED-EL Cochlear implants.

V. Study Duration

A. Enrollment Period

1. 4 years

B. Study Timeline

1. Candidacy evaluation, preoperative evaluation, surgery, initial postoperative follow-up, initial activation, and post-initial activation evaluations (1, 3, 6, 9, and 12-months post-initial activation)

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- C. The study endpoint for each subject will be the 12-months post-initial activation follow-up interval.

VI. Methods

All procedures will be conducted by UNC investigators, including board-certified otologists and an audiologist. Fully informed consent will be obtained from all subjects.

A. Participants

Subjects must meet the following inclusion criteria and not exhibit any of the exclusion criteria.

1. Inclusion Criteria

- a. Scheduled to undergo a surgical procedure that will result in profound hearing loss in the surgical ear
 - i. Unilateral, vestibular schwannoma with planned translabyrinthine surgery or unilateral Meniere's disease with planned labyrinthectomy
 - ii. Diagnosed by UNC investigators
- b. PTA \leq 35 dB HL in the contralateral ear
 - i. No evidence of retrocochlear dysfunction
- c. Unaided CNC word score \geq 80% in the contralateral ear
- d. Greater than 18 years of age at implantation
- e. Realistic expectations
- f. Willing to obtain appropriate meningitis vaccinations
- g. No reported cognitive issues
 - i. Pass the Mini Mental State Examination (MMSE) screener
- h. Able and willing to comply with study requirements, including travel to investigational site
- i. Obtain CDC recommended meningitis vaccinations prior to surgery

2. Exclusion Criteria

- a. History of implantable technology in either ear, such as a bone-conduction implant
- b. Non-native English speaker
 - i. Speech perception materials are presented in English
- c. Inability to participate in follow-up procedures (i.e., unwillingness, geographic location)

3. Enrollment

- a. This study seeks to enroll ten (10) subjects.

B. Timeline

Appendix B graphically depicts the timeline and associated measures.

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1. Candidacy Evaluation
 - a. Medical Evaluation
 - i. Diagnosis of unilateral vestibular schwannoma with planned translabyrinthine surgery or unilateral Meniere's disease with planned labyrinthectomy
 - ii. Associated imaging studies
 - a. This is standard of care for these patient populations
 - b. May also be completed at Preoperative Evaluation
 - iii. Discussion of current treatment options (surgical approach and associated hearing loss, and hearing device options for use postoperatively)
 - iv. Determine if potential subject meets candidacy criteria
 - b. Audiologic Evaluation
 - i. Unaided air- and bone-conduction thresholds in both ears
 - a. Air-conduction assessed with insert phones
 - ii. Unaided word recognition with CNC words in both ears
 - a. Unaided word recognition testing is conducted in quiet in the effected ear
 - b. Masking will be presented to the contralateral ear if indicated
 - iii. Tympanometry in both ears
 - iv. Determine if potential subject meets candidacy criteria
 - c. Informed Consent
 - i. Review and discussion of consent form
 - ii. Provide time for subject to review consent form and ask questions
 - iii. Provide subject with a signed copy of the completed consent form
2. Preoperative Evaluation
 - a. Medical Evaluation
 - i. Subjects will undergo a medical assessment
 - ii. Associated imaging studies
 - a. This is standard of care for these patient populations.
 - b. May have been completed at Candidacy Evaluation.
 - iii. Counseling on cochlear implantation surgical procedure and postoperative considerations, including MRI limitations due to internal magnet
 - a. MED-EL SYNCHRONY cochlear implant is approved up to 3 Tesla with magnet in place (magnet can be removed to eliminate shadow if necessary).
 - b. Audiologic Evaluation
 - i. Obtain a case history, including but not limited to:
 - a. Onset of hearing loss
 - b. Resulting impairments from vestibular schwannoma or Meniere's disease (i.e., dizziness)

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- ii. Unaided air- and bone-conduction thresholds in both ears
 - a. Air-conduction assessed with insert phones
 - iii. Unaided word recognition with CNC words in both ears
 - iv. Tympanometry in both ears
 - v. Counseling on cochlear implant external technology, test battery, and postoperative timeline
3. Surgery

Two surgical scenarios are considered dependent on the subjects' etiology (i.e. vestibular schwannoma or unilateral Meniere's Disease with intractable vertigo). Due to the etiology of the impairment, subjects will be scheduled to undergo these surgical approaches whether or not they elect to participate in the study. Both surgical approaches, however, result in profound hearing loss in the surgical ear. Both surgical approaches also include steps taken during a cochlear implantation procedure, thus limiting the additional operative time needed for cochlear implant placement.

Risk factors associated with cochlear implantation are listed in Section X "Risk Analysis."

All surgical procedures will take place at the UNC Memorial Hospital or UNC ACC operating rooms. All procedures will be completed by board-certified otologists.

- a. Vestibular Schwannoma Subjects: Translabyrinthine Approach
 - i. This surgical approach allows wide access to various parts of the ear. As such, most surgical steps required for cochlear implantation have already been drilled. Thus, implantation will only take an additional 5 minutes or less. The overall operative times for vestibular schwannoma removal with a translabyrinthine approach range from 6-12 hours.

It is pertinent to note that the auditory nerve will have to be preserved for these procedures. For tumors of less than 2 cm in size this appears to be a reasonable goal. For larger growths, however, this might be impossible. Hence, intraoperative preservation of the structural integrity of the nerve will be a prerequisite for implantation, which will be performed once resection of the schwannoma has been completed.

During the surgical procedure there will be nerve monitoring as well as visual confirmation of auditory nerve integrity. Once the cochlear implant is in place, integrity testing will be performed (including but not limited to EABR, ART, and telemetry).

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- b. Unilateral Meniere's Disease with intractable vertigo Subjects:
Labyrinthectomy
 - i. A labyrinthectomy in this population is curative; however, a labyrinthectomy will render the subject profoundly hearing impaired in the operated ear. The routine surgical approach for this procedure is approximately 2 hours and includes all steps typically drilled for cochlear implantation. Thus, cochlear implantation will only take an additional 5 minutes or less.
4. Postoperative Evaluations
- a. Initial Follow-Up (approximately 1-2 weeks postoperatively)
 - i. Medical Evaluation
 - a. This is standard of care.
 - b. Subject will be seen by the physician
 - ii. Audiologic Evaluation
 - a. Unaided air and bone conduction thresholds
 - i. Air-conduction assessed with insert phones
 - b. Initial Activation of External Speech Processor (approximately 2-4 weeks postoperatively)
 - i. Unaided air and bone conduction thresholds
 - a. Air-conduction assessed with insert phones
 - ii. Unaided word recognition with CNC words in both ears
 - a. Unaided word recognition testing is conducted in quiet in the effected ear
 - b. Masking will be presented to the contralateral ear if indicated
 - iii. Initial activation of external speech processor
 - a. Subjects will be fit with the commercially available MED-EL SONNET external speech processor (MED-EL Corporation, Innsbruck, Austria). Speech perception and localization measures will be conducted with the subject listening with the SONNET external speech processor for the aided conditions.
 - iv. Counseling on the external device and use
 - c. 1-month Post-Initial Activation
 - i. Completion of test battery listed in VI.C.
 - d. 3-months Post-Initial Activation
 - i. Completion of test battery listed in VI.C.
 - e. 6-months Post-Initial Activation
 - i. Completion of test battery listed in VI.C.
 - f. 9-months Post-Initial Activation
 - i. Completion of test battery listed in VI.C.

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- g. 12-months Post-Initial Activation (study endpoint)
 - i. Completion of test battery listed in VI.C

C. Test Battery

The following test battery will be completed at each post-initial activation interval (1, 3, 6, 9 and 12 months). All assessment and mapping will be conducted at the Carolina Crossing research lab by a board-certified audiologist.

1. Unaided Diagnostic Assessment

- a. Air- and bone-conduction thresholds in both ears
 - i. Air-conduction assessed with insert phones
- b. Unaided word recognition with CNC words in both ears
 - a. Unaided word recognition testing is conducted in quiet in the effected ear
 - b. Masking will be presented to the contralateral ear if indicated

2. Tympanometry for each ear

3. Sound Field Measures

The Carolina Crossing research lab features a 180° arc with 11 speakers spaced 18° apart. This arc will be utilized during the speech perception and localization measures.

- a. Aided thresholds with the external speech processor on and masking applied to the contralateral ear will be measured using pulsed, warble tones
 - i. Frequencies assessed: 250-8000 Hz, including all inter-octaves

b. Speech Perception Measures

Speech perception will be assessed in an aided (cochlear implant speech processor on) and unaided (cochlear implant speech processor off) condition.

Recorded materials will be presented at 60 dB SPL.

- i. Speech Perception in Quiet
 - a. Listening condition
 - i. Speech 0° azimuth
 - b. Speech perception materials
 - i. CNC words
 - ii. CID sentences
 - iii. HINT sentences (if >50% correct on CID sentences)
 - iv. AzBio sentences (if >50% correct on HINT sentences)

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- ii. Speech Perception in Noise
 - a. Listening conditions
 - i. Speech and noise 0° azimuth
 - ii. Speech 0° azimuth and noise to implanted side
 - iii. Speech 0° azimuth and noise to contralateral ear
 - b. Speech perception materials
 - i. HINT sentences
 - a. If >50% at SNR+10, then SNR+5
 - b. If >50% at SNR+5, then SNR+0
 - ii. AzBio sentences
 - a. If >50% at SNR+10, then SNR+5
 - b. If >50% at SNR+5, then SNR+0
 - iii. BKB-SIN sentences with adaptive SNR
 - iii. Listening Conditions
 - a. Cochlear implant only (contralateral ear masked)
 - b. Contralateral ear only (cochlear implant speech processor off)
 - c. Combined (Cochlear implant on + contralateral ear unmasked)
- c. Localization
- Localization will be assessed in an aided (cochlear implant speech processor on) and unaided (cochlear implant speech processor off) condition.
- i. The stimulus is a 200-ms speech-shaped noise, presented at 70-dB-SPL from one of the 11 speakers (evenly spaced -180 to 180 degrees), selected at random.
 - ii. The listener will be facing the center speaker during stimulus presentation. The task is to identify the source of the noise via a touchscreen monitor. No feedback is provided.
 - iii. Data will be analyzed in terms of error and adjusted constant error, as described by Grantham et al (2007).
 - iv. Listening Conditions
 - a. Contralateral ear only (cochlear implant speech processor off)
 - b. Combined (Cochlear implant on + contralateral ear unmasked)
4. Subjective questionnaires
- a. Speech, Spatial and Qualities of Hearing Scale (SSQ) Gatehouse & Noble (2004)
 - b. Abbreviated Profile of Hearing Aid Benefit (APHAB) Cox & Alexander (1995)

VII. Proposed Claims

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- A. Demonstrate the safety and effectiveness of cochlear implantation in populations suffering from unilateral profound hearing loss after labyrinthectomy or translabyrinthine surgical approaches.
 - 1. Demonstrate an improvement in speech perception abilities in an aided (cochlear implant on) versus an unaided (cochlear implant off) condition
 - 2. Demonstrate an improvement in localization abilities in an aided (cochlear implant on) versus an unaided (cochlear implant off) condition
 - 3. Demonstrate an improvement in subjective report in an aided (cochlear implant on) versus an unaided (cochlear implant off) condition

VIII. Statistical Analysis

- A. Descriptive summaries will be provided for the following: subject demographics, and frequency of major and minor complications/adverse events.
- B. A single-subject design will be utilized, where each subject serves as his or her own control, for analysis of objective and subjective results. A single-subject design was chosen in order to accommodate the heterogeneity that is well known to characterize auditory prosthesis research. Repeated-measures ANOVA will be calculated with a p-value of ≤ 0.05 for statistical significance. Statistical analysis will be conducted with SPSS software.
 - 1. Comparison in aided speech perception performance on word and sentence materials in the post-initial activation intervals
 - a. Also compare the difference between the aided and unaided conditions at each follow-up interval
 - 2. Comparison in localization abilities in the post-initial activation intervals
 - a. Also compare the difference between the aided and unaided conditions for each follow-up interval
 - 3. Comparison in subjective report in the post-initial activation intervals

If needed, statistical consultation will be sought from the North Carolina Translational and Clinical Sciences Institute (TraCS) or UNC Odum Institute.

IX. Endpoints

- A. Safety endpoint
 - 1. The primary safety endpoint is the evaluation of Adverse Events. All Adverse Events will be reported to the UNC IRB. If the UNC IRB or study investigators deem an Adverse Event unacceptable, then this would be sufficient terms to terminate the study.
- B. Primary effectiveness endpoint

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1. The primary effectiveness endpoint is the comparison of speech perception (VII.A.1), localization abilities (VII.A.2) and/or subjective report (VII.A.3) when the cochlear implant is on versus off.

X. Risk Analysis

A. Potential risks

The following are potential risks associated with this protocol. There are other risks associated with the surgical procedure and follow-up care that the subject would experience as a result of the surgical procedure for the treatment of their vestibular schwannoma or Meniere's Disease with intractable vertigo. The following are potential risks the subject may experience related to the study procedure.

1. Surgical

- a. The risks associated with this surgery are the same as those associated with the surgical procedures the subject would already undergo as part of their treatment for vestibular schwannoma or Meniere's Disease with intractable vertigo. There are no further risks anticipated from placement of the cochlear implant.
 - i. Risks associated with translabyrinthine surgical approach
 - a. Facial nerve injury
 - b. Incomplete tumor removal
 - c. CSF leak
 - d. Hemorrhage
 - e. Infection
 - ii. Risks associated with labyrinthectomy
 - a. Bleeding
 - b. Infection
 - c. Persistent disequilibrium
 - d. Facial nerve injury

2. Postoperative

- a. Swelling around the incision and/or coil site.
- b. Pain
- c. Reduced or loss of pinna sensitivity on the surgical side
 - i. Typically resolves 1-2 months postoperatively.
- d. The cochlear implant may not provide any auditory stimulation.
- e. The cochlear implant may provide auditory stimulation, but with a sound quality too poor to aid in the perception of speech.
- f. The cochlear implant may provide auditory stimulation, but with a sound quality too poor to aid in localization.
- g. Pain associated with the coil and/or placement of the external speech processor on the subject's ear.
- h. Discomfort from electric stimulation
- i. Facial nerve stimulation

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- j. Headache
- k. Dizziness
- l. Altered taste (i.e. reports of metallic tastes on the same side of the tongue as the surgical ear)
- m. Fatigue during follow-up assessment (completion of the test battery and/or mapping)
- n. The internal device may fail, requiring revision cochlear implantation

B. Risk Mitigation

1. Current hearing device options, including CROS hearing aids and bone-conduction devices, would still be available to the subject in the future if the subject does not benefit from the cochlear implant or elects to no longer use the cochlear implant.
2. Magnet strength will be assessed at each interval to ensure comfort at the coil site.
3. Reports of pain from the external speech processor placement will be addressed by different wearing options (i.e. moleskin between the external speech processor and the subject's ear, or different battery-wearing options to lighten weight on the pinna).
4. Mapping will be conducted at each post-initial activation interval to improve audibility and comfort of the sound quality from electric stimulation.
5. The MED-EL cochlear implant has MRI limitations*. Subjects may have CT scans or x-ray imaging postoperatively.
 - a. *The MED-EL SYNCHRONY cochlear implant is approved for MRI up to 3 Tesla with the magnet in place (magnet can be removed to eliminate shadow if necessary).
6. An otologist will conduct medical follow-up evaluations at the 3, 6 and 12-month intervals which is standard of care for cochlear implant recipients.

XI. Potential Benefits

- A. Improvement in speech perception abilities in noise with the cochlear implant due to utilization of auditory cues from both ears.
- B. Improvement in localization abilities with the cochlear implant due to utilization of auditory cues from both ears.
- C. Improvement in subjective benefit with the cochlear implant as compared to an unaided condition.

XII. Adverse Events

- A. Anticipated versus Unanticipated Events

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1. Anticipated Events: those events described as potential risks (section X.A.) of the protocol.
 2. Unanticipated Events: events not reported as potential risks (section X.A.).
 - a. Unanticipated serious adverse events are defined as any serious adverse event related to the health or safety or any life-threatening problem or death caused by, or associated with, a device, if that event, problem, or death that was not previously defined in nature, severity, or degree of incidence in the literature or investigational plan. It can also include any other unanticipated serious problem associated with a device that relates to the rights, safety or welfare of subjects.
- B. Reporting adverse events
1. Anticipated events will be reported to the FDA in the annual report
 2. Unanticipated events will be reported to the FDA and UNC IRB within 10 days of the investigator becoming aware of the event, as required by 21CFR 812.150.

XIII. Monitoring

- A. Subjects will be monitored on a case-by-case basis for ongoing or unanticipated medical complications. Adverse events will be tracked on a case-by-case basis and recorded in study binders at the time of occurrence and followed up at resolution. Any adverse event will be reported to the UNC IRB. Should there be concern for the safety of subjects because of their participation in the study by the investigators or the UNC IRB, the study would be halted at least temporarily and a detailed discussion with the investigators and UNC IRB would be undertaken to evaluate the viability of the study.
- B. Subjects can withdraw from the study at any time by notifying the Primary Investigator. If the investigator identifies the need to withdraw a subject from the study for any reason, this will be discussed in person during a scheduled evaluation. In either scenario, the subject will continue to receive care irrespective of their participation in the study. Should a subject not be able to receive auditory stimulation from the cochlear implant, or develops a complication related to participation in the study, their participation in the study will end when their study related morbidity has resolved or is no longer active. Again, this will not affect the medical care for the subject.

XIV. Confidentiality

- A. Subjects will be assigned a specific, anonymous subject number that will be associated with his or her data. Database entry will be by subject number

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only. All personal identifiers will be kept in a separate, secure data file that will be password protected and not associated with the study data. Only investigators will have access to the subject numbers.

- B. Subject specific binders will be maintained in a locked cabinet in the Carolina Crossing research lab. Individual data collection sheets will be coded with the subject number and placed in the subject specific binder at each interval. For analysis, the data will not include identifiable information.
- C. Data will not be shared outside the investigative team except during reporting of anonymous results.
- D. After the closure of the study, subject data will be retained for seven years. At that time, paper data will be shredded and destroyed in a HIPAA compliant manner. Electronic data will be destroyed following UNC policy.
- E. A description of the clinical trial will be available on <http://ClinicalTrials.gov>. This web site will not include information that can identify research subjects.

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Appendix A: Device Information

Appendix B: Procedure Timeline

| | | Candidacy Evaluation | Preoperative Evaluation | Surgery | Initial Follow-Up | Initial Activation | Post-Initial Activation Intervals (months) | | | | |
|-------------------------------|-------------------|----------------------|-------------------------|---------|-------------------|--------------------|--|---|---|---|----|
| | | | | | | | 1 | 3 | 6 | 9 | 12 |
| Informed Consent | | X | | | | | | | | | |
| Medical Assessment | | X | X | X | X | | X | X | | X | |
| Imaging Studies | | | X | | | | | | | | |
| Unaided Diagnostic Assessment | | X | X | | X | X | X | X | X | X | |
| Tympanometry | | X | X | | | X | X | X | X | X | |
| Sound Field Measures | Aided Thresholds | | | | | X | X | X | X | X | |
| | Speech Perception | | | | | X | X | X | X | X | |
| | Localization | | | | | X | X | X | X | X | |
| Subjective Questionnaires | | | | | | X | X | X | X | X | |