Cochlear Implantation in Cases of Single-Sided Deafness

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II. Introduction

Single-sided deafness (SSD) can be defined as moderate-to-profound sensorineural hearing loss with limited speech perception benefit in one ear and normal hearing in the contralateral ear. Though one ear is within the normal hearing limits, SSD results 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 & Tvete, 2010).

This patient population cannot utilize conventional amplification due to the severity of the hearing loss and poor speech discrimination abilities in the affected ear. Current treatment options include: contralateral routing of the signal (CROS) hearing aids, and bone-conduction devices. A CROS hearing aid is a two-part system that includes a microphone/transmitter on the affected ear and a receiver on the normal hearing ear. The microphone/transmitter sends the acoustic signal from the affected ear to the receiver, which is presented to the normal hearing ear. Bone-conduction devices utilize a percutaneous, implanted titanium abutment to send the acoustic signal from the affected side to the normal hearing ear via vibrations. The goal of both of these technologies is to send the signal from the affected side to the normal hearing side, thereby leaving the patient in a unilateral listening condition.

Though CROS hearing aids and bone-conduction devices provide the patient with auditory information from both sides to the better hearing ear, the ability to use binaural cues for speech perception in noise is variable (Kunst et al, 2007), and localization abilities have been found to be at chance (Bosman et al, 2003; Hol et al, 2010). For instance, Bosman et al (2003) compared three listening conditions in SSD subjects: unaided, CROS hearing aid and bone-conduction hearing aid. Subjects were allowed 4 weeks of listening experience for habituation with the CROS and bone-conduction hearing aids. Subjects reportedly experienced no difference in localization abilities between each condition, indicating the current technology available to this population could not improve localization abilities over the unaided condition.

It is of interest whether cochlear implantation of the affected ear would benefit the SSD population. 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 acoustic signal via electrical pulses within the cochlea, which is interpreted by the brain as sound. A steady growth in speech perception acquisition has been reported in conventional cochlear implant subjects up to 6-12 months of listening experience with the external speech processor (Pelizzone, Cosendai, & Tinembart, 1999). Presumably, cochlear implantation may provide the SSD population improvements in speech perception in the affected ear, which cannot benefit from appropriately fit hearing aids. Cochlear implantation may provide a benefit over current treatment options in the SSD population, as it stimulates the auditory pathway on the affected

side, thus allowing for ipsilateral representation of acoustic signals arriving to each ear independently.

Bilateral stimulation of the auditory system has been shown to improve speech perception in spatially-separated noise and localization abilities. These gains have been reported in bilateral cochlear implant recipients (van Hoesel & Tyler, 2003; Nopp, Schleich & D'Haese, 2004; Grantham et al, 2007). For instance, Grantham et al (2007) assessed the localization abilities of bilateral cochlear implant subjects at approximately 5 months of listening experience and then again 10 months later. The authors reported localization abilities did not differ significantly between these two intervals, indicating the ability to use binaural cues for improved localization developed after even limited listening experience with the external speech processors. Considering this subject population has bilateral hearing impairment, it is of interest whether the performance acquisition would be different in an SSD case with cochlear implantation since there is the added benefit of a normal hearing ear.

Cochlear implantation has been reported as a viable treatment option in 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 SSD cases as compared to CROS hearing aids and bone-conduction devices (Arndt et al, 2011). The limitation to this comparison, however, was the subjects had limited listening experience with the alternative treatment options (i.e. CROS hearing aids or bone-conduction device). Though other studies reported no difference in abilities with these technologies after 4 weeks of listening experience (Bosman et al, 2003), long-term duration of listening experience may influence speech perception and localization abilities. Considering this, a control condition of long-term users of current treatment options (i.e. bone-conduction devices) may provide a more accurate comparison with SSD cochlear implant recipients.

The primary goal of this project is to determine whether subjects with SSD experience an improvement in speech perception, localization, and quality of life with a cochlear implant as compared to an unaided listening condition. Secondary aims include: 1) a comparison of speech perception, localization, and quality of life outcomes in the study population to a SSD control group with long-term listening experience with a current treatment option (i.e. bone-conduction device), and 2) a within-subject comparison of speech perception and localization abilities with cochlear implantation versus the bone-conduction test device.

III. Objectives

A. The primary purpose of this feasibility study is to demonstrate the effectiveness of cochlear implantation in subjects with SSD
    1. Postoperative results will be evaluated with speech perception measures, localization tasks, and subjective reports

B. Compare outcomes of cochlear implantation to that of current treatment options (i.e. bone-conduction devices) for SSD cases
    1. Compare speech perception, localization, and subjective outcomes to a control group of implantable bone-conduction device recipients
    2. Assess cochlear implant subjects with a bone-conduction test device and/or previous BAHA device at the preoperative and 12 month follow-up intervals
        a. Comparison of individual subject speech perception and localization abilities between the cochlear implant and bone-conduction device

IV. Definitions

Adjusted Constant Error: the rms deviation of the mean responses from the diagonal, computed after compensating for bias. This procedure reduces the bias when evaluating the relationship between the average response on the azimuth and signal source on the azimuth.

Bimodal: Cochlear implant in one ear and a conventional hearing aid in the contralateral ear

Bone-Conduction Device: A device on the poorer hearing ear that picks up the acoustic signal on the effected side and transmits to the better hearing ear via vibrations through the skull. This is accomplished by either securing the oscillator to the head with a headband or via a percutaneous, implanted titanium abutment.

Cochlear Implant (CI): A two-part system, including the internal electrode array and external speech processor that stimulates the auditory pathway on the effected side. 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 acoustic signal via electrical pulses within the cochlear space, which is interpreted by the brain as sound.

Constant Error: the rms deviation of the average responses from the source positions

Contralateral Routing of Signal (CROS) Hearing Aids: A two-part system consisting of a transmitter microphone on the deafened ear and a receiver on the normal hearing ear. The transmitter sends the signal from the deafened ear to the normal hearing ear. The auditory pathway on the normal hearing ear receives the sound.

Interaural Level Difference (ILD): The difference in sound level between the two ears, dependent on the location of the sound source and the orientation of the head. This binaural cue is typically dominated by high frequencies.

Interaural Timing Difference (ITD): The difference in the time a sound arrives to one ear as compared to the other, dependent on the location of the sound source and the orientation of the head. This binaural cue is typically dominated by low frequencies.

Pure Tone Average (PTA): The average threshold (dB HL) from 500, 1000, and 2000 Hz

Random Error: the standard deviation of responses at each signal source position, averaged across all potential signal sources

Root-Mean-Square (rms) Error: The difference between the location on the azimuth of the sound source and the subject's response on each trial for the localization task

Single-Sided Deafness (SSD): Severe-to-profound sensorineural hearing loss with limited speech perception in one ear and a normal to mild hearing in the contralateral ear

V. Investigational Device

A. Subjects will be implanted with the commercially available MED-EL CONCERT cochlear implant with the standard 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 CONCERT 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.

   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 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.

   Subjects will be fit with the Opus 2 speech processor. The Opus 2 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 Opus 2

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 6.0 Fitting Software will be used to program the Opus 2 speech processor. The MAESTRO 6.0 software, which 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 OPUS 1 or OPUS 2 processor, 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.

VI. Study Duration

A. Enrollment Period
   1. 4 years

B. Study Timeline
   1. Cochlear implant subjects
      a. Each subject's involvement will last approximately 1.5 years, including: candidacy evaluation, preoperative evaluation, surgical procedure, initial activation of the external speech processor, and post-initial activation evaluations (1, 3, 6, 9 and 12-months post-initial activation)

   2. Bone-conduction device control group
      a. One evaluation interval to complete the test battery outlined in section VII.D.

C. Study Endpoint
   1. Cochlear implant subjects
      a. The 12-months post-initial activation interval

   2. Bone-conduction device control group
      a. Completion of the test battery (1 interval) defined in section VII.D.

VII. Methods

All procedures will be conducted by UNC investigators, including board-certified otologists, audiologists, and speech-language pathologists. Fully informed consent will be obtained from all subjects.

A. Participants: CI subjects
Subjects must meet the following inclusion criteria and not exhibit any of the exclusion criteria.

1. Inclusion Criteria
    a. Unilateral moderate-to-profound sensorineural hearing loss
        i. Unaided residual hearing thresholds measured from 250-8000 Hz (PTA ≥70 dB HL in the ear to be implanted)
        ii. Normal to mild residual hearing thresholds from 250-8000 Hz in the contralateral ear (≤35 dB HL at each frequency, 250-8000 Hz)
    b. Greater than or equal to 18 years of age at implantation
    c. Duration of moderate-to-profound sensorineural hearing loss less than or equal to 5 years
        i. Either reported by subject or documented in previous audiograms
        ii. Can be less than or equal to 10 years if the subject consistently utilized hearing technology (such as a bone conduction device or conventional hearing aid) within the past 5 years
    d. Previous experience with a current treatment option for SSD, including a conventional hearing aid, bone-conduction device, or CROS/BICROS technology.
        i. At least one month of listening experience with device
        ii. Dissatisfaction with and/or discontinued use of current treatment option due to: insufficient gain, poor sound quality, and/or lack of perceived benefit.
    e. Aided word recognition in the ear to be implanted of 60% or less as measured with CNC words (50-word list)
        i. When listening with an appropriately fit hearing aid and masking applied to the contralateral ear
        ii. Aided testing will be conducted in a sound-proof booth with the subject seated 1 meter from the sound source, facing 0° azimuth. Recorded materials will be presented at 60 dB SPL.
        iii. The hearing aid output will be measured using NAL-NL1 targets.
    f. Realistic expectations: *a verbal acknowledgement of the potential benefits and risks, and postoperative variation in performance. For instance, cochlear implantation will not restore normal hearing*
    g. Willing to obtain recommended meningitis vaccinations per CDC recommendations
    h. No reported cognitive issues
        i. Pass the Mini Mental State Examination (MMSE) screener
    i. Able and willing to comply with study requirements, including travel to investigational site and study-related activities

2. Exclusion Criteria
    a. Non-native English speaker
        i. Speech perception materials are presented in English
    b. Conductive hearing loss in either ear

c. Compromised auditory nerve, including those with a history of vestibular schwannoma
d. Ossification
e. Inability to participate in follow-up procedures (i.e., unwillingness, geographic location)
f. History of meningitis, autoimmune disease, or any medical condition that contraindicate middle or inner ear surgery or anesthesia
g. Meniere's disease with intractable vertigo
h. Trauma that precludes inner ear surgery
i. Case of sudden sensorineural hearing loss that has not been first evaluated by a physician
j. Pregnancy
    i. Subjects who are pregnant or become pregnant prior to surgery are excluded due to the potential risk of anesthesia to an unborn child.
        a. Subjects who become pregnant after surgery may continue to participate in study procedures
k. Tinnitus as the primary purpose for seeking cochlear implantation
l. Subject obtains a severe or catastrophic score on the Tinnitus Handicap Inventory (Newman, Jacobson & Spitzer, 1996).

3. Enrollment
    a. This study seeks to enroll twenty (20) subjects

B. Participants: Control group
Subjects must meet the following inclusion criteria and not exhibit any of the exclusion criteria.

1. Inclusion Criteria
    a. Unilateral moderate-to-profound sensorineural hearing loss
        i. Unaided residual hearing thresholds from 250-8000 Hz (PTA ≥70 dB HL on the implanted side)
        ii. Normal to mild residual hearing thresholds from 250-8000 Hz in the contralateral ear ≤35 dB HL at each frequency, 250-8000 Hz
    b. Recipient of bone-conduction device on affected side
        i. Recipient of the Bone-Anchored Hearing Aid (BAHA)
            a. Either the Cochlear BAHA Connect or Attract system
        ii. At least 12 months of listening experience with the BAHA system
    c. Greater than or equal to 18 years of age
    d. Duration of moderate-to-profound sensorineural hearing loss less than or equal to 5 years at time of implantation with bone-conduction device (BAHA)
        i. Either reported by the subject or documented in previous audiograms
    e. Willingness to participate in test battery

2. Exclusion Criteria
    a. Non-native English speaker

i. Speech perception materials are presented in English
b. Conductive hearing loss in either ear
c. Compromised auditory nerve, including those with a history of vestibular schwannoma
d. Inability to participate in test battery

3. Enrollment
   a. This study seeks to enroll at least 10 subjects in the control group

C. Timeline

Appendix A graphically depicts the timeline and associated measures

The Candidacy Evaluation and Preoperative Evaluation can either occur during the same visit or two different visits.

1. **Candidacy Evaluation.** This interval may overlap with the Preoperative Evaluation interval.

   a. Audiologic Evaluation
      i. Unaided air- and bone-conduction thresholds in both ears
         a. Air-conduction assessed with inserts
      ii. Unaided word recognition in both ears
         a. Measured with recorded CNC words (50-word list)
         b. Masking provided when appropriate
      iii. Tympanometry in both ears
      iv. Aided word recognition in the affected ear
         a. Measured with recorded CNC words (50-word list)
         b. Masking applied to the contralateral ear
      v. Completion of the Tinnitus Handicap Inventory
      vi. Determine if potential subject meets candidacy criteria

   b. Medical Evaluation
      i. Determine if potential subject is healthy enough to undergo cochlear implantation
      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 alternative treatment options
      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**. This interval may overlap with the Candidacy Evaluation interval.

   The Preoperative Evaluation will be completed within 6 months of the surgery date.

   a. Audiologic Evaluation
      i. Obtain a case history, including but not limited to:
         a. Onset of hearing loss
         b. Progression to moderate-to-profound sensorineural hearing loss
         c. Suspected etiology of hearing loss
      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
         a. Measured with recorded CNC words (50-word list)
         b. Masking provided when appropriate
      iv. Tympanometry in both ears
      v. Subjects will complete the test battery detailed in section VII.D.
         a. Two listening conditions:
            i. unaided
            ii. bone-conduction test device or BAHA
               a. The bone-conduction test device will be the Cochlear BAHA Intenso on a headband
               b. If the subject has a BAHA (Cochlear Connect or Attract system) then her or she may use the external processor associated with that system.
         b. Subjects who listen with a hearing aid in the contralateral ear may utilize this technology during this listening condition
            i. Hearing aid output will be measured using the NAL-NL1 targets
      vi. Counseling on cochlear implant external technology, realistic expectations, study test battery, and postoperative timeline

   b. Medical Evaluation
      i. Subjects will undergo a medical assessment and review of medical history
      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 Concert device approved for 0.2 or 1.5 Tesla

3. **Surgery: Cochlear Implantation**

   Risk factors associated with cochlear implantation are listed in Section XI “Risk Analysis.”

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

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 thresholds
            i. Air-conduction assessed with an insert phone in the contralateral ear
            ii. Bone-conduction thresholds assessed in the surgical ear

   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. Measured with recorded CNC words (50-word list)
         b. Masking provided when appropriate
      iii. Initial activation of external speech processor
         a. Subjects will be fit with the commercially available MED-EL Opus 2 external speech processor (MED-EL Corporation, Innsbruck, Austria), and/or alternative external speech processor. Speech perception and localization measures at follow-up intervals will be conducted with the subject listening with the Opus 2 external speech processor for the aided conditions.
         b. Mapping will be completed by board-certified audiologists. Mapping procedures will be similar to conventional cochlear implant recipients.
      iv. Counseling on the external device and use

   c. One-Month Post-Initial Activation
      i. Completion of test battery listed in VII.D.
      ii. Speech perception assessed with the cochlear implant on and contralateral ear masked
         a. CNC words
      iii. Mapping of the external speech processor

   d. Three-Months Post-Initial Activation
      i. Completion of test battery listed in VII.D.
      ii. Speech perception assessed with the cochlear implant on and contralateral ear masked
         a. CNC words

iii. Mapping of the external speech processor

e. Six-Months Post-Initial Activation
   i. Completion of test battery listed in VII.D.
   ii. Speech perception assessed with the cochlear implant on and contralateral ear masked
      a. CNC words
   iii. Mapping of the external speech processor

f. Nine-Months Post-Initial Activation
   i. Completion of test battery listed in VII.D.
   ii. Speech perception with the cochlear implant on and contralateral ear masked
      a. CNC words
   iii. Mapping of the external speech processor

g. Twelve-Months Post-Initial Activation (study endpoint)
   i. Completion of test battery listed in VII.D.
      a. Additional listening condition: bone-conduction test device or BAHA
   ii. Speech perception with the cochlear implant on and the contralateral ear masked
      a. CNC words
   iii. Mapping of the external speech processor

D. Test Battery

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

1. Unaided Diagnostic Assessment

   a. Air-conduction thresholds in both ears
      i. Air-conduction assessed with insert phones
      ii. Assess bone-conduction thresholds if there is a PTA shift of >15 dB as compared to the previous interval

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.

   Postoperative aided sound field assessment will be completed with the subject listening with the Opus 2 speech processor.

Subjects who utilize a hearing aid in the contralateral ear may continue to use this technology during the sound field test conditions where the contralateral ear remains open. Hearing aid output will be measured using NAL-NL1 targets.

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

b. Speech Perception Measures
   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. AzBio sentences

   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. AzBio sentences
            a. If >50% at SNR+10, then SNR+5
            b. If >50% at SNR+5, then SNR+0
         ii. BKB-SIN sentences with adaptive SNR

   iii. Listening Conditions
      a. Cochlear implant speech processor off
         i. Contralateral ear only
      b. Cochlear implant speech processor on
         i. Cochlear implant + contralateral ear

c. Localization
   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 intensity level for each stimulus presentation will be randomly varied (10 dB around 70 dB SPL)
   iii. The listener will be facing the center speaker during stimulus presentation. The task is to identify the source of the noise. No feedback is provided.
   iv. Listening Conditions

a. Cochlear implant speech processor off
    i. Contralateral ear only
b. Cochlear implant speech processor on
    i. Cochlear implant + contralateral ear

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)
    c. Tinnitus Handicap Inventory, Newman, Jacobson & Spitzer (1996)

E. Aural Rehabilitation
    1. Subjects will participate in two aural rehabilitation sessions with a board-certified speech-language pathologist. One session will be after the initial activation of the external speech processor. This will occur either on the same day as the initial activation or within the first 2 weeks of listening experience. The second session will be scheduled in conjunction with the 1-month post-initial activation interval.

VIII. Proposed Claims

A. Demonstrate the effectiveness of cochlear implantation in SSD subjects

    1. Demonstrate an improvement in speech perception abilities, localization, and/or subjective benefit in an aided (cochlear implant on) versus an unaided (cochlear implant off) condition

B. Cochlear implantation provides similar or superior speech perception, localization, and/or quality of life as compared to that found with bone-conduction devices

    1. Comparison with control group performance
    2. Comparison within subject when listening with bone-conduction test device

IX. 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 of aided speech perception performance on word and sentence materials in the post-initial activation intervals to evaluate trends over time

a. Comparison of the difference between the aided and unaided conditions at each follow-up interval

2. Comparison of localization abilities in the post-initial activation intervals
   a. Comparison of the difference between the aided and unaided conditions for each follow-up interval
   b. Compute the overall rms error, random error, constant error, and adjusted constant error, as described by Grantham et al (2007)

3. Comparison of subjective report scores in the post-initial activation intervals

C. The incidence of interference between ears will be assessed by comparing the speech perception performance in the 0° azimuth conditions for the contralateral ear only versus cochlear implant + contralateral ear conditions for each subject, as well as the individual's subjective report.

A sample size for the cochlear implant recipient cohort of 20 subjects was selected due to known variability in conventional cochlear implant recipient outcomes and to allow for possible dropouts (approximately 20%). A comparable study, Hansen, Gantz & Dunn (2013) evaluated 29 cochlear implant subjects with SSD, which included etiologies of sudden sensorineural hearing loss, Meniere's disease, and vestibular schwannoma. Authors reported a high degree of variability in their sample. This project will not enroll all of the etiologies included in the Hansen, Gantz & Dunn (2013) analysis (such as, Meniere's Disease with intractable vertigo or history of vestibular schwannoma), therefore a smaller sample size was selected. The inclusion/exclusion criteria associated with this study, as compared to the heterogeneity of the Hansen, Gantz, & Dunn (2013) subject sample, will allow for more generalized comments about subjective and objective outcomes of cochlear implantation in cases of SSD.

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

X. 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 result in termination of the study.

B. Primary effectiveness endpoint
   1. The primary effectiveness endpoint is the comparison of speech perception, localization abilities and/or subjective report when the cochlear implant is on versus off.

XI. Risk Analysis

A. Potential risks

The following are risks associated with the MED-EL Concert implant, which is also included in the device description:

1. Loss of residual hearing
2. Increased vertigo
3. Delay of healing of the scar
4. Impairment of the sense of taste
5. Potential for swallowing difficulties
6. Numbness
7. Increased tinnitus
8. Stimulation of the facial nerve
9. Temporary pain and uncomfortable sounds during stimulation

The following are potential risks the subject may experience related to the study procedure:

1. Surgical
    a. Facial nerve injury
        i. Facial nerve monitoring is conducted during the surgical procedure
    b. Infection
        i. All subjects will be counseled regarding bacterial meningitis and recommended vaccinations
    c. Bleeding
    d. Cerebrospinal fluid (CSF) leak
    e. Pain
    f. Scarring

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. Movement of the internal receiver
    i. Discomfort from electric stimulation
    j. Facial nerve stimulation
    k. Headache

l. Dizziness
m. Altered taste (i.e. reports of metallic tastes on the same side of the tongue as the surgical ear)
n. Fatigue during follow-up assessment (completion of the test battery and/or mapping)
o. The internal device may fail, requiring revision cochlear implantation
p. The sound from the cochlear implant may interfere with the better hearing ear.

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.
   a. The test battery includes a listening condition to assess the monaural performance of the contralateral ear. Interference of the cochlear implant on the performance of the contralateral ear can be evaluated by comparing the contralateral ear only condition to the cochlear implant + contralateral ear conditions when tested at 0° azimuth, as well as, review the subjective benefit via the subjective questionnaires. If interference is found to impact speech perception and subjective benefit, the subject may elect to discontinue use of the cochlear implant and would still have access to currently approved technologies for SSD.
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 when warranted.
   a. *The MED-EL CONCERT cochlear implant is approved for MRI of 0.2 or 1.5 Tesla
6. An otologist will conduct medical follow-up evaluations at the 6 and 12-month intervals, which is standard of care for cochlear implant recipients.
7. Age appropriate vaccinations per the CDC recommendations will be completed by each subject prior to implantation. Subjects will be counseled regarding meningitis vaccinations and directed where to obtain them by their implanting physician.

XII. 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 preoperative performance.

The potential benefits of cochlear implantation in cases of SSD are suspected to outweigh the risks listed in Section XI.A. The study sample will include subjects with previous history with current hearing technology options for SSD, who are dissatisfied with this technology and/or have discontinued use of the technology. This sample is similar to those in previously published reports who have benefited from cochlear implantation.

This study also includes a comparison to a currently approved technology option for SSD, bone-conduction technology. This comparison will be used to assess outcomes between technologies, but also to determine whether individual subjects experience differences in performance between the two technologies. The risks associated with cochlear implantation in this population are also reduced considering subjects may continue to use currently approved technologies for SSD if they do not obtain subjective and objective improvements from cochlear implantation.

XIII. Adverse Events

A. Anticipated versus Unanticipated Events
   1. Anticipated Events: those events described as potential risks (section XI.A.) of the protocol

   2. Unanticipated Events: events not reported as potential risks (section XI.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.

   3. Serious Adverse Event: Serious injury means an injury or illness that: 1) is life-threatening, 2) results in permanent impairment of a body function or permanent damage to a body structure, or 2) necessitates medical or surgical intervention to preclude permanent impairment to a body function or permanent damage to a body structure.
      a. Permanent means an irreversible impairment or damage to a body structure or function, excluding trivial impairment or damage.
      b. Revision cochlear implantation will be considered a serious anticipated adverse event.

B. Reporting adverse events
   1. All adverse events will be reviewed by the PI during the preparation of the annual reports to the FDA and UNC IRB. Combined adverse events will be listed in an excel spreadsheet. Frequent adverse events will be discussed with co-investigators.

   2. Anticipated events will be reported to the FDA in the annual report

3. 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.

XIV. 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 and for any reason 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. Subjects may also be withdrawn if residual hearing changes in the contralateral (better hearing ear) to a moderate hearing loss of worse. In either scenario, the subject will continue to receive care irrespective of their participation in the study.

C. Investigative Team
   1. The Principal Investigator will review completed Consent Forms and Case Report Forms, including determining candidacy.
   2. The Principal Investigator will ensure that study site Standard Operating Procedures are followed by the study team.
   3. Responsibilities for all study team members will be recorded in a Study Delegation Log. Not all team members will be responsible for all activities.
   4. Communications between the Principal Investigator and study team will be maintained in the regulatory binder.
   5. Source data will be maintained with completed Case Report Forms (such as, speech perception score sheets) when available.

XV. 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 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 included 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.

XVI. References

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Appendix A: Procedure Timeline

Intervals		1	2	3	4	5	6	7	8	9	10
		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						
Cochlear Implant Surgery				X							
Imaging Studies			X								
Unaided Assessment	**AC Thresholds**	X	X		X*	X	X	X	X	X	X
	BC Thresholds	X			X	X**					
	CNC Words	X				X					
Tympanometry		X	X			X	X	X	X	X	X
Sound Field Measures [Unaided AU]	**Speech Perception** in Quiet		X				X	X	X	X	X
	Speech Perception in Spatially Separated Noise		X				X	X	X	X	X
	Localization		X				X	X	X	X	X
Sound Field Measures [BC Device]	**Aided Thresholds** (contra masked)		X								X
	Speech Perception in Quiet		X								X
	Speech Perception in Spatially Separated Noise		X								X
	Localization		X								X
Sound Field Measures [Cochlear Implant On]	**Aided Thresholds** (contra masked)						X	X	X	X	X
	Speech Perception (contra masked)						X	X	X	X	X
	Speech Perception in Quiet (contra open)						X	X	X	X	X
	Speech Perception in Spatially Separated Noise (contra open)						X	X	X	X	X
	Localization (contra open)						X	X	X	X	X
Subjective Questionnaires			X				X	X	X	X	X
Aural Rehabilitation						X	X				

*Air conduction thresholds assessed in the contralateral ear only.

**Only if fluctuation noted in AC thresholds