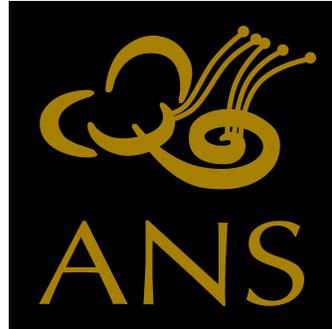


SELECTED ABSTRACTS
in order of presentation

**ORAL
PRESENTATIONS**



54th Annual Spring Meeting

AMERICAN NEUROTOLOGY SOCIETY

***May 3-4, 2019
JW Marriott Austin
Austin, TX***

Five Years of Electric-Acoustic Stimulation (EAS) Listening Experience: Hearing Preservation and Benefits of Acoustic Representation of the Fundamental Frequency

*Elizabeth Perkins, MD; Margaret Dillon, AuD
Kevin Brown, MD, PhD*

Objectives: To compare long term speech recognition performance of cochlear implant (CI) recipients with and without hearing preservation. To determine the influence of acoustic representation of 125 Hz on speech recognition with electric-acoustic stimulation (EAS).

Study Design: Prospective clinical trial

Setting: Tertiary referral center

Patients: Twenty-six subjects with preoperative bilateral, normal to moderate low-frequency hearing sloping to severe-to-profound high-frequency hearing loss and an aided CNC word score in the ear to be implanted of less than or equal to 60% correct.

Interventions: Subjects underwent cochlear implantation with a short electrode array (FlexEAS) and grouped into either preserved low-frequency hearing fit with EAS (<80 dB HL at 125 Hz; EAS group) and those with unaidable low-frequency hearing (CI-alone group).

Main outcome measures: Pre- and post-operative CNC words in quiet, and AzBio sentences in a 10-talker babble (10 dB SNR).

Results: At 5 years, the speech recognition of the CI-alone group (n=9) continued to exceed preoperative abilities (t(8)=-5.83, p<0.001). The EAS group (n=17) demonstrated significantly better performance on CNC words (t(13.2)=3.53, p=0.004) and AzBio sentences (t(16.9)=2.60, p=0.02) compared to the CI-alone group. The EAS group was stratified by frequencies of aidable residual hearing [125 Hz only (n=5), 125 & 250 Hz only (n=8), and >250 Hz (n=4)]. Each subgroup had significant improvement in speech recognition scores, including those with aidable hearing at only 125 Hz.

Conclusion: Even when residual hearing was lost, subjects experienced a significant improvement in speech recognition. The acoustic representation of 125 Hz provides benefit for EAS users due to better resolution of the fundamental frequency.

Define Professional Practice Gap & Educational Need: 1. Long-term, prospective data on speech perception outcomes of hearing preservation failures following cochlear implantation with the MED-EL FlexEAS (Flex 24) has yet to be reported
2. Of those patients that failed hearing preservation, the value of hearing at the fundamental frequency of 125 Hz has yet to be determined

Learning Objective: 1. To compare long term speech recognition performance of cochlear implant recipients with and without hearing preservation. 2. To determine the influence of acoustic representation of 125 Hz on speech recognition with electric-acoustic stimulation

Desired Result: Attendees will have a better understanding of the importance of hearing at 125 Hz in electroacoustic stimulation. In addition, attendees will gain knowledge of long-term outcomes of CI recipients with and without hearing preservation with the MED-EL FlexEAS electrode.

Level of Evidence - Level V - Case series, studies with no controls

Indicate IRB or IACUC Approval: Approved

General Health Quality of Life Instruments Underestimate the Impact of Bilateral Cochlear Implantation

*Theodore R. McRackan, MD, MSCR; Joshua E. Fabie, BS
Prashant N. Bhenswala, MD; Shaun A. Nguyen, MD
Judy R. Dubno, PhD*

Objective: Determine the extent to which bilateral cochlear implantation increases patient-reported benefit as compared to unilateral implantation and no implantation.

Data Sources: PubMed, Scopus, CINAHL, and Cochrane databases searches were performed using the keywords ("Cochlear Implant" or "Cochlear Implantation") and ("bilateral").

Study Selection: Studies assessing hearing/CI-specific (CI) and general-health-related (HR) quality of life (QOL) in adult patients after bilateral cochlear implantation were included.

Data Extraction: Of the 31 articles meeting criteria, usable QOL data were available for 16 articles (n=355 bilateral CI recipients).

Data Synthesis: Standardized mean difference (Δ) for each measure and weighted effects were determined. Meta-analysis was performed for all QOL measures and also independently for hearing/CI-specific QOL and HRQOL.

Conclusion: When measured using hearing/CI-specific QOL instruments, patients reported very large improvements in QOL comparing before cochlear implantation to bilateral CI ($\Delta=2.07$ [1.76 to 2.38]) and medium improvements comparing unilateral CI to bilateral CI ($\Delta=0.51$ [0.32 to 0.71]). Utilization of parallel vs. crossover study design did not impact QOL outcomes ($\chi^2=0.512$, $p=0.47$). No detectable improvements were observed in either CI transition when using HRQOL instruments (no CI to bilateral CI: $\Delta=0.40$ [-0.02 to 0.81]; unilateral CI to bilateral CI: $\Delta=0.22$ [-0.02 to 0.46]). The universal nature of HRQOL instruments may render them insensitive to the medium to large QOL improvements reported by patients using hearing/CI-specific QOL instruments. Given that HRQOL instruments are used to determine the economic benefit of health interventions, these measurement differences suggest that the health economic value of bilateral cochlear implantation has been underestimated.

Define Professional Practice Gap & Educational Need: 1. Lack of knowledge regarding the quality of life improvement after bilateral cochlear implantation as reported through patient reported outcome measures, which are evaluated by the FDA and CMS. 2. inconsistencies between outcomes after bilateral cochlear implantation as measured using hearing/cochlear-specific quality of life instruments and general health quality of life instruments. 3. Lack of awareness of the above differences can impact the health economic evaluation of bilateral cochlear implantation.

Learning Objective: 1. Attendees will understand the quality of life improvement after bilateral cochlear implantation reported using hearing/cochlear implant-specific instruments. 2. Attendees will understand the measurement differences after bilateral cochlear implantation between hearing/cochlear implant-specific and general health-related quality of life instruments. 3. Attendees will understand how the lack of general health quality of life improvement undervalues the health economic benefit of bilateral cochlear implantation

Desired Result: 1. Attendees will be able to discuss the hearing-and cochlear implant-specific quality of life improvements from no cochlear implants to bilateral cochlear implants. 2. Attendees will be able to discuss the hearing-and cochlear implant-specific quality of life improvements from unilateral cochlear implantation to bilateral cochlear implantation.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Exempt

Slim Perimodiolar Arrays are as Effective as Slim Lateral Wall Arrays for Functional Hearing Preservation after Cochlear Implantation

*Erika Woodson, MD; Rebecca Nelson, MD
Thomas Haberkamp, MD; Sarah Sydlowski, AuD, PhD*

Objective: To compare functional hearing preservation (HP) with a slim perimodiolar array (SPA) and a slim lateral wall array (SLW) in cochlear implantation (CI)

Study design: Retrospective chart review

Setting: Tertiary referral center

Patients: All adult, post-lingual CI recipients with serviceable preoperative hearing serially implanted with SPA or SLW electrodes from July 2015 to August 2018.

Intervention(s): Cochlear implantation

Main outcome measure(s):

Hearing preservation (HP). Patients with a low frequency pure tone average (LFPTA) (125, 250, 500 Hz) threshold < 80dB were considered HP candidates based on preoperative audiograms. Postoperative audiograms were obtained before activation. Successful HP was defined as retention of LFPTA <80 dB. The change in LFPTA (deltaLFPTA) was also calculated.

Results: 123 patients were implanted with either the SPA or SLW electrodes, 81 (40,42) of whom were HP candidates with postoperative audiograms. Average preoperative LFPTA was 53.5 dB and 52.4 dB for SPA and SLW respectively, with a mean deltaLFPTA of 24.1 and 24.6 dB. Successful HP was achieved in 22 (55%) and 22 (52%). Preoperative LFPTA, deltaLFPTA, and postoperative LFPTA were not significantly different (p=0.39, 0.47, 0.28) between electrodes.

Conclusions: The SPA is as effective at immediate functional HP after CI as a SLW.

Define Professional Practice Gap & Educational Need: 1. Lack of contemporary knowledge of the perimodiolar electrode as a design which supports hearing preservation.

Learning Objective: 1. Attendees will recognize that perimodiolar electrode arrays can achieve similar clinical results as lateral wall arrays for functional hearing preservation.

Desired Result: Attendees will recognize that hearing preservation is achievable with a perimodiolar array and will integrate this knowledge into their surgical decision-making.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

Predicting Changes in Tinnitus after Unilateral Cochlear Implantation in Adults

*Peter R. Dixon, MD; David Shipp, MA
Kari Smilsky, MCLSc; Vincent Y. Lin, MD
Trung Le, MD, PhD; Joseph M. Chen, MD*

Objective: Identify characteristics associated with odds of improved tinnitus after cochlear implantation

Study design: Retrospective cohort

Setting: Academic center

Patients: Adult unilateral cochlear implant (CI) recipients implanted between 1996 and 2017 with pre-implant tinnitus

Interventions: Candidate predictors included 25 pre-operatively measured characteristics

Main outcome measure: Clinically significant improvement in Tinnitus Handicap Inventory (THI) or tinnitus resolution at 1-year post-activation

Results: Of the 345 patients with tinnitus, 228 (66.1%) had improved or resolved at 1-year post-activation. Identified independent predictors were baseline hearing in noise test in quiet condition (HINTq), hearing handicap inventory (HHI), THI, and device manufacturer. Confidence that each variable is truly an independent predictor in our population was high. Each of the 4 identified predictors was selected in more than 57% of 1,000 bootstrap replicates of the dataset. Each 10% increase in HINTq was independently associated with 15% reduction in odds of improved or resolved tinnitus (OR 0.85). Each 10-point increase in THI and HHI was associated with 1.2 and 1.3 times higher odds of the composite outcome respectively. Relative to Advanced Bionics (AB), those implanted with Cochlear devices had 76% lower odds of improved or resolved tinnitus (OR 0.24) and Med-El devices had 30% lower odds of improved or resolved tinnitus (OR 0.70).

Conclusion: Patients with worse pre-implant sentence recognition and higher handicap from hearing impairment and tinnitus have higher odds of improved tinnitus after CI. Advanced bionics CI systems may be independently associated with higher odds of improved tinnitus compared with Cochlear and Med-El devices. Potential explanations for this finding are discussed.

Define Professional Practice Gap & Educational Need: Lack of understanding of factors that influence tinnitus-related quality of life after unilateral cochlear implantation in adults

Learning Objective: Identify patients who are more likely to have improved or resolved tinnitus after cochlear implantation

Desired Result: Improve ability to predict changes in tinnitus after cochlear implantation for the purposes of counselling patients, particularly in situations where a cochlear implant is being considered as a treatment for debilitating tinnitus.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

Cognitive Functions in Adults Receiving Cochlear Implants: Predictors of Speech Recognition Outcomes and Changes after Implantation

*Aaron C. Moberly, MD; Michael S. Harris, MD
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Christin Ray, PhD, CCC-SLP*

Hypothesis: Significant variability in speech recognition persists among adults who receive cochlear implants (CIs). Two hypotheses were tested: (1) pre-operative cognitive skills assessed visually would predict post-operative speech recognition at 6 months after CI; and (2) cochlear implantation would result in benefits to cognitive processes at 6 months.

Background: Neurocognitive functions, such as working memory, processing speed, inhibition-concentration, and nonverbal reasoning, have been identified as contributors to speech recognition in adults with hearing loss, and particularly in CI users. There is also mounting evidence that cochlear implantation can lead to improvements in cognitive functioning. This study examined whether pre-operative cognitive functions would predict speech recognition after cochlear implantation, and whether cognitive skills would improve as a result of implantation.

Methods: Twenty postlingually deafened adult CI candidates were tested pre-operatively using a visual battery of tests to assess working memory, processing speed, inhibition-concentration, and nonverbal reasoning. Six months after implantation, participants were assessed for recognition of isolated words and words in sentences in quiet, and cognitive tests were repeated.

Results: Word and sentence recognition at 6 months of CI use were predicted by pre-operative working memory capacity ($\beta = .38$ to $.64$), and less so by nonverbal reasoning ($\beta = .18$ to $.31$). Improvements in processing speed and a measure of working memory were demonstrated from pre- to post-CI.

Conclusions: Findings provide evidence that pre-operative cognitive factors contribute to speech recognition outcomes for adult CI users, and support the premise that implantation may lead to improvements in some cognitive functions.

Define Professional Practice Gap & Educational Need: 1. Lack of contemporary knowledge regarding effective pre-operative predictors of post-operative cochlear implant patient performance. 2. Inconsistencies in the literature regarding the effects of cochlear implantation on cognitive functions.

Learning Objective: 1. To understand potential pre-operative cognitive predictors of outcome performance for adult cochlear implant users 2. To become aware of possible cognitive effects of cochlear implantation in adults.

Desired Result: Attendees will be better able to counsel their patients regarding pre-operative contributions to post-operative performance, as well as the potential benefits to cognition of receiving and using a cochlear implant.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Preclinical Evaluation of Compounds Targeting Schwannoma in an NF2 Mouse Model.

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Objective/Hypothesis: A genetically modified mouse model of NF2 may be an *in vivo* system for testing therapeutics that may have an effect on NF2 related vestibular schwannoma (VS). 100% of the postn-Cre NF2 (flox/flox) mice develop schwannoma in the dorsal root ganglia (DRG) and intracranially. Mice also progressively develop hearing loss as determined by auditory brainstem response testing (ABR). Multiple chemotherapeutic agents that showed previous *in vivo* or *in vitro* positive data were assessed. The objective of the current study is to validate a preclinical chemotherapy for reduction in size of VS.

Study Design: *In vivo* mouse study.

Methods: Fourteen mice were treated for a 3-month period with agent and compared to a control group that was gavage fed the vector alone. ABR testing was performed throughout the study period at monthly intervals. Mice were examined via necropsy section and DRG were assessed for tumor size and compared.

Results: Tumor size, as determined by volume of DRG schwannoma, was reduced by Brigatinib, Dasatinib, and AR42 compared to controls. GSK2126458, Panobinostat, and CuDC-907 showed no difference. The behavior of the mice was similar to the control. ABR testing showed a statistically significant trend toward less decline in hearing for the treated mice with Brigatinib, Dasatinib, and AR42.

Conclusions: Brigatinib, Dasatinib, and AR42 suppresses growth of DRG schwannoma in a novel genetically engineered mouse model of NF2. This is further data that supports use of these compounds in human trial.

Define Professional Practice Gap & Educational Need: Preclinical testing for chemotherapies for NF2 related disease has a lack of awareness in the Neurotology community of the research direction of treatments in preclinical models.

Learning Objective: To illustrate progress of testing preclinical chemotherapies for NF2 in preclinical NF2 mouse model.

Desired Result: To expand knowledge of chemotherapies for future clinical trials and application of that knowledge.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Vestibular Schwannoma Tumor Size is Correlated with Acute Vestibular Symptoms after Gamma Knife Therapy

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Objective: To assess how vestibular schwannomas tumor characteristics correlate with vestibular symptoms after Gamma Knife (GK) surgery.

Study Design: A retrospective chart review of patients undergoing gamma knife treatment for vestibular schwannoma at this institution from 2005 to 2018 was performed.

Setting: Tertiary referral center

Patients: All patients receiving GK surgery for vestibular schwannomas were evaluated. Patients with neurofibromatosis 2 or prior surgery were excluded.

Main outcome measures: Clinical records were assessed for tumor dimensions, cochlear radiation dose, development of post-treatment vestibular symptoms, and necessity of vestibular rehabilitation.

Results: Out of 134 patients, all patients received a radiation dose between 12 and 13 Gy. The average age was 60 years, with 51.9% of patients male and 48.1% female. Nineteen (14.2%) patients developed new and 25 (18.7%) patients developed worsening vestibular symptoms (vertigo, dizziness, and imbalance) within 6 months after GK. Out of 13 patients undergoing vestibular rehabilitation, 10 reported an improvement. Pre-treatment tumors were significantly smaller for patients who developed new or worsening acute vestibular symptoms (mean 1.51 cm vs 1.74 cm, $p = 0.0357$), with 24.5% of patients with tumors smaller than 1.6 cm offered vestibular rehabilitation at 6 months compared to just 9.1% of those with tumors greater than 1.6 cm ($p = 0.0248$, OR=3.25, 95% CI (1.23,8.58)).

Conclusions: Vestibular schwannomas smaller than 1.6 cm were significantly associated with higher rates of post-GK vestibular symptoms requiring rehabilitation. Tumor size may be used to counsel patients on the likelihood of post-GK vestibular symptoms and vestibular rehabilitation.

Define Professional Practice Gap & Educational Need: It is difficult to predict the likelihood of developing post-gamma knife vestibular symptoms for vestibular schwannoma patients. There are currently few effective prognostic markers for predicting vestibular symptoms after gamma knife radiation. Vestibular symptoms have a significant impact on quality of life, and we felt there was a gap in understanding the pre-treatment tumor characteristics that contribute to potential post-treatment vestibular symptoms. Our work identifies tumor size as a potential prognostic indicator of post-treatment vestibular symptoms, which will help physicians better counsel patients on expectations with gamma knife therapy for vestibular schwannoma.

Learning Objective: To understand the influence of pre-gamma knife tumor size on the likelihood of developing post-gamma knife acute vestibular symptoms. -To identify the increased risk of developing acute vestibular symptoms requiring vestibular rehabilitation for patients with smaller tumors.

Desired Result: We hope that physicians will consider the pre-treatment size of vestibular schwannomas when counseling patients on the likelihood of post-gamma knife vestibular symptoms.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

NEUROTOLOGY FELLOW AWARD

What Genes Can Tell: A Closer Look at Vestibular Schwannoma

*Ksenia A. Aaron, MD; Zarko Manojlovic, PhD
Sharon Chang, BS; Eric Kwok, BS; Nathan Tu, MD, MPH
Kyle Hurth, MD, PhD; Rick A. Friedman, MD, PhD*

Objective: Comprehensive molecular profiling of radioresistant and cystic vestibular schwannoma (VS) subtypes.

Study Design: Our study utilized somatic whole-exome sequencing (WES), RNA-sequencing, and correlated clinical data from 14 selected fresh frozen tumor samples with matched blood.

Setting: Hospital setting research facility.

Patients: Patients that were diagnosed with VS and necessitated surgery for treatment. Inclusion: Cystic, radioresistant and malignant transformation tumors matched to age and tumor volume, with solid naïve VS samples as control; Exclusion: NF-2 patients.

Intervention(s): WES was based on the custom probes for more informative copy number analysis, and probes that tile across known regions of known cancer translocations. The DNA, derived from the blood, was utilized as the internal control to reduce false-positive calling. For WES data, we achieved a mean coverage of 124X for VS and for RNA-seq, we generated an average of 80 million read pairs.

Main Outcome Measure(s): Analysis of genetic landscape of various VS subtypes by performing deep next-generation sequencing.

Results: The mutation rate of cystic, radioresistant and malignant transformation samples had drastically higher number of non-silent mutations vs the naïve ($p=0.0014$). In addition to already published data, such as frequency of 22q loss, somatic mutational analysis unraveled significantly mutated genes such as FOXD4, IGFN1, FNM2, NOTCH4 and ALK.

Conclusions: High quality, high-resolution WES allowed us to identify potential differences in the genomic and molecular landscape of cystic and radioresistant VS. Our results can help advance the understanding of the pathophysiology of these tumor subtypes and pinpoint the molecular targets for alternative treatment strategies.

Define Professional Practice Gap & Educational Need: Approximately 10% of vestibular schwannomas (VS) display either cystic and radioresistant features. These VS tumor subtypes are a different clinical entity as they are usually characterized by unpredictable biologic behavior with frequent involvement of cranial nerves and a relatively rapid rate of growth. There is a lack of knowledge in the precise etiology of these VS subtypes, even though various mechanisms have been proposed.

Learning Objective: Using high-quality, high-resolution whole-exome sequencing to evaluate molecular profiling of radioresistant and cystic VS.

Desired Result: Results from our study can help advance our understanding of the pathophysiology of these VS tumor subtypes and pinpoint the molecular targets in alternative treatments.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Effects of Single-Fraction Radiation on Merlin-Deficient and Normal Schwann Cells in Vitro

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Nagy Elsayyad, MD; Michael Ivan, MD
Cristina Fernandez-Valle, PhD; Fred F. Telischi, MD
Christine T. Dinh, MD*

Background: Vestibular schwannomas are benign tumors of the cochleovestibular nerve that develop from *NF2* mutations leading to merlin dysfunction and/or loss. Although tumor control rates with stereotactic radiosurgery are >85% at 10 years, hearing preservation rates approach 25%. The first steps toward optimizing radiation protocols are determining the molecular and cellular effects of radiation on wild type (WT-SC) and merlin-deficient Schwann cells (MD-SC).

Hypothesis: WT-SCs are more resistant to specific dosages of single fraction (SF) radiation than MD-SCs through differential expression of apoptosis, DNA damage and repair.

Methods: Human and murine WT-SCs and MD-SCs were seeded on 96-well plates and 16-well culture slides and treated with SF-radiation (0-18 Gy). Cell-based assays were performed to assess viability, cytotoxicity, and apoptosis. Immunohistochemistry was performed to determine expression of DNA breaks and activation of DNA repair mechanisms. Statistical analysis was performed with Mann-Whitney U and Kruskal-Wallis tests.

Results: SF-radiation initiated double-strand DNA breaks in all cell-lines; however, there was differential activation of DNA repair mechanisms, cleaved caspase-3/7 expression, and loss of membrane integrity. Rat WT-SCs demonstrated remarkable resistance to SF radiation. In contrast, human WT-SCs demonstrated dose-dependent reductions in viabilities. Viabilities, however, were significantly better than human and mouse MD-SCs at several radiation dosages.

Conclusion: MD-SCs are more susceptible to SF-radiation-induced loss than WT-SCs. WT-SCs may activate multiple DNA repair mechanisms to evade radiation injury at specific radiation dosages. Further investigations into the radiobiology of vestibular schwannoma and normal nerve are critical in understanding and improving clinical outcomes in the future.

Define Professional Practice Gap & Educational Need: 1. The most optimal stereotactic radiosurgery protocol to maximize tumor control and hearing preservation rates in sporadic vestibular schwannoma is controversial. 2. There is a need to understand how radiation affects vestibular schwannoma and adjacent normal nerve on molecular and cellular levels to identify better radiation strategies to maximize tumor control and hearing preservation rates.

Learning Objective: Addressing both 1 and 2 above, we aim to understand the differences in radiobiological response of normal and pathological merlin-deficient Schwann cells that can potentially affect clinical outcomes when treating vestibular schwannoma.

Desired Result: - Gain in physician knowledge that radiation causes cellular injury by initiating double-strand DNA breaks at specific radiation dosages. - Gain in physician knowledge that evasion of radiation injury can occur through activation of DNA repair mechanisms. - Gain in physician knowledge of how understanding the radiobiology of vestibular schwannoma and adjacent nerve constituents can aid in identifying radiation protocols that can improve clinical outcomes.

Level of Evidence - Does not apply-you will be asked to explain - in vitro study

Indicate IRB or IACUC Approval: Exempt

The Role of The Spiral Ligament in Sensorineural Hearing Loss in Humans: A Temporal Bone Study

Karen B. Teufert, MD; Fred H. Linthicum Jr., MD

Hypothesis: Spiral ligament fibrocyte pathology may be the primary cause of sensorineural hearing loss (SNHL).

Background: Animal studies show that cell loss in the spiral ligament precedes loss of hair cells and/or neurons, suggesting fibrocyte pathology as the primary cause of sensory cell degeneration. However, involvement of other structures confounds the role of spiral ligament.

Methods: Sixty-nine temporal bones from patients with varying degrees of SNHL or normal hearing, having normal cochlear sensorineural structures, were studied using quantitative evaluation of spiral ligament fibrocytes under light microscopy. Double staining with hematoxylin was used to quantify fibrocytes of each type. Fibrocyte quantity was compared between SNHL and normal hearing, and correlation coefficients were computed between PTA and fibrocyte counts. Expression of ion transport mediating enzymes Na,K-ATPase, CAII, CK, and connexin 26 was assessed by immunohistochemistry to evaluate fibrocyte function.

Results: All correlations between PTA and spiral ligament were negative; the fewer the fibrocytes, the poorer the hearing (higher PTA). Five of 25 comparisons achieved significance, primarily in middle cochlear turn segments. Significant correlation coefficients (all $p < .05$) were small to moderate (-.347 to -.428), increasing when including only subjects tested within two years of death (-.472 to -.558). Preliminary results using CAII antibody and double hematoxylin staining suggest functionality of fibrocytes may be a more important factor.

Conclusions: Fibrocyte quantity may be a contributing factor to hearing loss severity in humans, but explains only a portion of variability in SNHL. Fibrocyte functionality may be a more critical factor, but further study is required.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge.

Learning Objective: Papers reporting data on animals have suggested that cell loss in the spiral ligament precedes the loss of hair cells and/or neurons in both space and time suggesting that fibrocyte pathology may be the primary cause of the hearing loss and ultimate sensory cell degeneration in animals, but this has not been shown in humans. Previous studies by our institution have suggested that the spiral ligament may play a role in sensorineural hearing loss (SNHL) but the involvement of other structures (stria vascularis, hair cells, dendrites, spiral ganglion cells, endolymphatic sac) in those cases makes it difficult to assess whether the hearing loss was caused by degeneration of those structures or if the spiral ligament pathology was the primary cause of hearing loss, as proposed by others. Therefore, the learning objective of the present study is to determine whether spiral ligament fibrocyte pathology may be a primary cause of SNHL in humans. Temporal bones from patients with varying degrees of SNHL will be selected after exclusion of other possible causes of SNHL, such as hair cell degeneration, loss of dendrites, or decreased spiral ganglion counts. Temporal bones of patients with normal hearing and normal inner ear structures will be used for comparison.

Desired Result: The study will help attendees understand the concept that spiral ligament fibrocyte pathology may be the primary cause of sensorineural hearing loss (SNHL) and that fibrocyte quantity may be a contributing factor to hearing loss severity in humans, but explains only a portion of variability in SNHL. Fibrocyte functionality may be a more critical factor, but further study is required.

Level of Evidence - Level V - Case series, studies with no controls

Indicate IRB or IACUC Approval: Exempt

Anatomical and Functional Consequences of Microneedle Perforation of Round Window Membrane

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Hypothesis: Microneedles can create microperforations in the round window membrane (RWM) without causing anatomic or physiologic damage.

Background: A means for reliable delivery of agents into the inner ear for therapeutic purposes remains a formidable challenge. A novel approach harnesses microneedles to facilitate intracochlear access via the RWM for both diagnostic and therapeutic purposes. In this study, we investigate the anatomical and functional consequences of microneedle perforations on guinea pig RWMs in vivo.

Methods: Single 3D-printed, 100 μm diameter microneedles were used to perforate the guinea pig RWM via the postauricular sulcus (n=18). Hearing was assessed both before and after microneedle perforation using compound action potential (CAP) and distortion product otoacoustic emissions (DPOAE). Confocal microscopy was used ex vivo to examine RWM to measure the size, shape, and location of the resulting microscopic perforations and document healing at one week.

Results: The microneedles created precise perforations measuring $99.7\pm 31.7 \times 36.3\pm 19.7 \mu\text{m}$ without tearing the membrane. Compared to pre-perforation CAP and DPOAE measurements, some guinea pigs experienced temporary threshold shift immediately following RWM perforation but all guinea pigs recovered and showed no lasting hearing loss at 1 week post-perforation. At 1 week, all perforations were observed to heal.

Conclusion: Microneedles can be used to create temporary microperforation in the RWM that heal without causing anatomic or physiologic dysfunction. Microneedles have the potential to mediate safe and effective means of intracochlear delivery for inner ear therapeutics.

Define Professional Practice Gap & Educational Need: Drug delivery to the inner ear remains a challenge for the field. Microneedle perforations via the round window membrane have been proposed as a solution for gaining access to the cochlea. As such, there is a need for understanding how this procedure may affect hearing and cochlear structures.

Learning Objective: Participants will learn about microneedle perforation of the round window membrane and will gain a better understanding of the consequences of applying microperforations to round window membrane.

Desired Result: Participants may consider a new method for access to the cochlea for both diagnostic and therapeutic purposes.

Level of Evidence - Does not apply-you will be asked to explain - Basic science in vivo research

Indicate IRB or IACUC Approval: Approved

ANS TRAINEE AWARD

Neurotrophin Signaling in Various Degrees of Hearing Loss using MicroRNA Perilymph Profiling

*Matthew Shew, MD; Helena Wichova, MD; Jacob New, PhD
Athanasia Warnecke, MD; Thomas Lenarz, MD, PhD
Hinrich Staecker, MD, PhD*

Hypothesis: Perilymph microRNA (miRNA) profiling of the human inner ear can help predict neuronal status in the inner ear through neurotrophic factor signaling in cochlear implant (CI) candidates.

Background: Hearing loss (HL) is the most common neurodegenerative disease and we currently have no inner ear biopsy equivalent. In previous work we have shown that miRNA profiling in inner ear perilymph is feasible and may offer significant insight into what is occurring on a molecular level in humans with active inner ear disease.

Methods: We analyzed the human inner ear transcriptome and compared it perilymph microRNA expression profile in 18 CI candidates. Using bioinformatic programs, the expressed miRNAs were evaluated specifically on their ability to impact neurotrophic factor signaling.

Results: A total of 9 patients underwent hearing preservation (PTA<80dB) and 9 non-hearing preservation CI (PTA >80dB). A variety of neurotrophic factor signaling cascades were identified in active human inner ear disease. In those patients with residual hearing at time of CI placement, miRNAs related to BDNF and NT-3 signaling were differentially expressed within the scala tympani perilymph compared to individuals without residual hearing. These included miR-1207-5p, miR-103-3p, miR-100-5p, miR-221-3p, miR-200-3p.

Conclusions: Patients with residual hearing had differential expression of miRNA related to neurotrophic factor signaling, which has been strongly implicated in spiral ganglion health and can potentially be assayed through perilymph sampling. miRNA may serve as a biomarker in the perilymph to predict neuronal status of the inner ear which may serve as a therapeutic and prognostic marker for patients undergoing CI.

Define Professional Practice Gap & Educational Need: 1. Large gap in knowledge in what is occurring on a molecular level in patients with active inner ear disease, specifically various degrees of hearing loss. 2. Lack of understanding what is occurring on a cellular level in patients with and without residual hearing undergoing cochlear implantation 3. Inconsistency in ability to biopsy the inner ear in patients with active inner ear disease.

Learning Objective: To evaluate microRNA (miRNA) perilymph profiling in patients with various degrees of hearing loss while undergoing cochlear implantation. By analyzing miRNA perilymph profile we can gain significant insight to what may be occurring on a molecular level and help predict neuronal status in the inner ear through neurotrophic factor signaling in cochlear implant (CI) candidates.

Desired Result: By understanding the differential expression of miRNA related to neurotrophic factor signaling we can gain significant insight into spiral ganglion health. miRNA profiling in patients with hearing loss may serve as a biomarker in the perilymph to help predict neural status within the inner ear and serve as a promising therapeutic and prognostic marker for patients undergoing CI placement.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

NEUROTOLOGY FELLOW AWARD

Intratympanic Diltiazem-Chitosan Hydrogel as a Novel Otoprotectant Against Cisplatin-Induced Ototoxicity in a Mouse Model

*James G. Naples, MD; Michael J. Ruckenstein, MD
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Hypothesis: Intratympanic (IT) administration of the calcium-channel blocker (CCB), diltiazem, via chitosan-glycerophosphate (CGP) hydrogel vehicle will protect against cisplatin-ototoxicity.

Background: Cisplatin induces calcium-mediated apoptosis of cochlear outer hair cells (OHCs). Previous work demonstrated that IT diltiazem in solution provides otoprotection by reducing auditory brainstem response (ABR) threshold shifts in the setting of cisplatin-ototoxicity. We evaluate the role of a novel otoprotectant, IT CGP-diltiazem, against cisplatin-ototoxicity and analyze its effect on ABR and cochlear morphology.

Methods: Baseline pure-tone and click-evoked ABRs were performed in CBA/J mice. A control group (IT CGP-Saline, n=8) and treatment group (IT CGP-Diltiazem 2mg/kg, n=10) underwent baseline ABRs. A single dose of IT-CGP hydrogel was administered just prior to intraperitoneal cisplatin (14mg/kg). On Day 7, post-treatment ABRs were performed and cochleae were harvested. Specimens were dissected and hair cells were quantified using anti-myosin VIIa immunostaining.

Results: The mean threshold shifts on Day 7 was significantly reduced at all frequencies in both click- and tone-evoked ABRs in CGP-diltiazem-treated mice compared to control mice. The greatest reduction was at 24 and 32 kHz, where CGP-saline mice had a shift of 30.6 (± 7.72) and 37.5 (± 7.01)dB, respectively, compared to CGP-diltiazem mice with a shift of 7.22 (± 2.12) and 6.67 (± 2.58)dB ($p=0.0059$ and 0.0055). In the CGP-diltiazem group, preserved basal OHCs showed a significant correlation with reduced threshold shifts at 24kHz ($p=0.032$) and 32kHz ($p=0.009$).

Conclusions: This preliminary work suggests that IT CGP-diltiazem may offer otoprotection that reduces ABR threshold shifts and preserves OHC in the basal cochlea against cisplatin-induced ototoxicity.

Define Professional Practice Gap & Educational Need: Cisplatin-induced ototoxicity represents a type of acquired, permanent sensorineural hearing loss for which there is no available treatment. While there is a preponderance of research exploring potential therapies, few have translated into the clinical setting. This work aims to bridge that practice gap by providing a potentially new alternative through intratympanic diltiazem. The attempt to repurpose diltiazem offers a concept that may allow translation of this potential therapy into the clinical setting.

Learning Objective: The learning objective is that the audience understands the hypothesis and concept that underlies why the calcium-channel blocker, diltiazem, was chosen for its otoprotective potential. At the end of the presentation, the audience will understand that diltiazem has consistently reduced ABR threshold shifts in animal models, and may preserve inner ear structures. The audience should also recognize the foundational work that shows significant promise for potential translation of this idea, and how this idea can be applied to their practice in the future.

Desired Result: The desired result is that the audience learns of the potential for calcium-channel blockers and diltiazem as otoprotectants. This work can be applied as a foundation for future clinical and basic science work to explore other concepts of how to apply this class of drugs, which may have applications beyond ototoxicity for other destructive inner ear disorders.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Neuroprotection of NIR Light in an Animal Model of Cochlear Implantation

Arne Ernst, MD, PhD; Dietmar Basta, PhD

Abstract as submitted: It is the aim of the present animal study to investigate the influence of a near-infrared light (NIR) pre-treatment on outer hair cell loss (OHC) in cochlear implantation. NIR is known to be neuroprotective in acting on the respiratory chain, i.e. cytochrome-c-oxidase, thus, reducing apoptosis, inflammation and other mechanisms of acute neurotrauma. This leads in turn to a preservation of neuronal structure and function which was shown for different models (e.g. stroke, retinal surgery)

16 guinea pigs were bilaterally implanted with a cochlear implant electrode (insertion speed 200 μm , electrode diameter 0.32 mm, insertion depth 7mm). One side was pre-treated with NIR (15 min, 808 nm, 130 mW), the other not so that it served as control.

After 3months of continuous acoustic stimulation, the animals were sacrificed and the organ of Corti was dissected and the remaining OHC analysed. With no pre-treatment, there was a complete loss of OHC. The pre-treated side showed a reduction of 26.4 % of OHC loss, i.e. about one quarter of OHC survived the insertion trauma.

In essence, NIR seems to be an alternative mechanism to preserve residual hearing by acting as non-invasive neuroprotectant. This is interesting insofar that only steroids in different application modes have been shown to effectively reduce the sequelae of electrode insertion, thus, preserving residual hearing. Human applications of NIR are underway.

Define Professional Practice Gap & Educational Need: It is the learning objective to outline possible alternative, non-pharmacological approaches to preserve neuronal (cochlear) structures which are not yet known in detail as yet. This might become interesting in the future to preserve residual hearing in cochlear Implantation.

Learning Objective: Discuss NIR as possible treatment modality in patients with residual hearing, produce awareness among the scientific community About this non-invasive Approach.

Desired Result: Attendees should become Aware of other, non-pharmacological approaches to preserve residual Hearing in cochlear implantation.

Level of Evidence - Level I - Large RCTs with clear cut results

Indicate IRB or IACUC Approval: Approved

Evaluating the Industry Relationships of Physicians Presenting at the American Neurotology Society Spring Meetings

*Milap H. Desai, BS; Darshak M. Vekaria, BS
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Objective: 1.) Evaluate the accuracy of Financial Conflicts of Interest (FCOI) reporting by presenters and organizers at the American Neurotology Society (ANS) Spring meetings between 2014 to 2016 2.) Tabulate the reported monetary value of undisclosed FCOI. 3.) Determine the degree of compliance by presenters and organizers to the standards of the Accreditation Council for Continuing Medical Education.

Data sources: 1) Presenters and organizers along with FCOI reporting from ANS Spring meeting programs. 2.) Financial payments from Centers for Medicare and Medicaid Services Open Payments Database and Dollars for Docs. This is an IRB EXEMPT study.

Study selection: Open Payments and Dollars for Docs were used as the two primary sources to cross-check the disclosures of every presenter, panelist, and moderator listed on the ANS Spring Meeting programs.

Data extraction: The presenters, and organizers and associated financial disclosures were extracted and compared with Open Payments Database and Dollars for Docs.

Data synthesis: Monetary amount of undisclosed payments were calculated as were median amount of undisclosed payments. In 2014, 67% of physician presenters had undisclosed FCOI, with a median value of \$2798.38. In 2015, 49% of physicians has undisclosed FCOI with a median value of \$7637.13. In 2016, 35% of physicians had undisclosed FCOI with a median value of \$4165.14.

Conclusions: A considerable percentage of presenters, organizers at the ANS Spring Meetings had undisclosed FCOI. Presenters consistently had a higher median value of undisclosed FCOI than the organizers. There is a clear upward trend in the amount of physicians fully disclosing their conflicts of interest in both groups.

Define Professional Practice Gap & Educational Need: Inconsistencies in reporting of Financial Conflicts of Interests by presenters and organizers present a significant risk in unrecognized bias or influence in medical educational. The requirement for full disclosure of any relevant FCOI is to identify such relationships and to allow the audience to form its own judgment regarding the presentation. It is considered troubling if those in position to influence educational activity may not be providing full disclosure.

Learning Objective: 1.) Evaluate the accuracy of Financial Conflicts of Interest (FCOI) reporting by presenters and organizers at the American Neurotology Society (ANS) Spring meetings between 2014 to 2016 2.) Tabulate the reported monetary value of undisclosed FCOI. 3.) Determine the degree of compliance by presenters and organizers to the standards of the Accreditation Council for Continuing Medical Education.

Desired Result: Attendees should be able to explain and discuss the significance of disclosed and undisclosed Financial Conflict of Interests of those presenting at and those organizing ANS meetings.

Level of Evidence - Level V - Case series, studies with no controls

Indicate IRB or IACUC Approval: Exempt

Active Bone Conduction Implants Improve Patient Reported Outcomes Measures – A 12-Month Prospective Study

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Objectives: To evaluate patient reported outcome measures after implantation of an active bone conduction system in adult patients with single-sided deafness (SSD) or conductive-mixed hearing loss (CMHL).

Study Design: Prospective cohort study.

Setting: Tertiary referral center.

Patients: Adults who were implanted with the Bonebridge from 2013-2017.

Outcome Measures: Objective audiometric variables and Health Utilities Index (HUI), Tinnitus Handicap index (THI), Speech Spatial Qualities Questionnaire (SSQ), and Bern Benefit in Single-Sided (BBSS) Deafness Questionnaire were collected at 1-, 6-, and 12-months postoperatively. Comparative quantitative and regression analyses were completed to evaluate variable relationships.

Results: 50 patients with 12-month follow-up were included. 33 (66%) patients were implanted for CMHL, and 17 (34%) for SSD with a mean pre-operative pure-tone average of 79.7 db. Central Institute for the Deaf (CID) auditory test, Speech-reception thresholds (SRT), HUI-hearing subdomain, and SSQ performance were all improved at 1-month with a durable result through 12-months after implantation. There was no significant improvement in BBSS, or THI at any time interval.

Conclusion: Patient reported outcomes measures are critical in determining the utility of health interventions beyond objective performance data. Our study is the largest series published to date examining patient reported outcome measures with the Bonebridge in an adult patient population. We found that the Bonebridge active bone conduction system improved both objective audiologic performance and several patient reported outcomes measures. Future work is needed to develop a sensitive health utility measure for hearing loss so that formal cost-utility analyses may be performed.

Define Professional Practice Gap & Educational Need: 1. Lack of awareness and contemporary research of the patient-reported benefits (or lack thereof) of novel active bone conduction implants.

Learning Objective: 1. To describe the performance in patient-reported outcomes measures in adult patients after implantation of an active bone conduction system. 2. To discuss the 'best' candidates for an active bone conduction system and relay potential areas for future research and intervention in potential disparities in outcomes for different indications for active bone conduction implantation.

Desired Result: It is the authors' hope that attendees will consider the utility and shortfalls of active bone conduction implants in context of patients with either single-sided deafness or conductive-mixed hearing loss.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Subclinical Age-Related Hearing Loss is Associated with Cognitive Impairment

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Objective: Age-related hearing loss (HL), defined by a pure-tone average (PTA) >25 dB, has been associated with cognitive impairment and dementia. The objective is to assess whether hearing thresholds under the established 25 dB cutoff are associated with cognition.

Study Design: Multicentered, cross-sectional epidemiologic study (Hispanic Community Health Study; HCHS, 2008-2011; n=4,347)

Setting Four US communities (Miami, San Diego, Chicago, Bronx)

Main Outcome Measures: Cognitive ability measured by the Digit Symbol Substitution Test, Word Frequency Test, Spanish-English Verbal Learning Test (SEVLT), and Six-Item Screener

Results: Mean age was 57.6 years (SD=5.9, range=50-75). Among those with classically defined normal adult hearing (PTA \leq 25 dB), a 10 dB increase in hearing threshold was associated with a -1.61 (95% CI = -2.18, -1.04) raw score point difference in the Digit Symbol Substitution Test, adjusting for demographics, hearing aid use, and cardiovascular disease. Similarly, a 10 dB increase in hearing threshold was associated with a -0.71 (-1.07, -0.35) point difference on the Word Frequency Test, a -0.67 (-0.95, -0.40) point difference in Spanish English Verbal Test (SEVLT) 3 trials, a -0.40 (-0.55, -0.25) point difference in SEVLT recall, and a -0.08 (-0.12, -0.03) point difference in the Six Item Screener (all models $p < 0.001$).

Conclusions: Increasing hearing thresholds were independently associated with lower cognition among adults with subclinical hearing loss (PTA \leq 25 dB). The current 25 dB threshold for defining adult HL may be too high. Studies investigating whether treating HL can prevent impaired cognition/dementia should consider a lower threshold for defining HL.

Define Professional Practice Gap & Educational Need: The association between subclinical hearing loss and cognition is unknown. It is unclear what hearing threshold should dictate a recommendation to begin amplification.

Learning Objective: Physicians will understand that increasing hearing thresholds were independently associated with lower cognition among adults with hearing better than the current normal/abnormal threshold.

Desired Result: In counseling patients on hearing loss treatment, physicians will consider that subclinical hearing loss was associated with cognitive impairment. Physicians will also recognize the need for more research in this area.

Level of Evidence - Level III - Cohort and case-control studies

Indicate IRB or IACUC Approval: Approved

Impact of Auditory-Motor Musical Training on Melodic Pattern Recognition in Cochlear Implant Users

*Divya A. Chari, MD; Anirrudh Patel, PhD
Karen C. Barrett, PhD; Lauren Jacobs, BS
Patpong Jiradejvong, MS; Charles J. Limb, MD*

Objective: Cochlear implant (CI) users struggle with tasks of pitch-based prosody perception. Pitch pattern recognition is vital for both music comprehension and understanding the prosody of speech, which signals emotion and intent. Research in normal-hearing individuals shows that auditory-motor training, in which participants produce the auditory pattern they are learning, is more effective than passive auditory training. We investigated whether auditory-motor training of CI users improves speech prosody perception and pitch pattern recognition compared to purely auditory training.

Study design: Prospective cohort study.

Setting: Tertiary academic center.

Patients: Fifteen post-lingually deafened adults with CIs.

Intervention(s): Participants were divided into three one-month training groups: auditory-motor (intervention), auditory-only (active control), and no training (control). Auditory-motor training was conducted with the “Contours” software program and auditory-only training was completed with the “AngelSound” software program.

Main outcome measure: Pre- and post-test examinations included tests of speech perception (CNC, HINT sentence recognition), pitch discrimination, speech prosody perception, and melodic contour identification.

Results: Participants in the auditory-motor training group performed better than the auditory-only training group in the melodic contour identification test ($p < 0.05$). The auditory-motor and auditory-only training groups performed better in speech prosody perception and melodic contour identification tasks compared to the no-training group ($p < 0.05$).

Conclusions: These data suggest that short-term auditory-motor music training of CI users impacts pitch pattern recognition and speech prosody perception. No prior studies have examined the impact of instrumental music training on pitch pattern recognition; this study offers approaches for enriching the world of complex sound in the CI user.

Define Professional Practice Gap & Educational Need: 1. Lack of contemporary knowledge about performance of cochlear implant users in tasks of pitch-based prosody perception. 2. Lack of knowledge about the effect of auditory-motor training compared to purely auditory training on cochlear implant user performance. 3. Lack of understanding about the role of pitch pattern recognition in both music comprehension as well as understanding the prosody of speech.

Learning Objective: The learning objective is to investigate whether auditory-motor training of CI users improves speech prosody perception and pitch pattern recognition compared to purely auditory training.

Desired Result: Our data suggest that short-term auditory-motor music training of CI users impacts pitch pattern recognition and speech prosody perception. Our study offers approaches for enriching the world of complex sound in the CI user through auditory-training exercises.

Level of Evidence - Level II - Small RCTs with unclear results

Indicate IRB or IACUC Approval: Approved

The Use of Artificial Intelligence in Cochlear Implant Programming

Susan B. Waltzman, PhD; David C. Kelsall, MD

Objective: Cochlear implant (CI) technology and techniques have advanced over the years. The only component which has not changed is the programming of the implant devices. The purpose of this study is to compare performance in cochlear implant subjects using an expert experienced clinician (EC) standard MAP programming methods versus an Artificial Intelligence (AI) using standard of care and direct connect psychoacoustic test metrics as well as patient satisfaction based algorithm for programming and evaluation without the need for a sound booth.

Study Design: Prospective, non-randomized, multi-center FDA study using within-subject experimental design

Setting: T Private clinics, and tertiary referral centers

Patients: 50 adult patients CI recipients with ≥ 3 months combined experience with a Nucleus 5, 6, Kanso, or 7 series sound processor.

Intervention: Diagnostic and Therapeutic

Main Outcome measures: CNC words and AzBio sentences in noise (+10dB SNR) were performed in a sound booth followed by a direct connect psychoacoustic battery (including audiometry, loudness scaling, phoneme discrimination, and speech perception with varied input levels) using the experienced expert clinician (EC) program MAP (EC). at Visit A. The tests were repeated approximately one month later at visit B using the optimized AI program MAP. Subjective measures of patient satisfaction were also measured.

Results: Equivalent group mean performance for the EC Expert Clinician program MAP were compared to the AI program MAP for CNC words and AZ Bio sentences in noise (+10dB SNR). in preliminary analysis (Kruskal-Wallis ANOVA $P=0.934$). Group mean results revealed equivalent performance (Kruskal-Wallis ANOVA $P=0.934$) with both programming methods. Some patients had better performance with AI method while none performed more poorly. 73% The majority of subjects were very satisfied/somewhat satisfied with preferred the direct connect AI system compared to the sound booth.

Conclusion: The study demonstrated that the AI outcomes are equivalent or better to those using the traditional programming techniques. This and provides can substantially reduce the number of visits per patient allowing for increased volume, standardization across centers and a standardized approach to aftercare that reduces the need for costly booth set-up and perceived level of expertise needed to provide quality care. This may allow for more hearing health professionals to offer the technology increased access for to reach the many individuals who could benefit.

Define Professional Practice Gap & Educational Need: 1. Lack of efficiency in cochlear implant programming 2. Lack of standardization in cochlear implant programming 3. Lack of application of modern techniques to cochlear implant programming

Learning Objective: Physicians will be able to 1. Explain how artificial intelligence (AI) can be applied to cochlear implant programming 2. Discuss the benefits of using AI to program cochlear implants 3. Summarize the possible benefits of AI in terms of patient outcomes, satisfaction and efficiency

Desired Result: Attendees will 1. Be able to increase efficiency related to cochlear implant programming without sacrificing patient outcome 2. Be able to provide access to more patients in need of cochlear implant technology

Level of Evidence - Does not apply - it does apply at Level 2b

Indicate IRB or IACUC Approval: Approved

Intracochlear Pressure Transients During Cochlear Implant Electrode Insertion: Effect of Micro-mechanical Control on Limiting Pressure Trauma

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Hypothesis: Use of micro-mechanical control will result in reduced number and magnitude of intracochlear pressure transients when compared with electrode insertion by hand.

Background: It has been established that large intracochlear pressure spikes can be generated during the placement of cochlear implant electrodes, which may be a cause of insertion-related trauma. Here, we examine the effect of a micro-mechanical insertion control tool on intracochlear pressure during implantation.

Methods: Electrodes from three manufacturers were placed in four cadaveric heads both with a custom micro-mechanical control tool and by hand. Insertions were performed at three different rates: 0.2 mm/s, 1.2 mm/s, and 2 mm/s (n=20 each). Fiber-optic sensors measured intracochlear pressures. The effect of electrode type, speed, and device use on pressure magnitude was calculated using an N-way ANOVA. Chi-squared analysis assessed the relative number of insertions with transients with and without the device.

Results: Electrode insertion by hand produced pressure transients in the cochlea up to an ear canal equivalent of 174 dB SPL. Average pressures were significantly lower when utilizing the insertion device compared with insertion by hand ($p < 0.001$). No difference in magnitude was noted across electrode type or speed. A significantly lower proportion of insertions contained pressure spikes when the insertion device was used ($p < 0.001$).

Conclusion: Results affirm the importance of atraumatic techniques during electrode insertion and suggest that use of a micro-mechanical insertion control system may mitigate trauma from pressure events, both by reducing the amplitude and the number of pressure spikes resulting from cochlear implant electrode insertion.

Define Professional Practice Gap & Educational Need: 1. Limited understanding of the intracochlear environment during insertion of cochlear implant electrodes. 2. Unclear benefit of the use of an electrode insertion tool on minimizing insertion-related trauma to the cochlea.

Learning Objective: 1. Better appreciate the potential for causing cochlear trauma during cochlear implant electrode insertion. 2. Learn about cochlear implant insertion tools and develop an understanding of how such devices may potentially mitigate implantation-related trauma to the cochlea.

Desired Result: 1. Participants will improve understanding of one potential cause of loss of residual hearing following cochlear implant surgery. 2. Participants will evaluate the relative benefit of a cochlear implant electrode insertion tool compared with traditional hand insertion of electrodes in mitigating implantation-related trauma to the cochlea. 3. Participants will have objective data to consider when deciding whether or not to incorporate insertion tools into clinical practice when such devices become clinically available.

Level of Evidence - Does not apply

Indicate IRB or IACUC Approval: Exempt

Electrocochleographic Patterns in Patients with Sudden Sensorineural Hearing Loss Undergoing Cochlear Implantation

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Objective: The pathophysiology and locus of dysfunction associated with sudden sensorineural hearing loss (SSNHL) is poorly understood. The objective of this study was to quantify the electrophysiologic integrity of cochlear hair cells and the auditory nerve in patients with SSNHL undergoing cochlear implantation (CI). The central hypothesis was that the amplitude of the cochlear microphonic, reflective of cochlear hair cell function, would be greater among SSNHL patients relative to patients with gradually progressive hearing loss.

Study design: Case-control study

Setting: Two tertiary referral centers

Patients: The case cohort consisted of adult patients with SSNHL who met CI candidacy criteria. The control cohort consisted of a sample of post-lingually deaf adults with gradually progressive SNHL who met CI candidacy criteria.

Interventions: Intra-operative electrocochleography (ECochG); cochlear implantation.

Main diagnostic and outcome measures: Intra-operative ECochG recordings and post-operative speech perception testing.

Results: Intraoperative ECochG recordings were possible in all patients with SSNHL and the control cohort of patients with gradually progressive SNHL. Pre-operative demographic and audiological factors including duration of hearing loss, pre-operative pure tone averages, preoperative best-aided speech discrimination, and age at implantation were reviewed. Patterns involving the cochlear microphonic, indicative of cochlear hair cell function, and the auditory nerve neurophonic, reflective of the function of the auditory nerve, were compared between SSNHL patients and controls with gradually progressive SNHL. Post-CI speech outcomes were compared between groups. On average the SSNHL patients displayed large cochlear microphonics, reflecting significant hair cell presence, with absent or poor compound action potentials, indicating poor neural activity.

Conclusions: Intra-operative ECochG is a useful tool to study the pathophysiology and locus of dysfunction in patients with SNHL undergoing CI. Findings from this study provide insight into the poorly understood pathophysiology of SSNHL.

Define Professional Practice Gap & Educational Need: This study addresses a gap in our knowledge regarding the locus of functional impairment associated with sudden sensorineural hearing loss.

Learning Objective: This study applies use of intraoperative electrocochleography in a sample of patients undergoing cochlear implantation for sensorineural hearing loss associated with sudden sensorineural hearing loss compared to a control group of patients with gradually progressive sensorineural hearing loss.

Desired Result: From this presentation, attendees will: 1. Come away with a greater appreciation and understanding of the utility of electrocochleography to monitor and study intracochlear micromechanics and the function of the cochlear nerve. 2. Develop an understanding of how electrocochleographic patterns among sudden sensorineural hearing loss patients differ from those of progressive hearing loss patients and what implications this may have for loci of dysfunction in this group.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

Transgenic Mouse Model for Facial Nerve Synkinesis

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Hypothesis: Our central hypothesis is that inhibition of Schwann cell de-differentiation, in the post-injury setting will impact synkinesis.

Background: No therapies exist to improve the accuracy of facial nerve regeneration. Following peripheral nerve injury, adult reactive Schwann cells de-differentiate and express glial fibrillary acidic protein (GFAP); suggesting that reactive Schwann cells impact axonal regeneration precision.

Methods: Transgenic GFAP-thymidine kinase (TK) mouse model was employed, allowing selective downregulation of reactive GFAP expressing Schwann cells through ganciclovir (GCV) delivery via osmotic pump. Adult female transgenic GFAP-TK mice had the right facial nerve transected and repaired, they then were treated with saline or GCV, allowing for 10 animals in each group. At 6 weeks post-injury, mice were exposed to at least three separate air puff events while high speed videography recorded whisker. MatLab code processed video with publicly available BIOTACT algorithm.

Results: Whisker velocity was calculated using binning and Fourier transform statistical analysis. Saline treated animals confirmed our model's ability to detect aberrant movement such that intact (left) facial nerves caused whisker retraction, while repaired (right) facial nerves had protraction. Administration of GCV increased whisker protraction compared to saline. GCV did not impact intact animal whisker movement compared.

Conclusions: Inhibition of reactive Schwann cell proliferation appears to impacts degree of synkinesis, providing important insight in a potential therapeutic target for facial nerve injury.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge on how to treat synkinesis following facial nerve injury

Learning Objective: Explore transgenic mouse model that detects and impacts synkinesis

Desired Result: Appreciate role that Schwann cells play in synkinesis development.

Level of Evidence - Does not apply-you will be asked to explain - Basic science study

Indicate IRB or IACUC Approval: Approved

**Post Traumatic Complete Facial Palsy: Comparative Analysis of
Outcomes of Conservative Management vs surgical exploration:
A University Hospital Study and Review of Literature**

Diptarka Bhattacharyya, MD; Pravin Rajgadkar, MD

Introduction: Post traumatic facial nerve paralysis is common, being seen in up to 7-10% of blunt head trauma. Early surgical exploration is usually widely recommended, with decision making being based upon the onset, Imaging findings and Electro-diagnostic studies. However, evidence for benefit is still unclear, and is usually based on institutional protocols.

Materials and Methods: Retrospective anonymized single institutional study. Patient charts from 2010-2015 were reviewed. All patients were treated with systemic steroids.

Inclusion criteria:

1. Post traumatic complete Unilateral facial nerve palsy
2. Duration of onset known
3. Unfavorable Electroneuronography (<5%) and EMG

Exclusion criteria:

1. Displaced temporal bone fractures
2. No follow up data to 1 year, or documented recovery

Results: A total of 43 patients met the inclusion criteria. 41 patients had an identified temporal bone fracture (6 transverse, 35 patients had mixed/longitudinal). 19 patients underwent surgery within 4 weeks. 17 patients recovered in this group (95%). 24 patients initially declined surgery. 14 of them went on to NOT have surgery. Recovery rate was 92% in this group. 10 patients underwent delayed surgery, ranging from 4 weeks to 28 weeks. Recovery rate was 90%

Discussion and Conclusion: In this series of patients with undisplaced temporal bone fractures with complete facial palsy, conservative management, early and late surgery all appear to have the same recovery rate. None of the patients had a complete transection of the nerve. The utility and role of surgical treatment in this sub-group of patients needs to be carefully reviewed with larger studies

Define Professional Practice Gap & Educational Need: There is lack of clear evidence of benefit in early surgical exploration in Post traumatic complete unilateral facial palsy. The perceived improvement noted in some case series may simply be the natural history. In fact, the largest recovery of nerve function in any unilateral neuropathy, irrespective of intervention is expected within 4 weeks, so the perceived poorer outcomes from delayed exploration is susceptible to selection bias, and hence needs to be clearly reviewed.

Learning Objective: To reassess and analyse the role of early facial nerve decompression in patients with post traumatic unilateral complete facial nerve palsy, and consider that conservative medical management may provide equal outcomes.

Desired Result: 1. Assess temporal bone fractures and understand that in transverse temporal bone fractures, early surgical intervention may be indicated 2. Consider that improvement in Post traumatic Unilateral Facial Palsy often happens later than 4 weeks- extending up to 28 weeks; however, chances of spontaneous recovery decreases with time 3. The timing of facial nerve decompression does not appear to change outcomes

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

Association between Metformin Usage and Tumor Growth Rate in Vestibular Schwannoma Patients

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Objective: Laboratory work has suggested Metformin may possess novel anti-neoplastic properties. This study aims to assess the effect of Metformin on vestibular schwannoma growth rate

Study Design: Retrospective cohort comparison study

Settings: Stanford Hospital, a tertiary referral center, USA

Patients: Patients presenting with radiologically confirmed Vestibular schwannoma to Stanford medical center between January 1990 to October 2018. Patients who were received Metformin during the follow-up period were included and were compared to the control group who were not receiving Metformin.

Interventions: Treatment with Metformin.

Main outcome measures: Tumor growth.

Results: A total of 149 patients were analyzed, with 42 patients receiving Metformin. The mean age at presentation was 69.6 (± 11.7) years. There were 69 (46.3%) females and 80 (53.7%) males and there was no significant age difference between the groups. Tumor size at presentation was similar between two groups, 8 mm (4-13) in control group and 7.5 mm (4-14) in Metformin group.

The follow up period was 34.2 month (18.3-57.8) and 30.3 month (13.6 – 69.8) in the Metformin and control cohorts respectively and this was not significant different.

Tumor growth was significantly less common in Metformin cohort during follow up (33.3% vs 51.4%).

Conclusions: This preliminary result suggests Metformin may reduce vestibular schwannoma tumor growth rate and shows promise as a novel chemotherapeutic agent. Further studies are needed to validate this finding.

Define Professional Practice Gap & Educational Need: Lack of awareness regarding the potential effect of Metformin on vestibular schwannoma growth rate

Learning Objective: Demonstrate the effect of metformin therapy on vestibular schwannoma tumor growth rate.

Desired Result: The attendee will be able to discuss the potential utilization of metformin in follow up of vestibular schwannoma patients.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved

Delayed Tumor Growth in Vestibular Schwannoma: An Argument for Lifelong Surveillance

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Objective: Previous research has shown that tumor growth during observation of small-to-medium sized sporadic vestibular schwannomas (VS) occurs almost exclusively within 3 to 5 years. This has led some to consider ending surveillance after this interval. This study seeks to characterize a cohort of patients with tumors that exhibited late growth.

Study Design: Retrospective case review.

Setting: Tertiary referral center.

Patients: Adults with VSs who underwent MRI surveillance.

Intervention(s): None.

Main outcome measure(s): Linear tumor growth was measured in accordance with AAO-HNS guidelines. Delayed growth was defined as growth 5 years or more from the initial MRI.

Results: Of 361 patients with available data, 172 (47.6%) experienced tumor growth. Fourteen of these 172 patients (8.1%) experienced delayed growth, with the highest growth rate after the delay being 7.90 mm/year and the longest delay being 11.1 years. Additional treatment was recommended for 6 (43%) delayed growth patients. Of 68 tumors that remained in the IAC, 11 (16.2%) exhibited delayed growth. Of 66 tumors that presented in the CPA, 2 (3.0%) demonstrated delayed growth. Initial size was smaller for those exhibiting delayed growth compared to those with early growth (4.85 vs. 7.90 mm). For tumors within the IAC, those with early growth had a significantly higher growth rate than those with delayed growth (1.40 vs. 0.45 mm/year, $p = 0.001$)

Conclusions: Delayed growth was observed in 8.1% of growing VSs. Patient factors that predict delayed growth remain elusive. These findings support lifelong surveillance to detect growth that may impact management and outcome.

Define Professional Practice Gap & Educational Need: Lack of awareness regarding the proper length of vestibular schwannoma surveillance if serial imaging is the selected management

Learning Objective: Understand that lifelong surveillance of vestibular schwannomas is recommended given the delayed growth identified in our cohort and the potential for altered treatment outcomes due to this

Desired Result: Clinicians will prolong their MRI surveillance windows of vestibular schwannomas to identify patients that may have delayed growth, which can affect later treatment outcomes

Level of Evidence - Level V - Case series, studies with no controls

Indicate IRB or IACUC Approval: Approved

Rate of Initial Hearing Loss Predicts Risk of Non-Serviceable Hearing Among Observed Sporadic Vestibular Schwannoma

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Objective: To evaluate the association between rate of initial hearing loss and development of non-serviceable hearing in patients with sporadic vestibular schwannoma (VS) who elect initial observation.

Setting: Two tertiary care centers.

Patients: VS patients with serviceable hearing who underwent at least three audiograms before intervention or loss to follow-up. The rate of change in pure tone average (PTA) was calculated as the PTA from the second audiogram minus the PTA from the first audiogram, divided by the duration in months between the two.

Main outcome measure(s): Serviceable hearing, defined as the PTA ≤ 50 dB HL and word recognition score (WRS) $\geq 50\%$.

Results: Among 264 patients meeting inclusion criteria, 56 developed non-serviceable hearing during follow-up. Kaplan-Meier estimated rates of maintaining serviceable hearing (95% CI; number still at risk) at 1, 3, 5, 7, and 10 years were 97% (95-99; 203), 77% (70-84; 97), 66% (58-76; 38), 56% (45-70; 16), and 40% (25-63; 2), respectively. In a univariable setting, each 1-unit increase in the rate of initial PTA change was associated with a 73% increased likelihood of non-serviceable hearing (hazard ratio 1.73; 95% CI 1.31-2.28; $p < 0.001$). This difference persisted after adjusting for initial presenting PTA (hazard ratio 2.22; 95% CI 1.61-3.07; $p < 0.001$) and after adjusting for both PTA and WRS at the first audiogram (hazard ratio 2.27; 95% CI 1.67-3.09; $p < 0.001$).

Conclusions: Rate of initial PTA decline is a novel strong predictor of non-serviceable hearing in patients with observed VS and may be used to guide patient counseling and optimize management.

Define Professional Practice Gap & Educational Need: Lack of awareness regarding predictors of hearing decline in patients with sporadic vestibular schwannoma

Learning Objective: To describe a novel strong predictor of non-serviceable hearing in patients with sporadic vestibular schwannoma

Desired Result: This information can be used to guide patient counseling and optimize care.

Level of Evidence - Level V - Case series, studies with no controls

Indicate IRB or IACUC Approval: Approved

Factors Associated with Cranial Neuropathy following Gamma Knife for Vestibular Schwannoma

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Objective: Evaluate the incidence of and potential contributory factors to cranial neuropathy (CN) following Gamma Knife (GK) for primary treatment of vestibular schwannoma (VS).

Study design: A retrospective chart review was performed for all patients undergoing GK for VS at a single institution from 2005 to 2018.

Setting: Tertiary referral center.

Patients: All patients receiving primary GK treatment for VS were evaluated. Patients with NF2 or prior surgery were excluded from analysis.

Intervention: GK surgery.

Main outcome measures: The incidence of new onset sudden sensorineural hearing loss (SSNHL) requiring steroids, trigeminal paresthesia, facial nerve paresis, dysphagia, and vocal cord dysfunction was evaluated. Vestibular symptoms were excluded from analysis due to lack of objective assessments. Secondary end-points include association of CN with patient demographics, tumor characteristics, and radiation received.

Results: 134 patients with VS received primary GK therapy. Post-treatment CN developed in 34 patients (25.4%). 12 patients (9%) developed SSNHL requiring steroids, 11 experienced trigeminal paresthesia (8.2%), and 7 (5.2%) demonstrated facial paresis. The mean maximum cochlear dose was 15.49 Gy in patients with facial paresis compared to 12.42 Gy in patients who did not ($p=0.032$). Subjects with facial paresis were more likely to have a lateral tumor without a fundal cap on MRI (71%) compared to subjects without facial paresis (43%, $p=0.70$)

Conclusions: In the treatment of VS with GK, elevated maximum cochlear dose and lack of a fundal cap on MRI were associated with facial paresis. These factors should be considered during GK treatment planning for VS.

Define Professional Practice Gap & Educational Need: 1. Lack of knowledge regarding incidence of acute cranial neuropathy following gamma knife for acoustic neuroma 2. Lack of knowledge regarding predisposing factors for acute cranial neuropathy following gamma knife for acoustic neuroma

Learning Objective: Evaluate the incidence of and predisposing factors towards development of acute cranial neuropathy following gamma knife for acoustic neuroma.

Desired Result: Attendees will be able to better counsel patients regarding the relative risks of gamma knife treatment for acoustic neuroma and identify those at a higher risk of developing facial paresis in the short-term.

Level of Evidence - Level IV - Historical cohort or case-control studies

Indicate IRB or IACUC Approval: Approved