SELECTED ABSTRACTS

IN ORDER OF PRESENTATION

ORAL PRESENTATIONS

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AMERICAN NEUROTOLOGY SOCIETY

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Abnormal Cochleovestibular Nerves and Pediatric Hearing Outcomes: "Absent Cochlear Nerves" Can Derive Benefit from Cochlear Implantation

Elina Kari, MD; John L. Go, MD
Janice Loggins, AuD; Laurel Fisher, PhD

Objective: Analyze imaging and hearing characteristics of children with cochleovestibular nerve (CVN) abnormalities and correlate these imaging characteristics with hearing and language outcomes after hearing aid fitting, cochlear implantation (CI) and/or auditory brainstem implantation (ABI).

Study Design: Retrospective.

Setting: Tertiary referral academic center.

Patients: Twenty-eight children with CVN abnormalities with magnetic resonance (MRI) and/or computed tomography (CT).

Intervention(s): none.

Main Outcome Measure(s): Ability to determine presence or absence of a cochlear nerve, cochleovestibular abnormalities, and correlate imaging findings with response to auditory stimulation.

Results: A total of 26 children with bilateral sensorineural hearing loss and abnormal CVNs and 2 children with unilateral findings (28 patients total) were evaluated (MRI/CT). There were equal numbers of males and females. Twelve children (39%) had comorbid conditions. Fifty-four (54) ears were identified with CVN abnormalities and analyzed. Fifteen (28%) ears were implanted with a CI and 8 (15%) with an ABI. The absence of a cochlear nerve was associated with an abnormal cochlear aperture, a narrow IAC and cochlear malformation. Thirteen (50%) ears with abnormal CVNs (n=26) exhibited normal cochlea.

Hearing data were available on 23 anomalous ears. Eleven (49%) exhibited reproducible hearing thresholds either with or without a hearing aid, CI, or ABI. Some achieved open-set word recognition.

Conclusions: Current imaging modalities cannot accurately characterize the functional status of the cochleovestibular nerve or predict a child's benefit with either a CI or ABI. Several children who would have otherwise been denied a CI exhibited responses to auditory stimuli after implantation.

Define Professional Practice Gap & Educational Need: Current imaging technology does not predict pediatric hearing outcomes and current literature typically describes "aplastic" or "absent" cochlear nerves. Our data show that despite this "absence", many children exhibit responses to sound and in some cases open set word recognition after hearing aids, CIs or ABIs. Our data highlight the need for novel imaging technologies and demonstrate that many of these children may achieve the same benefit from a CI than from an ABI.

Learning Objective: To better understand the limits of MRI/CT in the evaluation of children with congenital SNHL and abnormal cochleovestibular nerves. To better appreciate that an absent cochlear nerve does not predict lack of auditory awareness or lack of benefit from a CI

Desired Result: Attendees will consider CI for children with CVN abnormalities Attendees will understand the limitations of current imaging technologies and potentially revise their imaging protocols.

Indicate IRB or IACUC Approval: Approved

An In-vitro Insertion-force Study of Magnetically Guided Lateral-wall, Cochlear-implant Electrodes

Lisandro Leon, MS; Frank M. Warren, MD
Jake J. Abbott, PhD

Hypothesis: Insertion forces are reduced by magnetically guiding the tip of lateral-wall electrodes during insertion.

Background: Steerable electrodes have the potential to minimize intracochlear trauma by reducing the contact between the electrode tip and the cochlear walls. We have experimented with lateral-wall electrodes with magnets at their tips. Magnetic torque can be applied to the tip so that it can be guided away from the medial wall through the cochlear hook and the lateral wall of the basal turn. To date, steerable electrodes have only been designed to curve in the direction of the basal turn.

Methods: Automated insertions of electrodes with magnets are conducted into a scala-tympani phantom with a force sensor attached to it to provide the measurements needed to evaluate our hypothesis. An external magnet is used to apply magnetic bending torque to the magnetic electrode tip with the goal of directing the tip down the lumen. Experiments are conducted to mimic both cochleostomy and round-window insertions

Results: T-test results indicate that magnetic guidance reduces insertion forces for all electrodes tested with certain electrode models achieving more than 50% reduction. For cochleostomy insertions, this benefit can be expected beyond 8 mm insertion depth while eliminating direct-tip contact with the lateral wall. For round-window insertions, direct-tip contact with the medial wall through the cochlear hook was also eliminated.

Conclusions: Significant insertion force reduction can be obtained by applying magnetic guidance to the insertion of lateral-wall electrodes. This augments the superior flexibility of lateral-wall electrodes with a steerable mechanism.

Define Professional Practice Gap & Educational Need: Clinicians are typically too busy or not connected with academic researchers to realize what the current state of the art is with engineered medical devices.

Learning Objective: In this specific instance, a new technology is being developed to guide the insertion of a standard cochlear-implant electrode array with a robotic magnetic manipulator.

Desired Result: Our goal is simply to educate the clinician of a possible robotic cochlear-implant insertion method that enables a lateral-wall electrode array to be navigated through the lumen using a non-stylet-based method.

Indicate IRB or IACUC Approval: Approved

NEUROTOLOGY FELLOW AWARD

Real-time Intracochlear Electrocochleography Obtained Directly through a Cochlear Implant

Michael S. Harris, MD; William J. Riggs, AuD
Brendan P. O'Connell, MD; Kanthaiah Koka, PhD
George Wanna, MD; Robert Labadie, MD, PhD
Oliver F. Adunka, MD

Hypothesis: Electrocochleography (ECochG) obtained through the cochlear implant (CI) will provide the surgeon unprecedented real-time feedback reflective of cochlear micromechanical changes occurring during electrode advancement.

Background: Contemporary CI surgery is performed without real-time feedback reflecting the impact of electrode insertion on cochlear micromechanical health. ECochG obtained at the round window (RW) has proven to be a highly efficacious method of monitoring cochlear micromechanics immediately before and after electrode insertion. ECochG obtained directly through the CI provides surgeons an opportunity to monitor cochlear dynamics and potentially tailor electrode placement.

Methods: ECochG was recorded directly from the apical electrode during CI electrode advancement via RW insertion. The cochlear microphonic and auditory nerve neurophonic response magnitude – the "on-going response" – indicative of the current generated by outer hair cell stereocilia and neural phase-locking of CN VIII, was analyzed at three points: upon RW entry, at its peak, and upon completion of full insertion.

Results: Detectable intracochlear ECochG was achieved in all patients. Comparison of the on-going response magnitude upon RW entry, at its peak, and upon completion of insertion revealed several distinct response patterns: the amplitude generally increased steadily with electrode insertion, but in several patients the on-going response amplitude fell below the peak amplitude upon completion of insertion. Implications for post-operative hearing prediction and in-clinic post-CI ECochG are discussed.

Conclusions: ECochG obtained directly from the CI electrode array is highly feasible, unencumbered by added instrumentation or dedicated acquisition time, and provides the CI surgeon previously unavailable feedback reflective of cochlear health.

Define Professional Practice Gap & Educational Need: 1. A progress-limiting gap exists in our ability to monitor in real-time the effects of cochlear implant electrode insertion on cochlear micromechanics. This talk addresses the use of intra-cochlear electrocochleography obtained directly through the cochlear implant as a solution to this problem. 2. There persists a lack of fundamental knowledge regarding the impact of cochlear implant electrode placement on cochlear electrophysiology. This talk presents the electrophysiologic response patterns observed in a sample of cochlear implant users. 3. The field of cochlear implant surgery is currently limited in its ability to achieve the goal of minimally traumatic cochlear implantation and hearing preservation. Intracochlear electrocochleography, as discussed here, has the potential to allow the cochlear implant surgeon to better achieve these goals.

Learning Objective: 1. The learner will appreciate the impact that cochlear implant electrode insertion has on the delicate micromechanics of the cochlea. 2. The learner will be exposed to the variability that exists across patients in electrocochleographic response to electrode insertion and the distinct response patterns observed. 3. The learner will consider the utility of intracochlear electrocochleography obtained directly through the cochlear implant for minimally traumatic insertion, hearing preservation, and predicting post-implant performance.

Desired Result: 1. Attendees may have the opportunity to apply the knowledge learned from this study directly to their own cochlear implant practice: possibly by adopting this or a similar methodology or simply by becoming more cognizant of the impact of insertion on cochlear electrophysiology. 2. Attendees may eventually have the opportunity, on the basis of knowledge gained from this study, to inform patient expectations regarding functional outcomes depending on which of the electrocochleography response patterns they exhibit during insertion.

Indicate IRB or IACUC Approval: Approved

Assessing Cochlear Implant Outcomes in Older Adults Using HERMES, a National Web-Based Database

Stephanie Y. Chen, BM; Jedidiah J. Grisel, MD
Anne Lam, BS; Justin S. Golub, MD

Objective: Cochlear implant (CI) outcomes research has been limited to retrospective or single-institution studies in the US. The objective is to demonstrate the feasibility of using a novel, national, web-based CI database through evaluating CI outcomes in older adult

Study design: Analysis of a prospective, national, web-based database designed for CI outcome tracking (HERMES; HIPAA-secure, Encrypted, Research Management and Evaluation Solution)

Setting: Multi-centered at 14 private practice and academic US medical centers

Patients: Older (age≥75, n=43) or younger (age<75, n=88) adult CI patients (n=131 total, n=139 ears)

Main outcome measure(s): AzBio scores, CI usage, postoperative complications

Results: Older adults had slightly lower performance on most recent AzBio (57.0%, n=24, 12.5 months) compared to younger adults (75.2%, n=47, 12.3 months; p<0.01, Mann Whitney). However, on multiple regression, age was not a significant predictor of AzBio scores after controlling for sex, hearing loss duration, time since implantation, and use (p=0.10). Most recent CI use was similar but significantly different (10.6 hours/day in older, n=14 vs. 12.8 in younger, n=26; p<0.01). Usage also did not decline over time (p=0.97 in older vs. p=0.22 in younger). The most common complications were similar (26% vs. 30% for vertigo; p=0.58) or less frequent (5% vs. 21% for tinnitus; p=0.02) in older and younger adults, respectively.

Conclusions: We demonstrate the feasibility of a novel user-friendly, web-based, national CI database to analyze CI outcomes. Older age was not a significant predictor of AzBio scores after adjusting for multiple factors. Additionally, CI use did not decline over time.

Define Professional Practice Gap & Educational Need: Lack of awareness of a national database to evaluate cochlear implant outcomes

Learning Objective: Gain knowledge of a new national, web-based prospective cochlear implant database

Desired Result: 1. Use of the database to evaluate cochlear implant outcomes by conducting larger scale, prospective studies 2. Consider contributing to a database to enable better quality research on cochlear implant outcomes

Indicate IRB or IACUC Approval: Approved

Early Outcomes with a Slim, Modular Cochlear Implant Electrode Array

Jonathan L. McJunkin, MD; Jacques Herzog, MD
Andrew Drescher, MD; Richard A. Chole, MD
Craig A. Buchman, MD

Objective: Describe outcomes from cochlear implantation with a new, slim modiolar electrode array.

Study Design: Cohort study

Setting: Tertiary referral centers

Patients: Adult cochlear implant candidates

Interventions: Cochlear Implantation with CI532 (Cochlear Corp).

Main Outcome Measures: Pre- and postoperative speech perception scores, audiometric behavioral thresholds, electrode impedance/neural response telemetry measures and postoperative CT reconstructions of array location.

Results: 48 patients are implanted to date. There were 2 tip rollovers identified with intraoperative x-ray and resolved with re-insertion. There were no open circuits on impedance testing. At 1-month post-activation, mean CNC word scores improved from 13% to 46% and mean AzBio (quiet) scores improved from 16% to 63%. Mean preoperative pure tone thresholds were 70 dB, 74 dB, 84 dB and 88 dB at 250 Hz, 500 Hz, 1 kHz and 2 kHz, respectively. After 1-month of stimulation, mean thresholds are 85 dB, 91 dB, 104 dB and 102 dB at these frequencies. Many patients had $\leq$ 20dB change in thresholds. CT reconstructions in 8 patients show scala tympani placement of the entire array with a wrap factor of 60% (range 57-64%) and a mean insertion angle of 408^{o} (360-433^{o}). Mean neural response telemetry (NRT) thresholds at 1-month are 165 (+/-21) CUs. At the time of presentation, 3-month outcomes on at least 50 patients will be presented.

Conclusions: CI532 array insertion results in consistent scala tympani location and provides expected audiologic performance. Initial hearing preservation results are promising.

Define Professional Practice Gap & Educational Need: 1. New technology and device design 2. Lack of outcomes for new technology

Learning Objective: The objective of this research is to present early outcomes with a slim, modiolar cochlear implant array.

Desired Result: Attendees will gain a better understanding of the slim, modiolar array cochlear implant and its outcomes.

Indicate IRB or IACUC Approval: Approved

Intracochlear Measurements and Histologic Findings Relevant to Cochlear Implantation in Malformed Cochleae: A Human Temporal Bone Study

Reuven Ishai, MD; Joseph B. Nadol Jr., MD
Alicia M. Quesnel, MD

Hypotheses: 1) The cochlear duct length in temporal bones (TBs) with incomplete partition type II (IP-II) and cochlear hypoplasia (CH) is significantly smaller than normally formed cochleae. 2) The spiral ganglion cell (SPG) counts in TBs with MC are not significantly reduced.

Background: Understanding the cochlear duct and scala tympani dimensions in various types of malformed cochleae (MC), such as IP-II and CH, may inform the surgeon's choice of electrode array in these cases.

Methods: TBs from patients with MC including IP-II, CH type II, and CH type III were identified, and compared to TBs from patients with normally formed cochleae whose hearing met cochlear implantation criteria. A 2D cochlear reconstruction was performed. The cochlear duct and number of SPG were evaluated. The size of scala tympani in the basal turn of each cochlea was measured.

Results: The average length of cochlear duct in the MC (n=9, 3IP-II, 6CH) was significantly shorter than normally formed cochleae (n=8) in TBS from possible cochlear implant candidates (21.8mm vs. 33.2mm, t-test, $p << 0.05$). The height of scala tympani in lower/upper basal turns of the MC (1.0mm) was not different than the normally formed cochleae (0.9mm), ($p=0.07$). The average SPG count (in % of normal age-matched) was significantly lower in TBS with cochlear malformations (15% vs. 46%, $p<<0.05$).

Conclusion: The cochlear ducts lengths are shorter in IP-II and CH compared to normal cochleae, but the scala tympani is not smaller; this may inform electrode array selection. MC had significantly lower SPG counts.

Define Professional Practice Gap & Educational Need: Lack of awareness

Learning Objective: Evaluation of the the length of cochlear duct in temporal bones with malformed cochleae, and quantification of spiral ganglion cell populations in these malformed cochleae.

Desired Result: Understanding the histopathology of various types of malformed cochleaemay inform the surgeon's choice of electrode array.

Indicate IRB or IACUC Approval: Exempt

Prospective Evaluation of Patients Undergoing Concurrent Translabyrinthine Excision of Vestibular Schwannoma with Concurrent Cochlear Implantation

Kevin D. Brown, MD PhD; Margaret Dillon, AuD
Meredith Anderson, AuD

Objective: Translabyrinthine (TL) vestibular schwannoma (VS) resection may be accomplished with preservation of the cochlear nerve, permitting successful, concurrent cochlear implantation. In this single institution, FDA – approved feasibility study, we wished to determine the success and outcomes of concurrent cochlear implantation at the time of TL resection of VS.

Study Design: Prospective cohort

Setting: Tertiary referral center

Patients: Patients with small VS <1.5 cm in size and speech understanding < 60% in affected ear.

Intervention: Concurrent TL VS resection and cochlear implantation.

Main Outcome Measure: Sound localization and speech understanding

Results: All cochlear nerves were anatomically preserved. Five out of 6 patients had auditory precepts at the time of activation. At 1 month following surgery, AzBio scores (0dB SNR, with sound front, noise to normal ear, speech to implant ear) were improved by an average of 10% with implant on, persisting to 6 months out from surgery. Localization 1 month after surgery was markedly improved with RMS 81 degrees ± 13 in the "implant off" condition and 39 degrees ± 9 in the "implant on" condition. This was likewise maintained out 6 months.

Conclusions: These data demonstrate preservation of potential electrical hearing in TL VS surgery is consistently possible, with excellent improvement in sound localization. The delay in improvement of speech perception may reflect trauma to the cochlear nerve at the time of surgery, which may continue to improve.

Define Professional Practice Gap & Educational Need: To become aware of possible preservation of electrical hearing in vestibular schwannoma patients undergoing translabyrinthine surgery

Learning Objective: The learner will understand outcomes following translabyrinthine surgery to remove vestibular schwannomas as they relate to sound localization and speech understanding.

Desired Result: Attendees will be able to select patients from their practice that may benefit from concurrent vestibular schwannoma surgery and cochlear implantation.

Indicate IRB or IACUC Approval: Approved

ANS TRAINEE AWARD

Selective Stimulation of Facial Muscles following Chronic Intraneural Electrode Array Implantation and Facial Nerve Injury in the Feline Model

Yarah M. Haidar, MD; Ronald Sahyouni, BA
Omid Moshtaghi, BS; Hamid R. Djalilian, MD
John C. Middlebrooks, PhD; Harrison W. Lin, MD

Background: Our group has previously shown that activation of specific facial nerve (FN) fiber populations and selective contraction of facial musculature can be achieved through acute intraneural multi-channel microelectrode array (MEA) implantation in the feline model.

Hypothesis: Selective stimulation of facial muscles will be maintained in the setting of (1) chronic MEA implantation and (2) acute MEA implantation following FN injury recovery.

Methods: This study included seven cats. In three cats with normal facial function, chronic intraneural implantation was performed and tested biweekly for three months. Electrical current pulses were delivered to each channel individually, and elicited electromyographic (EMG) voltage outputs were recorded for each of several facial muscles. For FN injury experiments, two cats received a standardized hemostat-crush injury, and two received a transection-reapproximation injury to the FN. These four underwent acute implantation of a 4-channel penetrating MEA three months' post-injury.

Results: Stimulation through individual channels selectively activated restricted nerve populations, resulting in versatile contraction of individual muscles in cats with chronic array implantation and following nerve injury. Increasing stimulation current levels resulted in increasing EMG voltage responses in all cases.

Conclusion: We have established in the animal model the ability of a chronically implanted MEA to selectively stimulate restricted FN fiber populations and elicit contractions in specific FN, adding more evidence to the feasibility of a FN implant system. Likewise, following FN injury, selective stimulation of restricted FN fiber populations and subsequent contraction of discrete facial muscles can be achieved following acute MEA implantation.

Define Professional Practice Gap & Educational Need: To date, surgical management of patients with chronic facial paralysis has limited utility with inconsistent outcomes. This work serves to elucidate the functional and histological changes that occur following chronic microelectrode implantation and stimulation post-facial nerve injury in reanimating facial musculature following facial paralysis.

Learning Objective: To understand the utility of selective stimulation of facial muscles in the setting of (1) chronic muti-electrode array implantation and (2) acute multi-electrode array implantation following facial nerve injury recovery.

Desired Result: Attendees will further understand the ability of intraneural stimulation in rehabilitation of injured nerves.

Indicate IRB or IACUC Approval: Approved

MitoQ as Novel Agent for Protecting against Amikacin Ototoxicity

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Bailey Milne-Davies, BS; Jerin K. Joseph, BS
Patrick J. Antonelli, MD

Hypothesis: Mitoquinone (MitoQ) attenuates amikacin ototoxicity in guinea pigs.

Background: MitoQ, a mitochondria-targeted derivative of the antioxidant ubiquinone, has improved bioavailability and demonstrated safety in humans. Thus, MitoQ is a promising therapeutic approach for protecting against amikacin-induced ototoxicity.

Methods: Both oral and subcutaneous administration of MitoQ were tested. Amikacin-treated guinea pigs (n=12 to 18 per group) received water alone (control), decyl-TPP (positive control), or MitoQ 0.03 or 0.075g/L-supplemented drinking water; or injected subcutaneously with 3 mg/kg MitoQ or saline (control). Auditory brainstem response and distortion product otoacoustic emission were measured before MitoQ or control solution administration and after amikacin injections. Cochlear hair cell damage was assessed using scanning electron microscopy and Western blotting.

Results: With oral administration, animals that received 0.03g/L MitoQ had better hearing than controls at 24 kHz only at 3-weeks ($p=0.017$) and 6-weeks ($p=0.027$) post-amikacin. With subcutaneous administration, MitoQ-injected guinea pigs had better hearing than controls at 24 kHz only, 3-week post-amikacin ($p=0.013$). DPOAE amplitudes were decreased after amikacin injections, but were not different between treatments ($p>0.05$). Electron microscopy showed no difference in outer hair cell loss between treatments. Western blotting demonstrated limited attenuation of oxidative stress in the cochlea of MitoQ-supplemented guinea pigs.

Conclusions: Oral or subcutaneous MitoQ provided limited protection against amikacin-induced hearing loss and cochlear damage in guinea pigs. Other strategies for attenuating aminoglycoside-induced ototoxicity should be explored.

Define Professional Practice Gap & Educational Need: There is a lack of contemporary knowledge regarding the efficacy of clinically available antioxidants for the prevention of aminoglycoside ototoxicity. The mitochondria-targeted antioxidant, MitoQ, has shown potential as a prophylactic agent for the prevention of hearing loss induced by ototoxic drugs such as the aminoglycoside antibiotic, gentamicin, but it is unclear if this holds true for other aminoglycosides.

Learning Objective: At the conclusion of this presentation, the attendees will learn that the mitochondria-targeted antioxidant, MitoQ, provides limited protection against amikacin-induced cochlea oxidative damage and hearing loss.

Desired Result: The attendees may be able apply this knowledge by recognizing that although the mitochondria targeted antioxidant MitoQ has previously been shown to attenuate gentamicin- and cisplatin-induced ototoxicity, it provided very limited protection against amikacin-induced ototoxicity. Moreover, while oral MitoQ appear to be well-tolerated, with no significant adverse effects, subcutaneously injected MitoQ reduced weight gain in guinea pigs. Many questions need to be addressed if MitoQ is to be developed as a therapeutic against drug-induced hearing loss. Clinicians and researchers should consider other strategies for attenuating drug-induced ototoxicity.

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The Small Molecule Oral Drug Candidate SENS-341 Effectively Reduces Cisplatin-induced Hearing Loss in Rats

Mathieu Petremann, MS; Christophe Tran Van Ba, MS
Désiré Challuau; Stéphanie Bressieux, BS
Jonas Dyhrfjeld-Johnsen, PhD

Hypothesis: SENS-341 protects against cisplatin ototoxicity in rats.

Background: SENS-341 is a small molecule, orally administered drug candidate. Among pediatric and adult cancer patients, ~20% or more suffer significant hearing loss when treated with platinum-based chemotherapies (Frisina et al., 2016; van As et al., 2016) and currently no treatment exists. As SENS-341 acts on oxidative stress, neuro-inflammation, excitotoxicity and apoptosis downstream of the effector of an inner ear insult, the goal of this study is to evaluate whether the drug candidate could be effective in the protection against cisplatin-induced hearing loss.

Methods: After baseline audiometry (ABR at 8/16/24 kHz and DPOAE at 4/8/16/24/32 kHz) Wistar rats were randomized to receive either daily oral placebo (n=7) or SENS-341 (n=8) treatment for 14 days initiated 15 min before slow intravenous infusion of 8 mg/kg cisplatin. ABR thresholds and DPOAE amplitudes were evaluated at D7 and D14 after cisplatin administration.

Results: ABR thresholds were elevated by up to 30 dB at D7 and D14 after cisplatin administration in placebo treated rats and DPOAE amplitudes reduced by up to 19 dB. In SENS-341 treated animals, ABR threshold shifts were significantly reduced ($p=0.008$ and $p=0.012$ respectively) by 10-22 dB depending on stimulus frequency. Similarly, SENS-341 treatment significantly reduced the DPOAE amplitude loss at 70 dB SPL stimulus intensity by 2-14 dB at D7 ($p=0.04$) and D14 ($p=0.041$).

Conclusions: Daily, oral SENS-341 treatment significantly reduced cisplatin-induced hearing loss in rats. SENS-341 appears to be a good candidate for clinical development in cisplatin-induced ototoxicity.

Define Professional Practice Gap & Educational Need: There is a lack of knowledge and awareness of whether the small molecule, oral drug candidate SENS-341 can be effective as a therapeutic agent for the treatment of hearing loss induced by cisplatin.

Learning Objective: At the conclusion of this presentation, the attendees will learn that the small molecule, oral drug candidate SENS-341 reduced cisplatin-induced hearing loss in rats and can be further developed as a treatment of ototoxicity in chemotherapy patients.

Desired Result: The attendees may be able apply this knowledge by recognizing that SENS-341 may be a promising future therapeutic agent for protecting against cisplatin-induced ototoxicity.

Indicate IRB or IACUC Approval: Approved

Age-related Increase in Serum Levels of Otolin-1 in Humans

Ryan D. Tabtabai, BS; Laura Haynes, PhD
George A. Kuchel, MD, PhD; Kourosh Parham, MD, PhD

Objective: To test the hypothesis that age-related demineralization of otoconia will result in an age-related increase in serum levels of otoconia matrix protein, otolin-1.

Study design: Cross-sectional observational clinical trial.

Setting: Clinical research center.

Patients: Seventy-nine healthy men and women ranging in age from 22 to 95 years old.

Interventions: Diagnostic.

Main outcome measures: Serum levels of otolin-1 in relation to age.

Results: Mean serum levels of otolin-1 serum levels of subjects divided into four age groups (1: 20-30 [n=20], 2: 50-65 [n=20], 3: 66-80 [n=20], 4: 84-95 [n=19] years old) demonstrated an increasing trend with age. The difference between otolin-1 levels of groups 2 and 3 (P=0.04), as well as 2 and 4 (P=0.031) were statistically significant, but there was no significant difference between the two oldest groups.

Conclusions: Otolin-1 serum levels are significantly higher in patients older than 65 years of age. This is consistent with previous scanning electron microscopy findings of age-related otoconia degeneration and increased prevalence of benign paroxysmal positional vertigo (BPPV) with age. Together with our previous finding that serum otolin-1 levels are elevated in patients with BPPV, results support the use of serum otolin-1 as a biomarker for the structural health of otoconia and BPPV.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge of age-related otoconia degeneration in humans as well as lack of biomarkers to assess the structural health of otoconia for both research and clinical applications.

Learning Objective: To test the hypothesis that age-related demineralization of otoconia will result in an age-related increase in serum levels of otoconia matrix protein, otolin-1.

Desired Result: Serum otolin-1 level is a promising biomarker for the structural health of otoconia and BPPV. Otolin-1 has applications in both research and clinical diagnosis where direct examination of otoconia in humans is challenging and diagnosis of BPPV can be obfuscated and time-consuming, respectively.

Indicate IRB or IACUC Approval: Approval

Connexin 26 Immunofluorescence in Temporal Bones with Cochlear Otosclerosis

Mia E. Miller, MD; Ivan A. Lopez, PhD
Akira Ishiyama, MD; Fred H. Linthicum, MD

Hypothesis: Connexin-26 (Cx26) expression is diminished in the spiral ligament of subjects with hearing loss and cochlear otosclerosis (CO).

Background: Human temporal bone (HTB) studies have demonstrated that CO is associated with hyalinization of the spiral ligament. We hypothesize that hyalinization is associated with a loss of fibrocytes and a decline in fibrocyte expression of Cx26. Cx26 and Connexin-30 encode gap junction proteins expressed in supporting cells of the organ of Corti, the spiral limbus, stria vascularis and in fibrocytes of the spiral ligament. These gap junctions are critical for potassium recycling and maintenance of the endocochlear potential. Diminished expression of these proteins would likely be associated with hearing dysfunction.

Methods: Histopathology and clinical characteristics of 45 HTB specimens with CO and spiral ligament hyalinization were reviewed. A subset with a history of sensorineural or mixed hearing loss but normal or near-normal hair cell counts were analyzed with light microscopy and immunohistochemical analysis. Immunofluorescence was qualitatively assessed and quantitatively reviewed using the computer image analysis software Fiji (*ImageJ*).

Results: H&E staining demonstrated hyalinization in the spiral ligament and loss of type II and type III fibrocytes. Immunostaining with Cx26 demonstrated diminished expression of Cx26 in not only the spiral ligament but also throughout the cochlea compared with normal controls.

Conclusions: The expression of the key gap junction protein, Cx26, is reduced in the spiral ligament and cochlea of subjects with CO, and likely plays a role in hearing loss in CO subjects with normal or near-normal cochlear hair cell counts.

Define Professional Practice Gap & Educational Need: 1. Lack of understanding of causes of sensorineural hearing loss in cochlear otosclerosis 2. The need to advance the study of the temporal bone with novel immunohistochemical techniques 3. Lack of awareness of differential protein expression in the human temporal bone in cochlear otosclerosis

Learning Objective: 1. Outline possible causes of sensorineural hearing loss in cochlear otosclerosis based on temporal bone analysis. 2. Apply advanced immunohistochemical techniques to archival human temporal bone specimens. 3. Demonstrate differential Connexin expression in human temporal bones with cochlear otosclerosis.

Desired Result: 1. Better understand the pathology of cochlear otosclerosis. 2. Recognize the need for further advanced study of the human temporal bone. 3. Explain to patients the state of the art in otosclerosis research.

Indicate IRB or IACUC Approval: Approval

Patulous Eustachian Tube Dysfunction: Patient Demographics and Comorbidities

Bryan K. Ward, MD; Yehia Ashry, MD
Dennis S. Poe, MD, PhD

Objective: Describe a large cohort of patients presenting with patulous Eustachian tube (pET) dysfunction.

Study design: Retrospective case series

Setting: Tertiary referral center

Patients: All outpatient visits (2004-2016) that were assigned ICD9 code (381.7-Patulous Eustachian tube) were screened. Only patients with observed TM(TM) movements during ipsilateral nasal breathing or acoustic reflex decay testing demonstrating transmitted nasal breathing were included(n=190,n=239 ears).

Main outcome measures: Demographics and nasopharyngoscopy/otomicroscopy findings by comorbidities.

Results: The majority(54%) was female and mean age of symptom onset was 38.0(SD 20.0) years. Common symptoms included voice autophony(93%), breath autophony(92%), aural fullness(57%), pulsatile tinnitus(17%), and crackling or rumbling sounds(14%). Symptoms increased in frequency and duration with time(65%), were exacerbated with exercise(27%) and improved with placing the head in a dependent position(65%), sniffing(28%), upper respiratory infection(8%), and ipsilateral internal jugular vein compression(12%). In 52% pET was bilateral. Common comorbidities include environmental allergy(49%), weight loss(35%), laryngopharyngeal reflux(33%), anxiety(31%), autoimmunity(13%) and neuromuscular disease(8%). Allergy and anxiety patients were younger and more likely to have tensor veli palatini spasm on exam($p<0.05$,chi-square). Allergy patients also had relief with sniffing and TM retraction($p<0.01$,chi-square). Weight loss patients reported mean loss 19.7kg(SD 23.1), were older, more rapidly diagnosed and more likely to have persistent symptoms ($p<0.05$). Initially, all patients were treated medically, with 47% eventually electing surgical intervention.

Conclusions: pET is progressive and often bilateral. In this large series of pET, in addition to weight loss and chronic medical conditions, allergy and stress/anxiety were identified as novel risk factors. Most patients can be treated medically.

Define Professional Practice Gap & Educational Need: Lack of awareness of common presenting features of patulous Eustachian tube. 2. Lack of knowledge of risk factors for patulous Eustachian tube and clinical examination findings that accompany those risk factors.

Learning Objective: To better understand the range of presentations of patients with patulous Eustachian tube and common clinical examination findings. In particular, to recognize the risk that patients with chronic sniffing pose to middle ear function and its association with patulous Eustachian tube dysfunction.

Desired Result: Attendees will better recognize a patient with patulous Eustachian tube when they present to their clinic. This can lead to earlier and accurate diagnosis, and may prevent

Indicate IRB or IACUC Approval: Approved

Radiographic Signs of Intracranial Hypertension in Patients with Meniere's Disease May Predict Poor Audiovestibular Outcomes

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Objectives: Describe the relationship between radiographic signs of intracranial hypertension (ICH) and audiovestibular presentations/outcomes in Meniere's Disease (MD).

Study design: Retrospective review.

Setting: Tertiary referral center.

Patients: 68 adults with MD were analyzed from 2011-2015 after meeting the following criteria: MRI and audiogram were performed within 1 month of presentation, duration of follow up was 6+ months, and there was no evidence of intracranial tumor(s), hydrocephalus, cerebral venous thrombosis, pregnancy, trauma or major infection.

Intervention(s): Three MRI signs of ICH were assessed: empty sella, optic nerve sheath dilation/tortuosity, and posterior globe flattening. Patients with 2+ signs were compared to those with 0-1 signs.

Main outcome measure(s): The following variables were compared between subgroups: age, gender, ethnicity, obesity and prevalence of bilateral MD. Pure tone average (PTA), air-bone gap (ABG) and word recognition scores (WRS) were compared at presentation and most recent follow up. The primary outcome was failed medical management with progression to surgery.

Results: 19 patients had 2+ signs of ICH. 49 had 0-1 signs. Patients with multiple signs were significantly more likely to be male (p=0.01), obese (p=0.02), and have worse mean PTA (53.0 vs. 39.1dB, p=0.02) and WRS (69% vs 84%, p=0.05) at presentation. ABG did not differ between the groups. Patients with 2+ signs were also significantly more likely to progress to surgery (84% vs. 42%, p=0.002) and have worse PTA and WRS at most recent follow up (p=0.02).

Conclusions: MD patients with multiple radiographic signs of ICH may have worse clinical presentations and treatment outcomes.

Define Professional Practice Gap & Educational Need: Lack of understanding regarding the association between idiopathic intracranial hypertension, obesity, and audiovestibular outcomes in Meniere's Disease.

Learning Objective: Describe the relationship between radiographic signs of intracranial hypertension (ICH) and audiovestibular presentations/outcomes in Meniere's Disease (MD).

Desired Result: Attendees will be provided evidence for a new predictor of audiovestibular outcomes in patients with Meniere's Disease. Using this information, they may consider obtaining MRI at the time of presentation in patients with Meniere's Disease (if not already doing so for asymmetric hearing loss) and in concert with a neuroradiologist review the imaging for signs of intracranial hypertension. If present, practitioners may modify their patient counseling and enact more rigorous medical management strategies.

Indicate IRB or IACUC Approval: Approved

Large Vestibular Aqueduct: Radiological Review of High-Resolution CT versus High-Resolution Volumetric MRI

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Objectives: To compare the diagnostic yield of high-resolution volumetric T2-weighted MRI(e.g. FIESTA-C, CISS, SPACE, CUBE) compared to high-resolution computed tomography(HRCT) for diagnosis of large vestibular aqueduct(LVA) and associated inner ear anomalies.

Study Design: Three board-certified neuroradiologists performed an independent, blinded radiological review for diagnosing LVA with 2:1 age-matched controls to eliminate bias.

Setting: Tertiary referral center

Patients: All patients between 2000-2016 with hearing loss who underwent both HRCT and volumetric T2-weighted MRI and diagnosed with LVA on either modality.

Main Outcome Measures: Diagnostic yield for LVA and associated inner ear anomalies using HRCT versus volumetric T2-weighted MRI.

Results: LVA was concurrently detected on both CT and MRI in 89.4% of cases(42/47). CT detected clinically significant LVA in 4 cases in which MRI was negative, while MRI detected clinically significant LVA in 1 case in which CT was negative. However, there was no statistical difference between MRI versus CT in detecting LVA($p=0.18$). The sensitivity for detecting associated cochleovestibular anomalies and the types of abnormalities uncovered between CT versus MRI differed and will be reported.

Conclusion: Historically, HRCT has been the imaging modality of choice for diagnosing LVA. However, this updated imaging review found a high concordance rate between the two imaging modalities. The diagnostic yield for LVA was not statistically different between high-resolution volumetric T2-weighted MRI versus HRCT. These data suggest that volumetric T2-weighted MRI-alone may be sufficient for diagnosis of inner ear anomalies and provides an added benefit over HRCT for interrogation of cochleovestibular nerve status and retrocochlear pathology. Future studies are needed to validate these early but promising findings.

Define Professional Practice Gap & Educational Need: It is not know which imaging modality (CT vs. MRI) has higher sensitivity for diagnosing a large vestibular aqueduct. Previous studies have employed older MRI technology (e.g. fast spin-echo T2-weighted images), however there has not been a study comparing CT to newer MRI technology which is currently widely available, specifically high resolution volumetric MRI, such as FIESTA or CISS sequences. We address this question in the current experiment.

Learning Objective: To compare the diagnostic yield of high-resolution volumetric T2-weighted MRI (e.g. FIESTA-C, CISS, SPACE, CUBE) compared to high-resolution computed tomography (HRCT) for diagnosis of large vestibular aqueduct (LVA) and associated inner ear anomalies. To provide guidance as to the best initial imaging test to obtain in the workup for hearing loss.

Desired Result: There is no consensus as to whether CT or MRI should be the initial imaging modality of choice when evaluating a patient for hearing loss. This study presents new evidence using the latest available MRI technology to provide guidance as to which imaging modality (CT vs. MRI) to choose.

Indicate IRB or IACUC Approval: Approval

NICHLOAS TOROK VESTIBULAR AWARD

Investigating Vestibular Blast Injury: Semicircular Canal Pressure Changes during High-Intensity Acoustic Stimulation

Anne K. Maxwell, MD; Renee M. Banakis Hartl, MD, AuD
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Daniel J. Tollin, PhD

Hypothesis: High-intensity acoustic stimulation causes measurable pressure waves in the semicircular canals.

Background: High-intensity acoustic trauma can cause hearing loss and balance disruptions. To examine the propagation of high-intensity acoustic stimuli to the vestibular end organs, we measured fluid pressure in the semicircular canals during both air- and bone-conducted high-intensity sound presentation.

Methods: Five full-cephalic human cadaveric heads were prepared bilaterally with a mastoidectomy and extended facial recess. Vestibular pressures were measured within the superior, lateral and posterior semicircular canals and referenced to intracochlear pressure within the scala vestibuli with fiber-optic pressure probes. Pressures were measured concurrently with stapes velocity via laser Doppler vibrometry for both air- and bone-conduction. Stimuli were pure tones between 100 Hz and 14 kHz presented with custom closed-field loudspeakers for air-conducted sounds and via commercially available bone-anchored device for bone-conducted sounds.

Results: Pressures recorded in the superior, lateral and posterior semicircular canals in response to sound stimulation were equal to or greater in magnitude than those recorded in the scala vestibuli (up to 10 dB higher). The pressure magnitudes varied across canals in a frequency-dependent manner.

Conclusions: High sound pressure levels were recorded in the semicircular canals with sound stimulation, suggesting that similar acoustical energy is transmitted to the semicircular canals and the cochlea. Since these intralabyrinthine pressures are comparable to intracochlear pressure levels known to cause trauma in the auditory system, our results suggest that the vestibular end organs may also be at risk for injury during exposure to high-intensity acoustic trauma.

Define Professional Practice Gap & Educational Need: Sound pressure levels known to correspond to acoustic trauma have been measured in the cochlea but these have never been measured before in the vestibular end organs. There is a lack of awareness if similar pressure waves are present or measurable in the vestibular end organs.

Learning Objective: To show that pressure waves are present and measurable within the vestibular end organs with high-intensity acoustic stimulation and that these are similar to levels known to cause acoustic trauma in the cochlea.

Desired Result: To increase knowledge of potential for vestibular system injury following high-intensity acoustic trauma.

Indicate IRB or IACUC Approval: Approved

Long-Term Outcomes for Surgical Treatment of Superior Canal Dehiscence Syndrome

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John P. Carey, MD

Objectives: To evaluate the long term outcomes of surgery for Superior Canal Dehiscence Syndrome (SCDS).

Study Design: Cross-sectional survey

Setting: Tertiary referral center

Patients: Adults who have undergone surgery for SCDS with at least one-year follow-up

Interventions: 55-item web-based survey of symptoms and quality of life

Main outcome measures: Resolution of characteristic SCDS symptoms: dizziness, imbalance, oscillopsia, tinnitus, etc., and patient-reported quality of life.

Results: 95 (43%) out of 219 eligible patients completed the survey (60% female, mean age 55). Surgery was performed predominantly by middle fossa craniotomy (91%). The mean follow-up time was 5.3 years (range 1-20). The most commonly bothersome symptoms pre-operatively were imbalance (43%), autophony (41%), and sensitivity to loud sounds (38%). The majority of patients reported improvement in overall symptoms (94%), and quality of life (90%), while a minority reported worse symptoms (3.2%) and quality of life (8.6%) at the time of survey. The majority of patients reported improved ability to function at work (76%) and socially (80%), while a minority reported worse ability to function at work (14%) and socially (11%). The symptoms with greatest mean improvement on a ten-point scale were autophony (6.5), pulsatile tinnitus (6.1), and sensitivity to loud sounds (5.2), while those with the least improvement were imbalance (2.4), dizziness (3.3), and headache (2.0).

Conclusions: This study represents the largest long-term follow up assessment of SCDS symptoms after surgical repair. Our results indicate a lasting benefit for the majority of patients, with auditory symptoms showing the most significant improvement.

Define Professional Practice Gap & Educational Need: 1. There are currently no large long-term studies of the outcomes of surgical treatment of Superior Canal Dehiscence Syndrome (SCDS). 2. Lack of adequate evidence on the long-term impact of surgery on quality of life. 3. Lack of knowledge of which symptoms of SCDS are more or less likely to improve after surgery.

Learning Objective: After this presentation, physicians will: 1. Understand the long-term benefits of surgical treatment of Superior Canal Dehiscence Syndrome (SCDS); 2. Understand the long-term impact of surgery on quality of life; 3. Understand that auditory symptoms show the most improvement.

Desired Result: Attendees will be able to use this unique, large long-term study to appropriately counsel their patients regarding the long-term outcomes of surgical treatment of Superior Canal Dehiscence Syndrome (SCDS).

Indicate IRB or IACUC Approval: Approved

Systematic Review of Hearing Outcomes after Radiotherapy for Vestibular Schwannoma

Adam R. Coughlin, MD; Tyler J. Willman, MD
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Objective: To determine the long-term serviceable hearing preservation rate for spontaneous vestibular schwannoma treated by primary radiotherapy

Data sources: The MEDLINE/PubMed, Web of Science, Cochrane Reviews, and EMBASE databases were searched using a comprehensive Boolean keyword search developed in conjunction with a scientific librarian. English language papers published from 2000 to 2016 were evaluated.

Study selection: Inclusion criteria: full articles, pre-treatment and post-treatment audiograms or audiogram based scoring system, vestibular schwannoma only tumor type, reported time to follow-up, published after 1999, use of either GammaKnife or linear accelerator radiotherapy. Exclusion criteria: case report or series with fewer than five cases, inadequate audiometric data, inadequate time to follow-up, neurofibromatosis type 2 exceeding 10% of study population, prior treatment exceeding 10% of study population, repeat datasets, use of proton beam therapy, and non-English language.

Data extraction: Two reviewers independently analyzed papers for inclusion. Serviceable hearing was defined as either PTA $\leq$ 50db with SDS $\geq$ 50%, AAO-HNS Hearing Class A or B, or Gardner-Robertson Grade I or II. Aggregate data was used when individual data was not specified.

Data synthesis: Means were compared with student t-test and Wilcoxon rank test.

Conclusions: 48 articles containing a total of 2002 patients with serviceable hearing were identified for analysis. The aggregate crude hearing preservation rate was 57.1% at an average reporting time of 40.7 months after radiotherapy treatment. Analysis of time-based reporting shows a clear trend of decreased serviceable hearing preservation extending to ten-year follow-up. This data encourages a future long-term controlled trial.

Define Professional Practice Gap & Educational Need: The current management of vestibular schwannoma includes observation, microsurgery, and radiotherapy. In addition to tumor control, hearing preservation is among the most important outcome factors which influence physician and patient decision making. The current literature reports a wide variation of hearing preservation rates following radiotherapy treatment of vestibular schwannoma. The majority of these articles report outcomes of single institution case series. This study attempts to more accurately define long-term serviceable hearing preservation rates and explore the factors influencing hearing preservation.

Learning Objective: Learn accurate hearing preservation rate following radiotherapy treatment of vestibular schwannoma. Understand the importance of time from treatment as critical factor when reporting in hearing preservation rates.

Desired Result: The physician should be able to better counsel patients with vestibular schwannoma on accurate, long term hearing preservation rates.

Indicate IRB or IACUC Approval: Exempt

Impact of Surgical Volume on Vestibular Schwannoma Surgical Outcomes

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Objective: Determine the effect of hospital surgical case volume on the outcomes of vestibular schwannoma (VS) surgery

Study Design: Analysis of University HealthSystem Consortium inpatient database

Setting: University HealthSystem Consortium member hospitals (includes virtually every US academic medical center)

Patients: 3,697 patients who underwent VS resection over a three year timespan (2012 – 2015) grouped by race, age, comorbidities, payer, and gender with the exclusion of patients with neurofibromatosis type 2

Intervention: Surgical resection of VS

Main Outcome Measures: Comparing post-operative outcomes (length of stay, morbidity, and mortality) at hospitals grouped by volume (low, medium, and high) and complications at hospitals grouped into deciles by volume

Results: Baseline patient characteristics in terms of age, sex, gender, and baseline comorbidities were similar between hospital groups. Patients undergoing VS at high-volume centers had the shortest length of stay followed by medium-volume hospitals, then low-volume hospitals ($p \leq 0.005$). Low-volume hospitals had significantly higher rate of complications including stroke, aspiration, and respiratory failure ($p \leq 0.0175$).). There was also a strong negative correlation between complication rates and hospital volume ($r = -0.8164$, $p = 0.0040$) when grouping hospitals into deciles by volume. However, patients at high-volume hospitals were more likely to be Caucasian (83.1%, $p = 0.0001$) and have private insurance (76.7%, $p < 0.0001$).

Conclusions: Volume of VS surgery performed at a hospital appears to impact length of stay and rates of postoperative complications. Most baseline demographics among hospital groups were similar though factors other than volume alone may impact patient outcomes.

Define Professional Practice Gap & Educational Need: 1) Lack of understanding of how surgical volume is associated with vestibular schwannoma surgical outcomes such as length of stay, complications, and mortality 2) Lack of understanding on the differences in patient demographics across hospitals of low, medium, and high surgical volume and how this may impact outcomes

Learning Objective: 1) Attendees will be able to identify differences in length of stay, complication rate, and mortality rate associated with hospitals of varying surgical volume 2) Attendees will have better understanding of the differences and similarities in patient demographics of low, medium, and high surgical volume hospitals

Desired Result: 1) Attendees will be more aware of how organizational practices and surgical experiences may lead to better outcomes and how they may implement these changes at their institution 2) Attendees will have a better understanding of contemporary outcomes for vestibular schwannoma surgery from a nationwide database. 3) Attendees will be able to improve care through mitigation of surgical risks

Indicate IRB or IACUC Approval: Exempt

Is Routine Chemical Prophylaxis Needed for Prevention of Deep Vein Thrombosis in Acoustic Neuroma Surgery?

Geoffrey C. Casazza, MD; Richard K. Gurgel, MD

Objectives: The benefit of routine chemical prophylaxis to prevent deep vein thrombosis (DVT) following skull base surgery is controversial. Chemical prophylaxis can prevent morbidity and mortality; however there are risks for devastating complications, including intracranial hemorrhage. Little is known about the safety of chemical prophylaxis following acoustic neuroma surgery.

Study Design: Retrospective case-control study.

Methods: A retrospective chart review of patients who underwent acoustic neuroma excision at the University of Utah from 2011 to 2016 was performed. Patients were divided by receipt of chemical DVT prophylaxis. Number of DVTs and post-operative complications (intracranial hemorrhage [IH], abdominal hematoma [AH], and post-auricular hematoma [PAH]) were recorded.

Results: 126 patients were identified, 55 received chemical prophylaxis and 71 did not. All patients received mechanical lower extremity prophylaxis. Two patients developed a DVT and no patient developed a pulmonary embolism. Both patients that developed a DVT received chemical prophylaxis. There was no statistically significant difference in the incidence of DVT's among the two groups ($p = 0.1886$). Five patients developed post-operative complications: 2 IH, 3 AH, and 0 PAH. All 5 patients with a complication received chemical prophylaxis ($p = 0.00142$). The relative risk for a complication was 14.14 (95% CI = 0.7987 to 250.4307; $p = 0.0778$).

Conclusions: There was a significant difference between numbers of post-operative complications but no difference between the numbers of DVTs. Interpretation of these results is limited due to a small sample size, however with a larger sample size we will likely generate similar results given the frequency of DVT in the entire population.

Define Professional Practice Gap & Educational Need: Lack of knowledge on the necessity of routine deep vein thrombosis prevention in acoustic neuroma surgery.

Learning Objective: Define the necessity of routine chemical deep vein thrombosis prophylaxis in acoustic neuroma surgery.

Desired Result: Develop an understanding of the benefits and risks of routine use of chemical deep vein thrombosis prophylaxis.

Indicate IRB or IACUC Approval: Approved

Audiologic Natural History of Small Volume Cochleovestibular Schwannomas in Neurofibromatosis Type 2

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Kelly A. King, PhD; Carmen C. Brewer, PhD
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Objective: To describe the natural history of audiologic features of neurofibromatosis type 2 (NF2), treatment-naïve, small volume (< 1000 mm3) cochleovestibular schwannomas (CVS).

Study design: Prospective, longitudinal cohort study.

Setting: Quaternary medical research institute.

Patients: NF2 patients with small volume, treatment-naïve CVSs enrolled in a prospective natural history study from 2008-2015 (n= 127 ears, 74 patients).

Interventions: Serial audiometry over a mean follow-up of 3.8 years.

Outcome measures: Pure tone audiometry at 500Hz, 1KHz, 2KHz, 3KHz, 4KHz, 8KHz, and four frequency PTA (4f-PTA) (.5, 1, 2, 4 KHz).

Results: Mean age at enrollment was 36.4 years (range 8 to 68) and mean 4f-PTA was 27.9 dB HL (range 0.00 to 118.3; SD=27.7). Progressive sensorineural hearing loss (SNHL) was defined as a loss of 10 dB or greater over the duration of follow-up. 4f-PTA worsened in 32.3% (n=41 ears) at a mean rate of 8.27 dB/year. This differed significantly from those whose hearing remained stable (n=86 ears , 67.7%, 1.4 dB/year, t-test, P=<0.001). 42.5% (n=54 ears) had progressive SNHL in at least one measured frequency. Progressive SNHL was seen most commonly at 8000Hz (n= 54 ears, 42.5%) and progressed at a rate of 6.2 dB/year. In affected ears, progression of hearing loss was most dramatic at 2000Hz with a rate of 9.0 dB/year (n=50 ears, 39.3%).

Conclusion: Within NF2, small volume CVSs with progressive SNHL and those without seem to represent two distinct populations. In tumors with progressive SNHL, hearing was affected most frequently at 8000Hz and most severely at 2000Hz.

Define Professional Practice Gap & Educational Need: Lack of contemporary knowledge of the natural audiologic history of NF2 related cochleovestibular schwannomas, particularly in the small volume subtype.

Learning Objective: To understand the nature and progression of hearing loss in NF2 related CVSs

Desired Result: Attendees' understanding of the natural progression of hearing loss in NF2 CVSs can be applied in treatment decision making as well as patient and family education.

Indicate IRB or IACUC Approval: Approved

Unlike in Vestibular Schwannoma, Cochlear Dysfunction is not Common in Meningioma of the Cerebellopontine Angle

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Sonaali Aggarwal, BA; Fred H. Linthicum Jr., MD
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Hypothesis: Cochlear damage in human meningioma of the cerebellopontine angle is not as common as in vestibular schwannoma (VS).

Background: Meningioma and VS of the cerebellopontine angle and internal auditory canal typically cause hearing loss. Cochlear damage is known to contribute to VS-induced sensorineural hearing loss. Cochlear histopathology in meningioma has not been reported.

Methods: Retrospective analysis of cochlear histopathology in 8 unoperated meningiomas of the cererebellopontine angle identified after screening human temporal bone collections from 3 academic medical centers. The findings were contrasted with those from 32 unoperated VSs (Roosli et al. 2012).

Results: Cochlear damage was not detectable in 50% of meningiomas, in contrast to only 25% of VSs. A predominant or exclusive hair cells loss was not found in any meningioma, but was present in 18.8% of VSs. The incidence of strial atrophy and spiral ganglion neuron loss was similar in both groups. However, cochlear hydrops was absent in all mengiomas and present in 28% of VSs. Endolymphatic and perilymphatic precipitate was infrequent in meningioma (12.5%) compared to VS (31.3% and an additional 12.5% with an exclusive perilymphatic precipitate).

Conclusions: Cochlear damage in human meningioma of the cerebellopontine angle is substantially rarer than in VS. This may explain the more commonly observed hearing improvement after surgical resection of meningioma than VS. The findings underline the importance of developing therapeutic strategies to prevent cochlear degeneration in tumors of the cerebellopontine angle and internal auditory canal.

Define Professional Practice Gap & Educational Need: 1. Cochlear histopathology in meningioma of the cerebellopontine angle has not been described. 2. Mechanisms of the more common hearing improvement after surgical resection of meningioma than vestibular schwannoma are not well understood.

Learning Objective: To identify differences in cochlear histopathology in meningioma and vestibular schwannoma of the cerebellopontine angle and internal auditory canal.

Desired Result: 1. To recognize that the infrequent cochlear damage in meningioma of the cerebellopontine angle may explain the observed hearing improvement after surgical resection of meningioma. 2. To appreciate that the much more common cochlear damage in vestibular schwannoma (VS) than meningioma may explain why surgical VS resection typically does not improve patients' hearing. 3. To highlight the need to develop therapeutic strategies that prevent cochlear degeneration in tumors of the cerebellopontine angle and internal auditory canal.

Indicate IRB or IACUC Approval: Exempt

Surgical Management of Tumors Involving Meckel's Cave and Cavernous Sinus: Role of a Lateral Sphenoidectomy Approach

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Objective: To study the indications and outcomes of lateral sphenoidectomy as part of a combined skull base approach in the treatment of tumors involving Meckel's cave and cavernous sinus.

Study design: Retrospective case series.

Setting: Tertiary referral center

Patients: Twenty-one consecutive patients (mean age: 45 years, range: 16 – 76) who underwent transzygomatic, extended middle fossa approaches for tumors involving Meckel's cave and cavernous sinus.

Interventions: Surgical access to Meckel's cave and cavernous sinus was achieved via extended middle fossa, trans-clinoid approach. Lateral sphenoidectomy was defined as drill-out of the greater sphenoid wing lateral to foramen rotundum. Reconstruction was achieved using combination of autologous and synthetic materials. Eleven patients (52%) received adjuvant radiation.

Main outcome measures: Tumor pathologies included meningioma (16 patients), epidermoid cyst (2), trigeminal schwannoma (1), and invasive pituitary adenoma (1). Mean (range) pre-operative tumor size was 4.1cm (1.3 – 9). Mean (range) length of follow-up was 4 years (range 0.1 – 10). Overall tumor control and gross total resection were achieved in 90% and 24% of patients, respectively. Lateral sphenoidectomy was performed in 15 patients (71%) for enhanced surgical access and/or tumor extension to the infratemporal fossa (4 patients). Post-operatively, cranial nerve deficits occurred in 11 (52%) patients (V – 7 patients; III, IV, or VI – 4; VII – 1; VIII – 1). CSF leak and hydrocephalus occurred in 1 and 4 patients, respectively.

Conclusion: In combination with middle fossa-based approaches to tumors involving Meckel's cave and cavernous sinus, lateral sphenoidectomy may play a viable role in tumor access and control.

Define Professional Practice Gap & Educational Need: 1. Lack of awareness 2. Lack of contemporary knowledge

Learning Objective: 1. Gain awareness in skull base approaches 2. Understand lateral sphenoidectomy as an option in a combined skull base approach

Desired Result: 1. Improve the care of patients with skull base tumors

Indicate IRB or IACUC Approval: Approved