SELECTED ABSTRACTS
in order of presentation

ORAL
PRESENTATIONS

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AMERICAN NEUROTOLOGY SOCIETY

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Podium presentations are Saturday & Sunday
High Prevalence of Comorbid Vestibular Migraine in Patients with Superior Semicircular Canal Dehiscence Syndrome

Miriam R. Smetak, MD, MS; Nauman F. Manzoor, MD; Kelsey Hatton, AuD, CCC-A
Alejandro Rivas Campo, MD; Marc L. Bennett, MD, MMHC
David S. Haynes, MD, MMHC; Matthew R. O'Malley, MD

Objective: To demonstrate the high prevalence of comorbid vestibular migraine (VM) and superior semicircular canal dehiscence syndromes (SSCD).

Study Design: Retrospective review of a SSCD database

Setting: University-based tertiary medical center

Patients: 96 patients diagnosed with SSCD from 2009 to 2017

Interventions: None

Main Outcome Measures: Comorbid diagnosis of VM, success of intervention aimed at SSCD

Results: Of the 96 patients identified with superior semicircular canal dehiscence (SSCD) at our medical center from 2009-2017, 37 (38.5%) were also diagnosed with vestibular migraine (VM). Diagnosis of VM was made based on clinical impression, history of migraine, and thorough neurotologic evaluation. Of these 37 patients, 6 (16.2%) were diagnosed with VM only after surgical correction of SSCD, while the other 31 received treatment of VM prior to consideration for surgical correction. 15 patients (40.5%) were treated with a combination of surgery and migraine therapy, of which 7 (58%) reported complete resolution of symptoms and 1 (6.7%) had worsening of symptoms. 12 patients were treated for VM alone, of which 5 (41.7%) had complete resolution of symptoms and 1 (8.3%) had no change. 11 patients (29.7%) were lost to follow up, none of which was surgically treated.

Conclusions: These results demonstrate the high prevalence of VM in the SSCD population. Distinguishing which symptoms can be attributed to each syndrome can be difficult, and often is not completely elucidated until after surgical treatment of SSCD. Unrecognized or undertreated VM may contribute to treatment failure of surgical correction of SSCD. Further research is needed to better understand the physiologic mechanism linking these two disorders.

Define Professional Practice Gap & Educational Need: A significant number of patients with superior semicircular canal dehiscence have persistence of symptoms after surgical correction of SSCD. Part of this treatment failure may be due to co-existence of vestibular migraine in this patient population.

Learning Objective: To better understand the patient-specific factors that lead to failure of surgical treatment for superior semicircular canal dehiscence, specifically the high prevalence of comorbid vestibular migraine.

Desired Result: A high level of suspicion should be maintained for the coexistence of vestibular migraine and superior semicircular canal dehiscence.

Level of Evidence – LEVEL V – Case series, studies with no controls

Indicate IRB or IACUC: Vanderbilt University Medical Center, IRB #181384. Approved 8/16/2018.
Circulatory Otologic Biomarkers in Meniere’s Disease and Vestibular Migraine

James G. Naples, MD; Khalili Rahman, BS; Drew Soda, BS
Michael J. Ruckenstein, MD; Kourosh Parham, MD, PhD

Objective: There is emerging evidence to suggest a role for prestin and otolin-1 as peripheral biomarkers of otologic disorders. Meniere’s disease (MD) is a peripheral otologic disorder that can be difficult to distinguish from central disorders that cause vertigo such as Vestibular Migraine (VM). Here we evaluate a potential role for prestin and otolin-1 as peripheral otologic-specific biomarkers in differentiating MD from VM.

Study Design: Prospective, cohort study

Setting: High-volume, University setting

Patients: 19 patients with Definite/Probable MD based on AAO-HNS criteria and 12 patients with VM based on ICHD-3 criteria were included in the study.

Interventions: Peripheral blood draw was performed, and serum evaluated with enzyme-linked immunosorbent assay (ELISA) to obtain prestin and otolin-1 values. Qualitative statistical analysis was performed between groups using independent samples t-test.

Main Outcome Measures: Prestin and otolin-1 levels between cohorts

Results: There were 19 MD and 12 VM patients who had serum collected for analysis. One of the VM patient samples was hemolyzed and removed from analysis. In the 19 MD patients, the mean prestin level was 2.33±0.81 ng/ml (mean ± SEM) compared to 0.64±0.10 ng/ml in the VM patients (p=0.011). Similarly, otolin-1 levels in MD patients (109.67±42.5 pg/ml) were significantly elevated relative to VM patients (30.96±6.00 pg/ml) (p=0.037).

Conclusions: Prestin and otolin-1 levels were elevated in MD subjects relative to VM subjects. These results suggest that otologic biomarkers may have a role in differentiating between MD and VM subjects.

Define Professional Practice Gap & Educational Need: Meniere’s disease is a peripheral otologic disorder that has symptoms which overlap with the central disorder of vestibular migraine. Emerging research has raised the prospect of inner-ear-specific biomarkers in circulation, such as prestin and otolin-1, which may have applications to otologic disorders. Application of these biomarkers would address the practice gap of differentiating MD and VM by potentially offering a tool to determine if the symptoms are otologic or central in nature.

Learning Objective: To recognize an emerging role for inner ear biomarkers in circulation as a potential tool to differentiate MD from VM.

Desired Result: The desired result is that physicians learn of the potential utility of inner ear biomarkers in differentiating patient with MD and VM. Additionally, we hope that these results lay the foundation for the possibility of offering biomarkers as a resource to improve diagnosis of MD and VM.

Level of Evidence – Level III

Indicate IRB or IACUC : IRB Protocol # 829041
Analyzing MicroRNA Profiles in the Human Perilymph and Serum in Patients with Meniere’s Disease

Matthew Shew, MD; Helena Wichova, MD; Kevin Sykes, PhD, MPH
Devin Koestler, PhD; Hinrich Staecker, MD, PhD

Hypothesis: microRNA (miRNA) profiles related to Meniere’s disease are reflected in the perilymph and serum of patients compared to other inner ear pathologies and healthy controls.

Background: There are significant gaps in knowledge on the pathophysiology of Meniere’s. MiRNA’s are small RNA sequences that regulate mRNA translation and play a role in different disease pathologies making them a promising diagnostic marker. MiRNA’s can be readily isolated from the human inner ear perilymph and exhibit disease specific profiles.

Methods: Perilymph sampling was performed in 10 patients undergoing surgery; 5 patients with Meniere’s disease and 5 patients with CHL. Serum was collected in 5 patients with bilateral Meniere’s disease and 5 age-matched controls. miRNAs were evaluated using Agilent miRNA gene chip, and IPA software was used to evaluate miRNA-mRNA interactions using a cochlear cDNA library.

Results: We identified 17 unique miRNAs within the perilymph that are specific to Meniere’s disease that regulate over 220 different genes. 7 key miRNAs are postulated to regulate aquaporin expression and 15 key miRNAs are postulated to regulate various inflammatory pathways. When comparing perilymph with serum samples, miRNA 1299 and 1270 were both differentially expressed in the perilymph and serum compared to controls. Both miRNAs are linked to inflammatory cascade regulation and 1299 is postulated to regulate aquaporin expression as well.

Conclusions: Patients with Meniere’s disease exhibit distinct miRNA expression profiles within human perilymph that are linked to aquaporin and inflammatory gene expression. Two key miRNAs were differentially.

Define Professional Practice Gap & Educational Need: The pathophysiology of Meniere’s disease has remained elusive and our lack of understanding has led significant gaps in both diagnosis and treatment. In this current study we used microRNA profiling of both the perilymph and serum in patients with active Meniere’s disease and controls to further understand the pathophysiology and try and identify a potential biomarker.

Learning Objective: Evaluate the microRNA profile in patients with Meniere’s disease. Using microRNA profile to further understand the pathophysiology of Meniere’s disease. Identify any potential biomarkers for Meniere’s disease by evaluating the microRNA profile in both the perilymph and serum of patients compared to controls.

Desired Result: Identify unique microRNA in the perilymph of patients with Meniere’s disease compared to controls (patients undergoing stapedectomy for conductive hearing loss). Identify unique microRNA in the serum of patients with active bilateral Meniere’s disease compared to healthy age matched controls. Identify unique and overlapping microRNAs in patients with active Meniere’s disease compared to controls, that could ultimately serve as biomarkers for Meniere’s disease.

Level of Evidence – Level III

Indicate IRB or IACUC: KUMC IRB - STUDY00142630
Natural History of Growing Sporadic Vestibular Schwannomas: An Argument for Observation Despite Documented Growth in Select Cases

John P. Marinelli, MD; Katherine A. Lees, MD; Colin L.W. Driscoll, MD; Brian A. Neff, MD; Michael J. Link, MD; Jamie J. Van Gompel, MD; Matthew L. Carlson, MD

Objective: Definitive treatment of sporadic vestibular schwannoma (VS) following documented growth is common practice at most centers in the United States. However, as a natural extension of this paradigm, very little evidence exists surrounding the natural history of growing tumors. The primary objective of the current work was to describe the natural history of VS following documentation of initial tumor growth.

Study Design: Retrospective cohort study.

Setting: Tertiary referral center.

Patients: Patients diagnosed with sporadic VS who elected continued observation despite having volumetric growth exceeding 20% of original tumor volume on interval magnetic resonance imaging (MRI).

Main Outcome Measures: Survival free of subsequent volumetric growth.

Results: Eighty-five patients met inclusion criteria at a median age of 66 years (IQR 55-71). Within this cohort, 40 patients demonstrated subsequent volumetric growth at a median of 1.7 years (IQR 1.0-2.6) from the date of initial MRI that documented growth. The median volumetric growth was 43% (IQR 28-57), and the median growth rate was 0.026 cm³ per year (IQR 0.009-0.107). Survival free of subsequent volumetric growth rates (95% CI; number still at risk) at 1, 2, 3, 4, and 5 years were 93% (87-99; 75), 67% (58-79; 45), 54% (43-67; 29), 44% (33-59; 19), and 41% (30-56; 12), respectively.

Conclusions: In a cohort exclusively comprised of VS with documented growth, over 40% of tumors demonstrated no subsequent growth after continued MRI surveillance. These data challenge the supposition that once growth occurs, all tumors will exhibit sustained growth. Continued observation after documented VS growth is a viable consideration in appropriately selected cases.

Define Professional Practice Gap & Educational Need: At many centers in the United States, documentation of growth of sporadic VS warrants its treatment. This widely held practice pattern naturally stems from the belief that growing tumors are likely to continue to grow. However, as a consequence of this commonly adopted paradigm, little evidence characterizes the natural history of growing tumors, and this lack of evidence precludes its consideration in the decision-making process surrounding the need for definitive management in patients with growing tumors.

Learning Objectives: Understand the natural history of growing sporadic VS within a tertiary referral center cohort. Describe the typical patient profile of those who successfully undergo continued observation despite early documentation of tumor growth.

Desired Result: Physicians will be able to identify which patients may be appropriate candidates for continued observation of their tumor opposed to pursuing immediate treatment following documented growth.

Level of Evidence: IV

Indicate IRB or IACUC: Mayo Clinic Institutional Review Board #15-008224.
Predicting Schwannoma Growth in a Mouse Flank Tumor Model
Using Targeted Imaging

Daniel R. Morrison, MD; Anna G. Sorace, PhD
Ellis Hamilton MS; Hailey A. Houson PhD
Jason M. Warram, PhD; Erika M. Walsh MD

Hypothesis: In a murine tumor model, fluorescent imaging characteristics using immunotargets may predict schwannoma growth.

Background: Vestibular schwannoma (VS) is a common pathology encountered in neurotology clinics. Many patients are observed with a “wait and scan” approach. Prior efforts to determine radiographic indicators of future growth have been unsuccessful. Using a mouse flank tumor model, we seek to determine if fluorescent imaging with directed immunotargets could be used to predict schwannoma growth rate.

Methods: Anti-VEGFR2 and anti-Her2/Neu were covalently linked to a near-infrared probe (IRDye800). Immunodeficient mice underwent flank injections with a rat-derived schwann (R3) cell line. When tumor growth was evident, either Anti-VEGFR2-IRDye800, anti-Her2/Neu-IRDye800, or IgG Isotype-IRDye800 (control) were injected via tail vein. The mice were serially imaged in a closed field device (Pearl, LI-COR Biosciences, Lincoln, NB). Fluorescent data were analyzed for tumor signal and correlated with tumor growth.

Results: All mice grew clinically evident tumors with variable growth rate. In both study groups, there were strong correlations between day 1 mean tumor fluorescence and eventual maximum tumor volume (p=0.002, 0.001; r²=0.92, 0.86). There was also strong correlation with maximum tumor signal and maximum tumor volume (p=0.003, 0.008; r² = 0.90, 0.91) There was no such correlation in the control group.

Conclusions: VS is a challenging problem for neurotologists and patients alike, with many patients opting for observation. We seek to identify immunotargets in a murine model that show promise in predicting schwannoma growth with advanced imaging techniques. Both Her2/Neu and VEGFR2 are promising targets that merit further investigation. Assessing tumor heterogeneity may identify spatial regions of increase growth patterns.

Define Professional Practice Gap & Educational Need: Management of vestibular schwannoma relies heavily on imaging, specifically MRI. Functional imaging may eventually provide additional insight as to the nature of the tumor and factor in the clinician’s management algorithm.

Learning Objective: Attendees will review current imaging modalities of vestibular schwannoma and learn of novel investigational imaging modalities that may have future applicability in clinical practice.

Desired Result: We seek to describe new imaging techniques which could eventually assist clinicians with diagnosis and management of vestibular schwannomas.

Level of Evidence - N/A – basic science study using animal model.

Indicate IRB or IACUC : IACUC 20327
A Protective Cap: Fundal Fluid Cap Predicts Inner Ear Radiation Dose and Hearing Outcomes in Radiosurgical Treatment of Vestibular Schwannoma

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Christopher A. Schutt, MD; Robert S. Hong, MD, PhD
Seilesh C. Babu, MD; Dennis I Bojrab, MD

Objective: To study the association between hearing preservation after gamma knife radiosurgical (GKRS) treatment for vestibular schwannoma (VS) with the presence of fluid signal lateral to tumor (fundal cap) in internal auditory canal (IAC) and the dose of radiation to the cochlea and labyrinth.

Study Design: Retrospective chart review.

Setting: Tertiary referral center.

Patients: Patients treated with GKRS for VS between March 2007 to March 2017. The diagnosis of VS was based on the clinical presentation and the typical radiological tumor appearance. Exclusion criteria included pretreatment PTA above 90 dB, neurofibromatosis type II, and follow-up less than 1 year.

Interventions: Therapeutic

Main Outcome Measures: AAO-HNS guidelines for reporting hearing results in patients pre-GKRS and post-GKRS for VS were followed, including patient stratification into AAO-HNS Classes A-D. Cochlear and labyrinthine doses were calculated using Leksell GammaPlan.

Results: Of the 96 patients included in the study, 42 had a fundal cap and 54 did not have any fluid signal in the lateral IAC. Mean labyrinth dose significantly differed for patients with (2.99±1.27 Gy) and without (3.91±1.55 Gy) evidence of a fundal cap (p=0.002). Mean labyrinth dose less than 3 Gy had 4- and 8-year hearing preservation rates of 83% and 62% compared with 59% and 21% in those with mean dose of 3 Gy or greater (p=0.003, log-rank test). Patients with no fundal cap had worse post-GKRS hearing (p=0.025, Fisher exact test).

Conclusions: A fundal cap is strongly associated decreasing mean labyrinth dose and both variables can predict hearing preservation.

Define Professional Practice Gap & Educational Need: Less than a handful of papers have been published on the relationship of a fluid fundal cap, cochlear/labyrinthine dose, and hearing preservation after gamma knife radiosurgery for vestibular schwannoma. This research will help fill a gap in knowledge and also help improve the quality of patient counseling.

Learning Objective: A fluid fundal cap is a quick and easy way to estimate inner ear radiation dose which will be delivered during gamma knife radiosurgery, and can also be predictive of hearing results

Desired Result: After looking at a patient’s MRI, physicians will be able easily to provide improved pre-treatment counseling for patients who are going to have gamma knife radiosurgery for vestibular schwannoma.

Level of Evidence: Level V

Indicate IRB or IACUC: Beaumont Hospital Institutional Review Board (IRB No. 2016-279)
Objective: To address variance in clinical care surrounding sporadic vestibular schwannoma (VS), a series of consensus statements were created using a modified-Delphi method to inform the development of a consensus guideline.

Study Design: Modified Delphi Method

Methods: The multidisciplinary Delphi task force was established with deliberate representation from key stakeholder societies and comprised 16 VS experts (8 neurotology and 8 neurosurgery). The modified Delphi consensus method encompassed a four-step process, comprised of one pre-voting round to establish a list of focus areas, and 3 subsequent voting rounds to successively refine individual statements and establish levels of consensus. Thresholds for achieving moderate consensus, at >67% agreement, and strong consensus, at >80% agreement, were determined a priori. All voting was performed anonymously via the Qualtrics online survey tool and full participation from all Delphi members was required before procession to the next round.

Results: Through the Delphi process, candidate items were developed and voted upon, encompassing: hearing outcomes (N=49), tumor control and imaging surveillance (N=20), preferred treatment (N=24), operative considerations (N=4), and complications (N=6). As a result of item refinement, moderate (4%) or strong (96%) consensus was achieved in 103 statements. A flowchart outlining the course of item development and select representative statements will be presented.

Conclusions: This Consensus Statement on Sporadic Vestibular Schwannoma addresses clinically pragmatic items that have direct application to everyday patient care. This document is not intended to define standard of care or drive insurance reimbursement, but rather to provide a general framework to approach VS care for providers and patients.

Define Professional Practice Gap & Educational Need: Currently there exists tremendous disparity in vestibular schwannoma patient counseling and management.

Learning Objective: To present the results of a recent multidisciplinary consensus statement on sporadic vestibular schwannoma care.

Desired Result: To establish a general framework to approach vestibular schwannoma care for providers and patients

Level of Evidence: Not applicable

Indicate IRB or IACUC: Exempt.
Objectives: Examine the role of psychological factors on measures of quality of life (QOL) and recovery outcomes following microsurgical resection of vestibular schwannoma (VS).

Study Design: Prospective cohort study

Setting: Tertiary academic center.

Patients: Adult (>18y) patients who underwent resection of their acoustic neuroma by either translabyrinthine, retrosigmoid or middle cranial fossa approaches.

Methods: Psychological measures of perceptions of injustice (Injustice Experience Questionnaire), anxiety (PROMIS-A), pain catastrophizing (Pain Catastrophizing Scale) and recovery expectancies were completed at the pre-operative consultation. At the 3-month post-operative visit, participants completed measures of QOL (Penn Acoustic Neuroma Quality-of-Life [PANQOL] scale and Short-Form 36 [SF-36]), physical and mental well-being, and occupational engagement. Demographic and medical data were collected.

Results: 73 patients completed both pre- and post-operative surveys (mean age: 47.1 years, 61.3% female). Prospective multivariate analyses revealed that patients with higher preoperative perceptions of injustice and anxiety experienced significantly lower postoperative QOL (p=0.006 and p=0.008, respectively) and lower physical (p=0.008 and p=0.004) and mental (p = 0.004 and p=0.003) well-being. Higher levels of catastrophizing were also prospectively predictive of lower post-operative QOL (p=0.008). Finally, patients who had lower recovery expectancies reported lower QOL (p=0.008), lower mental well-being (p=0.046) and were less likely to have returned to work within three months after surgery (p<0.001). Analyses controlled for age, tumor size and body-mass index.

Conclusions: Psychological factors account for significant variability in post-operative QOL and recovery following VS surgery beyond that which can be explained by medical variables. Assessing and targeting psychological risk factors pre-operatively may improve surgical outcomes.

Define Professional Practice Gap & Educational Need: There is a wide variability in quality of life and recovery outcomes between acoustic neuroma patients, despite similar tumors and surgeries. The individual and psychological differences that may explain this variability remain largely unknown.

Learning Objective: Participants will be able to understand the role of psychological variables on quality of life and recovery after vestibular schwannoma surgery.

Desired Result: The skull base surgeon should realize that beyond medical variables, psychological factors contribute for a significant amount of variability in post-operative outcomes after surgery.

Level of Evidence – Level III

Indicate IRB or IACUC: University of California – San Diego IRB #180978XL, 10/4/2018

Joe Saliba, MD, MSc & Junie S. Carriere, PhD - authors contributed equally to this work
Disease-specific Quality-of-Life in Sporadic Vestibular Schwannoma: A National Prospective Longitudinal Study Comparing Observation, Microsurgery, and Radiosurgery

Matthew L. Carlson, MD; Nicole M. Tombers, RN
Christine M. Lohse, MS; Michael J. Link, MD

Objectives: Traditional benchmarks used to assess vestibular schwannoma (VS) outcome include facial nerve function, hearing preservation, and tumor control. In recent years, quality-of-life (QOL) outcomes have come to the forefront of investigation.

Study Design: Prospective longitudinal study using the disease-specific Penn Acoustic Neuroma Quality-of-Life (PANQOL) index.

Setting: National survey

Patients: Patients diagnosed with unilateral VS who completed a baseline survey before treatment and at least one post-treatment survey.

Main Outcome Measures: Change in PANQOL scores from baseline to most recent survey.

Results: The 370 patients studied included 118 (32%) who elected observation, 172 (46%) with microsurgery, and 80 (22%) with stereotactic radiosurgery (SRS). Patients who underwent microsurgery were younger (p<0.001) and had larger tumors (p=0.001) than the observation and SRS groups, but there was no significant difference in duration of follow-up (average 2.1 years). After adjusting for age and tumor size, there were no statistically significant differences by treatment group in QOL changes from baseline for the facial (p=0.10), general health (p=0.94), balance (p=0.82), hearing (p=0.43), energy (p=0.35), and pain (p=0.26) domains or total score (p=0.93). However, there was a statistically significant difference for the anxiety domain (p=0.038). Specifically, the microsurgery group demonstrated significant improvement in anxiety from baseline to the most recent survey, improvement that was better than the observation (p=0.037) and SRS (p=0.18) groups.

Conclusions: In this first prospective study investigating differences in disease-specific QOL among VS treatment groups, treatment did not modify QOL for most domains. Microsurgery may confer an advantage with regard to patient anxiety, presumably relating to the psychological benefit of “cure” from having the tumor removed.

Define Professional Practice Gap & Educational Need: The management of vestibular schwannoma remains controversial and nuanced. To date, there is no compelling evidence to support one particular treatment strategy over another for small and medium-sized vestibular schwannoma.

Learning Objective: To present the results of a large national prospective disease-specific quality-of-life study in sporadic vestibular schwannoma that compares outcomes according to treatment modality.

Desired Result: Learners will understand the impact of treatment modality on vestibular schwannoma quality of life outcome, which in turn may inform patient counseling and choice of treatment.

Level of Evidence: Level II.

Indicate IRB or IACUC: 14-009331.
Objective: Currently, there exists no peripheral method of continuously monitoring facial nerve (FN) integrity during skull base surgery. Intermittent stimulation of the FN at the root exit zone is inherently retrospective. Methods that employ an electrode placed on the FN for continuous monitoring carry some risk of iatrogenic injury and require early access to the proximal FN. Herein, we present a novel method to noninvasively monitor the integrity of the entire FN, discuss feasibility of the technique, and comment on correlation with postoperative facial function.

Study Design: Prospective feasibility study.

Setting: Tertiary center.

Patients: Adult patients undergoing skull base surgery involving FN dissection.

Interventions: Blink reflex monitoring using bipolar electrodes to stimulate the supraorbital nerve and recording electrodes in facial musculature.

Main Outcome Measures: Presence and latency of R1 response (sensory nucleus of CN V to motor nucleus of CN VII), ratio of ipsilateral to contralateral R1, and immediate postoperative facial nerve function.

Results: Twenty patients were included. Fifteen (75%) underwent microsurgical resection of vestibular schwannoma. The remainder included glomus jugulare, facial nerve schwannoma, and other benign skull base pathologies. An ipsilateral R1 response was obtained in 12 cases (60%). Median R1 latency ratio for patients with postoperative FN paresis (House-Brackmann grade 2 or higher) was 1.24 compared to 1.06 for patients with normal postoperative FN function.

Conclusions: Blink reflex testing can be used intraoperatively to continuously monitor FN integrity. Preliminary data suggest correlation of R1 latency ratio with postoperative FN function. Further study is planned to assess this relationship and refine monitoring technique.

Define Professional Practice Gap & Educational Need: There is no currently available method to assess the integrity of the facial nerve continuously and noninvasively during lateral skull base surgery.

Learning Objective: To understand the emerging role of intraoperative blink reflex monitoring during skull base surgery and its potential prognostic implications.

Desired Result: The learner will be able to describe the blink reflex, its feasibility intraoperatively, and its potential utility as a method to monitor the facial nerve intraoperatively.

Level of Evidence – Level V

Indicate IRB or IACUC: IRB 16-007363
Surgical Approach for Human Inner Ear Tissue Extraction in an Organ Donor

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Bernhard Hirt, MD, PhD; Hubert Löwenheim, MD
Andreas Wagner, MD; Yona Vaisbuch, MD

Objective: Significant research efforts are underway into finding new therapeutics aimed at preventing inner ear cellular degeneration or regenerating cellular scaffold of the hearing organ. Unfortunately, fresh tissue of the human inner ear remains, for the most part, inaccessible for research purposes. The aim of our work is to present a surgical approach for harvesting of the inner ear tissue from organ donors with the objective that this technique will enable future advancement of human inner ear research.

Study Design: Surgical methodology.

Setting: Institute of Clinical Anatomy and Donor Network West.

Patients: Brain or cardiac death organ tissue donors.

Interventions: The inner ear tissue dissection and isolation and post-isolation processing.

Main Outcome Measures: Feasibility of fast and reproducible inner ear tissue harvest as well as optimal timing for tissue harvest based on the cause of death.

Results: The extraction procedure is described in three consecutive steps: the trans-canal exposure, the approach to the vestibule, and the extraction of the vestibule organ; and possible modifications for obtaining inner ear tissue, with a focus on the cochlear duct. We then compare the tissue extraction from organ donors looking at time since insult, type of insult (neurological versus cardiac death) and optimal conditions for tissue harvest.

Conclusions: Using our modified technique through the trans-otic approach, we are able to extract intact tissue of the vestibular and auditory end organ all as whole mount tissue. The time to appropriately access the inner ear tissue can be adapted according to the aspired type of experiment.

Define Professional Practice Gap & Educational Need: Feasibility to investigate healthy viable adult human inner ear tissue for research application is lacking. In comparison to tissue, that till now has been harvested from vestibular schwannoma or human embryos, we present an approach that enables fast harvesting human inner ear tissue from organ donors.

Learning Objective: The objective is to present the trans-canal/tran-sotic approach for vestibular and auditory end organ harvest and describe data on tissue viability based on the brain versus cardiac death.

Desired Result: We desire that the Otology and Neurotology community will be aware of this approach as a potential resource for future studies in the inner ear genetics and its application.

Level of Evidence - Level V

Indicate IRB or IACUC: Approved, Institute of Clinical Anatomy and Cell analysis, University of Tübingen, Germany Project ID: 237/2007BO1; Stanford University IRB: #50076
Hypothesis: A custom-built miniature endoscope can traverse the Eustachian tube and provide diagnostic-quality visualization of the middle ear space.

Background: In patients with middle ear pathology, surgical exploration is often necessary to confirm diagnosis and/or survey for recurrent disease. We hypothesized that surveillance surgery could be avoided if a miniature endoscope could be used to inspect the middle ear via the Eustachian tube.

Methods: Three formalin-preserved cadaveric temporal bones with fully intact Eustachian tubes were used for this pilot study. A custom-built, 1.6mm-diameter, steerable, flexible endoscope with integrated digital camera was used for video surveillance. An Eustachian tube dilation system was utilized to dilate soft tissues following which the endoscope was inserted into the middle ear space through the Eustachian tube. The camera was steered in multiple directions to provide wide-field views. Diagnostic validity was assessed using a 5-point Likert-scale survey distributed to attending otolaryngologists, neurotology fellows, and senior otolaryngology residents.

Results: Grading of the quality of endoscopic examinations in terms of illumination, focus, and overall experience yielded a mean score of 4.05/5 (standard deviation =1.00), corresponding to an adequate view for diagnostic purposes. The sinus tympani was the most difficult subsite to visualize (3.36/5), while ossicular chain and mesotympanum were the easiest to visualize (4.20/5 and 4.42/5, respectively).

Conclusions: The steerable flexible endoscope designed for this work provides diagnostic-quality video of a wide anatomic range of the middle ear space. This cadaver study is an important step towards the goal of in-vivo trans-Eustachian tube middle ear endoscopy.

Define Professional Practice Gap & Educational Need: 1. Diagnostic and surveillance surgeries for middle ear pathology are common but have associated morbidity. 2. Portions of the middle ear cavity are not easily visible through traditional transcanaal or transmastoid approaches.

Learning Objective: The latest miniature chip tip cameras and novel endoscope designs make trans-Eustachian tube middle ear endoscopy technically feasible.

Desired Result: Attendees will understand the current status of, and potential future applications for, transeustachian middle ear endoscopy

Level of Evidence – Not Applicable (cadaveric studies with proprietary device)

Indicate IRB or IACUC : Exempt
Fluorescent Detection of Vestibular Schwannoma Using Intravenous Sodium Fluorescein In Vivo

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Xue-Zhong Liu, MD, PhD; Fred F. Telischi, MD
Michael Ivan, MD; Christine T. Dinh, MD

Hypothesis: Intravenous sodium fluorescein (SF) preferentially deposits in vestibular schwannomas (VS), helping surgeons differentiate tumor from normal surrounding tissue.

Background: Because VS are closely associated with the facial nerve, brainstem, and cerebellum, clear identification of the tumor-tissue interface could improve surgical outcomes in difficult cases. SF is a fluorescent compound with preferential uptake in various intracranial tumors, causing tumors to emit green fluorescence after blue light excitation.

Methods: Mouse merlin-deficient Schwann cells were grafted onto the cochleovestibular nerve of 8 immunodeficient rats. Rats were randomized to receive intravenous SF (7.5 mg/kg; n=5) or saline (n=3). Relevant tissues were harvested at 1 hour and photographed in white and blue light. Sixteen surgeons identified and marked the tumor-tissue interfaces on images in a blinded manner. Fluorescence intensities (in total flux) of different tissues were measured using an in vivo imaging system (IVIS). Confocal images were performed on tissue cross-sections.

Results: Under blue light, tumors from SF rats demonstrated brighter green fluorescence under direct visualization, significantly higher fluorescence intensity measurements on IVIS imaging (p<0.001), and significantly more SF deposition on tissue cross-sections (p<0.001), when compared to surrounding tissues and placebo rats. Furthermore, surgeons distinguished the tumor-tissue interfaces significantly better using blue light in SF rats (p<0.05).

Conclusions: In a xenograft model of VS, intravenous SF preferentially deposits in tumors, compared to normal surrounding tissue. Under blue light, tumors emit an intense green fluorescence that can help surgeons differentiate tumor from critical structures nearby, which may improve clinical outcomes in complicated VS surgery.

Research Support: Alpha Omega Alpha Postgraduate Research Award (Szczupak), NIH/NIDCD 1K08DC017508 (Dinh), and NIH/NIDCD R01DC017264 (Fernandez-Valle & Liu)

Define Professional Practice Gap: Difficulty identifying the tumor and brain/nerve interfaces during vestibular schwannoma surgery can lead to brainstem, cerebellar, and cranial nerve injuries, which are devastating clinical outcomes in patients with vestibular schwannoma.

Educational Need: There is a need to inform physicians that fluorescence-guided microsurgery could potentially improve surgical outcomes in patients with vestibular schwannoma tumors.

Learning Objective: Understand the potential surgical utility of intravenous sodium fluorescein in detecting vestibular schwannoma and distinguishing tumor from critical structures nearby during vestibular schwannoma surgery.

Desired Result: Gain in physician knowledge that intravenous sodium fluorescein can preferentially deposit in vestibular schwannoma when compared to normal surrounding tissues. Gain in physician knowledge that intravenous sodium fluorescein and fluorescence-aided microsurgery can potentially improve surgical outcomes in complicated VS surgeries.

Level of Evidence: N/A

IACUC: University of Miami, IACUC #18-149
Objectives: To predict post-operative cochlear implant performance with heterogeneous text and numerical variables using supervised machine learning techniques.

Study Design: A supervised machine learning approach comprising neural networks and decision tree-based ensemble algorithms were used predict one-year post-operative cochlear implant performance based on retrospective data.

Setting: Tertiary referral center.

Patients: 1,604 adults who received one cochlear implant from 1989-2019. 282 text and numerical objective demographic, audiometric and patient-reported outcome survey instrument variables were included.

Outcome Measures: Outcomes for post-operative cochlear implant performance were discrete Hearing in Noise Test (HINT; %) performance and binned HINT performance classification (‘High,’ ‘Mid,’ and ‘Low’ performers). Algorithm performance was assessed using hold-out validation datasets and were compared using classification accuracy and root mean square error (RMSE) in the units of the target variable.

Results: Decision-tree algorithm HINT prediction performance produced a RMSE of 25.3%, and identified over 20 influential variables including pre-operative sentence-test performance, age at surgery, as well as specific tinnitus handicap inventory (THI), SF-36, and health utilities index (HUI) question responses as the highest influencers of post-operative HINT. Neural networks predicted post-operative HINT with a RMSE of 25.0%, and classification accuracy of 73.3% using both text and numerical variables. With text variables removed, neural network RMSE and accuracy improved to 0.57% and 95.4%, respectively.

Conclusion: Our results suggest that supervised machine learning can predict post-operative cochlear implant performance and identify pre-operative factors that significantly influence that performance. These algorithms can help improve the understanding of the diverse factors that impact functional performance from heterogeneous data sources.

Define Professional Practice Gap & Educational Need: Predicting functional post-operative performance in cochlear implantation has remained elusive. Part of the difficulty in determining who will be a ‘high performer’ after surgery are the numerous variabilities in patient disposition, surgical procedure and device characteristics.

Learning Objective: As a result of attending this presentation, audience members will be able to identify a role for novel machine learning approaches for predicting cochlear implant performance and recognize patterns of pre-operative variables that are influential on post-operative performance.

Desired Result: We anticipate that physician knowledge of machine learning applications to retrospective cochlear implant patient data will be advanced.

Level of Evidence – Level IV

Indicate IRB or IACUC : Approved by the Sunnybrook Health Sciences Center Ethics Review Board (ERB) through the Expedited/Exempt protocol.
Identification of Factors Associated with Second-Side Cochlear Implant Speech Recognition Outcomes in Adults

James R. Dornhoffer, MD; Yuan F. Liu, MD; Elise E. Zhao, BS
Ted A. Meyer, MD, PhD; Theodore R. McRackan, MD, MSCR

**Objective:** Assess the relationship between patient, hearing, and cochlear implant (CI)-related factors and second-sided CI speech recognition outcomes in bilaterally implanted adults.

**Study Design:** Retrospective review of a prospectively maintained CI database.

**Setting:** Tertiary academic center

**Patients:** 102 adults receiving bilateral sequential or simultaneous CIs

**Interventions/Main Outcome Measures:** Post-implantation Consonant-Nucleus-Consonant (CNC) word and AzBio sentence scores at 12 months.

**Results:** Of the patient, hearing and CI-specific factors examined, only first CI post-implantation speech recognition scores were independently associated with second CI speech recognition performance on multivariable linear regression analysis (CNC: $\beta=0.471 \ [0.298, 0.644]$; AzBio: $\beta=0.602 \ [0.417, 0.769]$). First-side post-CI CNC scores explained 23.0% of the variation in second CI CNC scores, while change in first-side AzBio scores explained 44.0% of the variation in second CI AzBio scores. Based on established 95% confidence interval, 24.8% and 34.1% of patients scored lower on their second CI CNC and AzBio score, respectively, compared to their first CI performance. Notably, age at implantation, duration of hearing loss, receiving simultaneous vs. sequential CIs, and pre-operative residual hearing (as measured by pure-tone average and aided speech recognition scores) were not associated with speech recognition scores at 12 months for the second CI.

**Conclusions:** The degree of improvement in speech recognition from first CI may predict performance from a second CI. This provides a degree of evidence-based expectations for patients considering a second CI. Such counseling should be guarded given the remaining unexplained variability in outcomes. Nonetheless, these data may help guide discussion of second CI vs hearing aid use for an unimplanted ear.

**Define Professional Practice Gap & Educational Need:** There is little evidence to help guide the decision between second CI and bimodal amplification (CI in one ear with hearing aid in the other) in patients with bilateral SNHL who have undergone initial unilateral CI.

**Learning Objective:** To explore demographic and audiologic factors that may be associated with second CI speech recognition performance.

**Desired Result:** Practitioners and researchers will recognize that the postoperative performance in speech recognition with one CI significantly correlated with performance on the second CI for patient undergoing bilateral implantation. As such, clinicians may offer limited evidenced-based guidance for patients pursuing a second CI vs. bimodal amplification with a hearing aid.

**Level of Evidence – Level IV: Historical cohort or case-controlled studies.**

**Indicate IRB or IACUC:** The study was approved by the Medical University of South Carolina IRB - Pro00071518

James R. Dornhoffer, MD & Yuan F. Liu, MD - Authors contributed equally to this work
Cochlear Implantation for Treatment of Tinnitus in Single-sided Deafness: A Systematic Review and Meta-analysis

Dylan A. Levy BS, Joshua A. Lee BA, Shaun A. Nguyen MD
Theodore R. McRackan MD, MSCR; Ted A. Meyer MD PhD
Paul R. Lambert MD

Objective: Quantify the benefit of cochlear implantation (CI) for tinnitus relief among individuals with single-sided deafness (SSD).

Data Sources: PubMed, Scopus and Cochrane databases were searched through July 10, 2019. Search strategies used a combination of subject headings (eg, MeSH in PubMed) and keywords for the following three concepts: single-sided deafness, cochlear implantation and tinnitus.

Study Selection: English articles that reported the pre-intervention (baseline) tinnitus-related patient-reported outcome measures (e.g. Tinnitus Handicap Inventory [THI] and Visual Analog Scale [VAS] for loudness) in patients with SSD that underwent CI were included.

Data Extraction: Number of patients, mean age, etiology of hearing loss, duration of deafness, baseline and follow-up THI and VAS scores.

Data Synthesis: A total of 17 studies met inclusion criteria encompassing 247 patients with SSD receiving a cochlear implant (mean age 50.2 years, range 23-71). For THI, CI resulted in a mean difference of –35.4 points [95% CI -55.8 to -15.0, p<0.001]. VAS decreased by –4.6 points [CI -6.0 to –3.3, p<0.001]. A weighted proportion of 14.9% [CI 6.4 to 26.1] of patients experienced complete resolution of tinnitus, while 74.5% [CI 63.1 to 84.5] experienced partial improvement; 7.6% [CI 4.1 to 12.6] of patients had no change in severity, and 3.0% [CI 1.0 to 6.7] experienced worsening of their tinnitus.

Conclusions: On both THI and VAS, patients reported significant reduction in their scores, representing an overall improvement in tinnitus severity while wearing the cochlear implant. Most patients with SSD will experience partial improvement or complete resolution of tinnitus with a cochlear implant.

Define Professional Practice Gap & Educational Need: Previous research has shown that in patients with SSD, CI improves not only hearing, speech recognition and quality of life, but substantially reduces the severity of tinnitus. Unfortunately, most investigations are limited to small sample sizes from international locations as CI using the MED-EL system for SSD in patients 5 years and older was only just recently approved by the US Food and Drug Administration. The paucity of large-scale studies limits the generalizability of published data and restricts any meaningful cross-study comparisons.

Learning Objective: Explain the extent of tinnitus-related benefit that patients with SSD might expect from CI.

Desired Result: Attendees should be able to counsel patients with SSD on tinnitus-related benefits following CI.

Level of Evidence - IV

Indicate IRB or IACUC: This project was exempt from IRB approval.
Role of Pre-Implant Patient Expectations in Adult Cochlear Implant Outcomes

Theodore R. McRackan, MD MSCR; Mark S. Costello, MD
Priyanka Reddy, BS; Judy R. Dubno, PhD

Objective: Pre-operative expectations affect patient outcomes many health conditions, but patient expectations are rarely studied in adult cochlear implant (CI) users. This study is a first step in assessing the role of pre-operative expectations on post-operative CI speech recognition, CI quality of life (CIQOL), and CI satisfaction.

Study Design: Cross-sectional study

Setting: Tertiary medical center

Patients: 41 adult CI patients

Interventions/Main Outcome Measures: Pre-operative expectation questionnaire results, pre-and post-operative speech recognition (CNC and AzBio) scores, post-operative CIQOL domain scores and global scores and visual analog scale (VAS) CI satisfaction scores. Cohen’s $d$ was used to express effect size.

Results: Patients with higher pre-operative CI performance expectations showed higher post-operative CIQOL scores compared to patients with lower pre-implant expectations. Specifically, social and emotional CIQOL domains demonstrated large effect sizes ($d=0.85-1.01$) and communication, entertainment, listening effort domains and the global score demonstrated medium effect sizes ($d=0.5-0.63$). Pre-operative expectations showed no association with pre-implant vs. post-implant change in CNC or AzBio scores. Determining the extent to which pre-operative expectations played in role in post-operative satisfaction with CIs was limited by the clustering of satisfaction scores in the upper range of the scale (VAS mean 81.1, SD±25.1, range 4-100).

Conclusions: This study provides preliminary evidence that patients’ expectations prior to cochlear implantation may influence their post-operative quality of life but not post-operative speech recognition. This suggests that an increased emphasis should be placed on measuring and counseling expectations in CI candidates. This assumption needs to be confirmed with larger sample sizes, more sensitive satisfaction measures, and a prospective research design.

Define Professional Practice Gap & Educational Need: Despite being extensively investigated, the patient and audiological factors that are routinely evaluated account for only a small degree of variation in CI outcomes (QOL and speech recognition ability). Patient expectation has been shown to have a substantial impact on outcomes and directly contribute to patient satisfaction in many health conditions. However, understanding patient pre-CI expectation and its impact on patient outcomes remains a major research gap in adult cochlear implantation.

Learning Objective: Determine the potential impact of patient pre-CI expectations on QOL, speech recognition and satisfaction outcomes

Desired Result: Practitioners and researchers will understand that pre-CI expectations may have a substantial impact on post-operative CIQOL. As such, this area may be a modifiable factor that could be addressed more completely in the pre-operative setting and investigated in controlled prospective trials.

Level of Evidence – Level IV

Indicate IRB or IACUC: Approved 12/20/17 Pro00073019
Objective: To characterize sensory organization and motor control among patients with imbalance; to evaluate the impact of age on abnormal posturography.

Study Design: Retrospective chart review.

Setting: Balance center; academic tertiary referral center.

Patients: Adults who underwent computerized dynamic posturography (CDP) for balance-related complaints from August 2017 to August 2018.

Main outcome measure: Sensory Organization (SOT) and Motor Control Testing (MCT).

Results: CDP was performed in 1037 patients, with majority yielding normal results (81% SOT and 96% MCT). Abnormal SOT scores were more likely among patients 65+ years than patients <65 years (33% vs 11%; p<0.01). There were no differences in each of the six conditions between older and younger patients. Patients 65+ years were more likely to demonstrate prolonged latencies on MCT (7.2% vs 3.1%; p<0.01). Correlation with video nystagmography results in the elderly showed that an abnormal composite SOT was significantly associated with abnormal random saccades (p<0.01), but not with abnormal smooth pursuit, Dix-Hallpike, positional, gaze, or caloric results. Abnormal SOT was associated with abnormal MCT in elderly patients (p<0.01). Further analysis of patients 65+ years demonstrated that the proportion of abnormal scores increases with age for both SOT (p<0.01) and MCT (p=0.05).

Conclusion: Our findings demonstrate a higher rate of deficits in SOT than MCT with age, suggesting that postural instability in the elderly may be attributable primarily to deficits in sensory organization. Furthermore, due to correlation of abnormal sensory organization with abnormal random saccades, we can postulate that underlying age-related central changes may drive postural instability and vestibular dysfunction.

Define Professional Practice Gap & Educational Need: To identify causes of postural instability and imbalance in the elderly.

Learning Objective: To understand that postural instability and imbalance in the elderly worsens with age but is primarily driven by alterations to sensory organization rather than motor control; to recognize that concurrent correlates of central vestibular dysfunction suggest that instability may be driven by age-related central changes.

Desired Result: To further spark understanding of vestibular dysfunction and postural instability among older patients in an aging population.

Level of Evidence – Level IV.

Indicate IRB or IACUC: Approved by the University of Pennsylvania Institutional Review Board. Approval #831279. Approval Date 7/27/2018.
Objective: To analyze audiometric data after surgical manipulation of the membranous labyrinth during repair of superior semicircular canal dehiscence (SSCD) or posterior semicircular canal occlusion (PSCO) for benign paroxysmal positional vertigo (BPPV).

Study Design: Retrospective chart review.

Setting: Tertiary referral center.

Patients: 79 patients who underwent repair of SSCD or PSCO between 2009 and 2019.

Main Outcome Measures: Pre- and post-operative hearing levels were recorded and pure tone averages (PTA) were calculated per AAO-HNS guidelines. Hearing outcomes at initial and last follow-up were compared. Sub-analyses were performed for surgical approach and age.

Results: 84 total procedures including 39 middle cranial fossa (MCF) for SSCD, 29 transmastoid SSCD, 2 combined approaches, and 14 PSCO. Mean preop PTA was 21.1 dB compared to 25.6 dB at initial postop (p=0.003) and 24.4 dB at last postop (p=0.012). There was no observed change in hearing during the follow-up period. MCF for SSCD did not result in statistically significant increase in PTA (2.96 dB, p=0.476). Transmastoid approaches for SSCD and PSCO were associated with a statistically significant increase in PTA of 5.16 dB and 5.98 dB (p=0.011 and 0.044, respectively). Patients under 50 did not demonstrate a change in hearing (increase in PTA of 1.4 dB, p=0.414); however, patients over 50 had a statistically significant increase in PTA of 7.8 dB (p=0.002).

Conclusions: Surgical manipulation of the membranous labyrinth resulted in statistically significant hearing loss in a pooled analysis. Transmastoid SSCD repair, PSCO, and patient age > 50 were subgroups associated with post-operative hearing loss.

Define Professional Practice Gap & Educational Need: There is a need for high-quality data on the risk of hearing loss after manipulation of the membranous labyrinth which occurs in surgical repair of SSCD and posterior semicircular canal occlusion procedures.

Learning Objective: To describe the change in hearing which results from surgical manipulation of the membranous labyrinth.

Desired Result: To demonstrate that surgical manipulation of the membranous labyrinth does not cause significant hearing loss and can be safely performed in the repair of SSCD and PSCO for BPPV.

Level of Evidence - Level V

Indicate IRB or IACUC: Ascension Providence #1487373.
Pre-existing Vestibular Symptoms Are Associated Acute Vestibular Symptoms after Gamma Knife Therapy for Vestibular Schwannoma

Dennis I. Bojrab II, MD; Christian G. Fritz BS; Kenny F. Lin, MD
Christopher A. Schutt, MD; Robert S. Hong, MD, PhD
Seilesh C. Babu, MD; Dennis I Bojrab, MD

Objective: To study if pre-existing patient symptoms and/or tumor characteristics are associated with acute vestibular symptoms after gamma knife radiosurgical (GKRS) treatment of vestibular schwannoma (VS).

Study Design: Retrospective chart review.

Setting: Tertiary referral center.

Patients: Patients treated with GKRS for VS between March 2007 to March 2017. The diagnosis of VS was based on the clinical presentation and the typical radiological tumor appearance. Exclusion criteria included pretreatment PTA above 90 dB, neurofibromatosis type II, and follow-up less than 6 months.

Interventions: Therapeutic

Main Outcome Measures: The presence of acute (<6 months after treatment) vestibular symptoms after GKRS. Pretreatment patient symptoms, including vestibular disorders, along with tumor and treatment characteristics were gathered from clinical records.

Results: All 98 patients included in the study received a radiation dose between 12 and 13 Gy to the 50% isodose line. Average age at time of GKRS was 61 years, with roughly equal numbers of men and woman (46.9%/53.1%). Acute vestibular symptoms within 6 months after GK occurred in 46 patients (46.9%). The average time from GK to the first medical record documentation of acute vestibular symptoms was 3.1 months. On multivariate analysis, pre-GKRS vestibular symptoms (imbalance/dizziness/vertigo) was significantly associated with acute vestibular symptoms within 6 months after GKRS therapy (p=0.001). Max tumor dimension and average mean cochlear dose were also included in the multivariate analysis, although neither was significant.

Conclusions: Patients with pre-existing vestibular symptoms are at an increased risk of experiencing post-treatment vestibular symptoms and should be counseled accordingly.

Define Professional Practice Gap & Educational Need: There is only one paper which was published earlier this year about acute vestibular symptoms after gamma knife radiosurgery. Our centers have fairly similar volumes (their study had 115 patients over 12 years and ours had 98 patients over 10 years), but our findings were quite different. We did not find that smaller tumors were associated with higher likelihood of acute vestibular symptoms as they did, but rather patients with pre-treatment vestibular symptoms had a higher likelihood of experiencing post-treatment acute vestibular symptoms. We feel that this is an important addition to the literature.

Learning Objective: Patients with pre-treatment vestibular symptoms have a higher likelihood of experiencing post-treatment vestibular symptoms in the first 6 months after gamma knife radiosurgery.

Desired Result: Physicians will be able to provide better pre-treatment counseling for patients who are going to have gamma knife radiosurgery for vestibular schwannoma.

Level of Evidence: Level V

Indicate IRB or IACUC: Beaumont Hospital Institutional Review Board (IRB No. 2016-279)
Single versus Multiple Cycles of Canalith Repositioning Procedure for Benign Paroxysmal Positional Vertigo: Randomized Controlled Trial

Suwicha Isaradisaikul Kaewsiri, MD; Sanathorn Chowsilpa, MD
Charuk Hanprasertpong, MD; Tayaporn Rithirangsiroj, MD

Objective: To compare the treatment outcomes and complications of single versus multiple cycles of canalith repositioning procedure (CRP) for unilateral posterior canal benign paroxysmal positional vertigo (PSC BPPV).

Study Design: Randomized controlled trial.

Setting: Tertiary academic center.

Patients: 143 PSC BPPV adults with unilateral positive Dix-Hallpike test (DHT)

Interventions: Single versus multiple cycles of CRP.

Main Outcome Measures: Rate of negative DHT, symptom improvement, complications, and dizziness handicap inventory score (DHI) after CRP at day 0, 7 and 28.

Results: Between single cycle and multiple cycle groups; patients’ characteristics included age (57.1 and 55.0 years), female to male ratio (2.35:1 and 2.64:1), numbers of vertigo attacks per day (2 and 2.5), affected ear (right vs. left; 1:1.2 and 1:1.2), DHI scores showed no difference. After CRP at day 7 and 28: 1) Rate of negative DHT (82.5% and 84.3%; p-value = 0.71, 89.5% and 88.9%; p-value = 0.84); 2) Rate of complete recovery or improved symptoms (96.5% and 92%; p-value = 0.37, 96.5% and 98.0% 0.62); 3) DHI grading scale (p-value = 0.08 and 1.0) between single cycle and multiple cycle groups showed no significant difference. Rate of complications in the single cycle group, day 0, (93.1%) was lower than in multiple cycle groups (78.9%); p-value = 0.014, power of test = 98.9%).

Conclusions: Single cycle of CRP is as effective as multiple cycle CRP, with a lower complication rate and decreased time for treatment. Single cycle CRP is a preferable treatment for unilateral PSC BPPV.

Define Professional Practice Gap & Educational Need: 1. CRP is a treatment of choice for PSC BPPV; variation of CRP technique has been reported. 2. Improvement of CRP technique with excellent treatment outcomes to maximize patient comfort should be investigated.

Learning Objective: 1. To confirm the effectiveness of this new technique of CRP and its complications. 2. Better CRP treatment techniques should improve patient care and shorten the physician’s time while implementing CRP treatment.

Desired Result: 1. Consider the use of single cycle CRP to treat PSC BPPV. 2. Initiate other treatment outcomes, long term results and further studies to confirm the use of single cycle CRP

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

Indicate IRB or IACUC: Approved, research ID: 3601; Chiang Mai University Hospital.
**Objective/Hypothesis:** Usher syndrome type IIIA (USH3A) is characterized by progressive loss of vision and hearing caused by mutations in the clarin1 gene (*CLRN1*). The pathogenic variant c.144T>G (p.N48K) in *CLRN1* is a common cause of Usher syndrome among Ashkenazi Jews, and the sensory deficit is predicted to be caused by failure of the *CLRN1*N48K protein to exit the endoplasmic reticulum (ER). Previous work in a zebrafish model of USH3A led to the hypothesis that the antimalarial drug Artesunate would liberate *CLRN1*N48K from the ER and prevent USH3A-deafness. Here, we tested that hypothesis in a mammalian model of USH3A.

**Study Design:** In vivo mouse study.

**Methods:** Thirty-six USH3A mice (20 treated and 16 untreated) were utilized in this study. The USH3A mice were subject to the following Artesunate dosing regimen – 15mg/kg/every other day from postnatal day 10 (P10) to P29, and 50mg/kg/day P30 to P45; the control mice were injected with saline. ABR thresholds were recorded at P46. A non-parametric student's t-test was used to ascertain statistical significance of the results.

**Results:** Compared to controls, the treated USH3A mice displayed 100 times more sensitive hearing at a low frequency (\(p<0.05\)), and a positive/encouraging trend at mid (16kHz) and high (32 kHz) frequencies (\(p\geq0.05\)), indicating that higher doses of Artesunate may result in better preservation of hearing at all frequencies.

**Conclusions:** Our work highlights the potential of Artesunate to prevent deafness in *CLRN1*c.144T>G patients. These findings can have a significant translational impact since medical management of these patients remains an unmet need.

**Define Professional Practice Gap & Educational Need:** Drug-based therapy for genetic progressive hearing loss has not been studied. In Usher syndrome Type IIIA, the same mutation causes both vision and hearing loss. Efficacy in the hearing phenotype can be used as a surrogate for efficacy in the visual phenotype.

**Learning Objective:** To illustrate the mechanism of rescuing the mutant protein to prevent progression of genetic hearing loss.

**Desired Result:** To expand the understanding of the translational impact that the mechanism of the rescuing unstable gene product can have on mitigating hearing loss in USH3A

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

**Indicate IRB or IACUC Approval:** Approved (IACUC protocol 2016-0258).
Objective: To compare white matter hyperintensities (WMHs) on T2-weighted magnetic resonance imaging (MRI) of patients with sudden sensorineural hearing loss (SSNHL) with an age-matched control group.

Methods: T2-weighted MRI scans of 150 patients with SSNHL were assessed for WMHs and compared with the data of 150 healthy age-matched adults. Assessments of WMHs included independent grading of deep white matter hyperintensities (DWMHs) and periventricular hyperintensities (PVHs). WMH severity was visually rated using Fazekas and Mirsen scales by two observers independently.

Results: Fazekas grades for PVHs ($p < 0.001$) and DWMHs ($p < 0.001$) of SSNHL patients were found to be significantly greater than those of healthy participants. The average Mirsen grades for DWMHs of healthy and SSNHL patients were evaluated to be $0.373 \pm 0.550$ and $2.140 \pm 0.859$, respectively. Mirsen grades for DWMHs of SSNHL patients were found to be significantly greater ($p < 0.001$) than those of healthy participants. The Mirsen scale was found to have higher sensitivity ($p < 0.001$) than the Fazekas scale in grading PVHs and DWMHs. No significant difference ($p = 0.24$) was found in specificities between the two scales.

Conclusions: Patients with sudden hearing loss have a much higher likelihood of having periventricular and deep white matter hyperintensities compared to age-matched controls. These findings indicate that sudden hearing loss patients are more likely to have microvascular changes in the brain, which may indicate a vascular origin to sudden sensorineural hearing loss.

Define Professional Practice Gap & Educational Need: The pathophysiology and management of SSNHL has remained subject of debate. Further investigation into discovering new and improved management solutions for better treating SSNHL has been called. For this reason, a need to educate otolaryngologists on new hypotheses for SSNHL etiology leading to new treatment strategies is warranted.

Learning Objective: To propose a new vascular etiology in SSNHL patients to ANS members which can relate this entity with other complex neurovascular disorders such as migraine. This can imply that SSNHL may have an underlying vascular or neurogenic inflammation pathophysiology similar to migraine offering new treatment strategies for SSNHL.

Desired Result: Informing neurologists of a possible new pathophysiology for SSNHL that can be a stepstone for future treatment options in patients with SSNHL.

Level of Evidence - III

Indicate IRB or IACUC: The study has IRB approval from the UC Irvine under the PI name of Hamid R. Djalilian.
Magnetic Resonance Imaging Fluid Signal Intensity in the Diagnosis of Temporal Bone Cerebrospinal Fluid Leaks

Joseph T. Breen, MD; Arun Raghavan, BS (presenter)

Objective: To examine the utility of objectively measuring signal intensity created by middle ear or mastoid fluid on magnetic resonance imaging (MRI) sequences in differentiating cerebrospinal fluid (CSF) leaks from other chronic middle ear effusions (MEEs).

Study Design: Retrospective imaging analysis.

Setting: Academic medical center.

Patients: Adults with MEE seen on MRI who were diagnosed as having either CSF or non-CSF MEE.

Interventions: Custom MATLAB software automatically segmented fluid collections within the middle ear and mastoid imaged on volume-acquired T2-weighted (3DT2) MRI sequences (e.g. CISS, FIESTA). The mean, standard deviation, and range of fluid signal intensity were compared to those of adjacent CSF in the posterior fossa.

Main Outcome Measures: The ratio of the mean signal intensity of the MEE to that of CSF was calculated. Signal intensity similarity (ratio approaching 1) was assumed to be diagnostic of CSF leak. Receiver operator characteristic analysis was performed to determine the best ratio threshold for accurately differentiating CSF leaks from other MEEs.

Results: Twenty-one patient with CSF leaks and 14 patients with other MEEs and adequate 3DT2 MRI sequences were included. Mean signal intensity ratio was 0.738 (+/- 0.020) for the leak patients and 0.475 (+/- 0.153) for the other MEEs (p = 0.00024). When a threshold ratio for diagnosis of CSF leak of 0.498 was selected, a sensitivity of 100% and specificity of 80% was obtained, with an overall accuracy of 91.7%.

Conclusions: Comparison of signal intensity between effusion and CSF can accurately diagnose CSF leak in patients with undifferentiated effusions.

Define Professional Practice Gap & Educational Need: Definitive diagnosis of a temporal bone cerebrospinal fluid leak may require invasive testing (myringotomy for beta-2 transferring testing). MRI is routinely obtained by some surgeons in preparation for CSF leak repair, and some middle ear effusions are incidentally noted on scans obtained for other reasons. The utility of objectively comparing MRI signal intensity of fluid in the middle ear and mastoid to that of adjacent CSF is not known.

Learning Objective: To describe the utility of MRI signal intensity measurement as a diagnostic test for temporal bone CSF leak.

Desired Result: The audience will understand the sensitivity and specificity of MRI signal intensity measurement in differentiating temporal bone CSF leaks from other middle ear and mastoid effusions.

Level of Evidence – IV

Indicate IRB or IACUC : University of Cincinnati 2017-2418