SELECTED ABSTRACTS

ORAL PRESENTATIONS

IN ORDER OF PRESENTATION

58th Annual Spring Meeting
AMERICAN NEUROTOLOGY SOCIETY

May 5-6, 2023
Sheraton Boston / Hynes CC
Boston, MA

Add-on Flexible Sensor Arrays for Real-time Monitoring of Cochlear Implant Electrode Insertion

Jay W. Reddy, PhD; Mohsen Tabrizi, PhD; Douglas A. Chen, MD
Abraham Jacob, MD; Maysam Chamanzar, PhD

Hypothesis: We hypothesize compact sensors integrated with cochlear implant (CI) electrodes can provide real-time force and position monitoring and feedback without contributing significantly to the implant stiffness.

Background: CI electrode mechanics and surgical techniques have been tuned to minimize insertion trauma. However, CI electrode insertion still results in undesired outcomes such as scalar translocation and tip-foldover, as well as structural damage and loss of residual hearing. We propose that integrated sensors can be used to measure clinically relevant features (i.e. wrapping factor, insertion force) and surgical events (i.e. tip-foldover, scalar translocation) to predict and potentially reduce these surgical risks.

Methods: We designed and fabricated novel stretchable, biocompatible, and ultrathin (< 20 μm) capacitive strain micro-sensor arrays using simulation and advanced lithographic microfabrication techniques. The sensors map the deformation and force at 16 points along the length of the CI electrode. The stiffness was characterized by a custom-made three-point bending setup comparing silicone electrode blanks (control) and sensor-attached samples.

Results: Computer simulations demonstrate sensitivity to CI electrode bending < 0.1 mm within the bend radius range of 0 to 4 mm, sufficient to clearly detect deformations associated with tip-foldover or scalar translocation. Experimental datasets show reliable attachment of the sensor to the CI electrode, with a small (<10%) contribution to the stiffness of the implant.

Conclusions: The strain sensors can be attached to CI electrodes to provide add-on force and position sensing capabilities without compromising the electrode flexibility, potentially enabling new fundamental understanding of electrode insertion dynamics and providing a novel intra-operative monitoring tool.

Professional Practice Gap & Educational Need: We lack knowledge of the dynamics of CI electrode insertion which leads to structural damage and residual hearing loss. This is tied to the lack of tools to enable high-resolution real-time monitoring of intracochlear electrode placement and forces. Polymer microfabrication provides the opportunity to integrate sensing modalities onto the electrode array itself, but a method for doing so without negatively impacting the highly-refined electrode array flexibility has yet to be demonstrated.

Learning Objective: To understand sensing modalities (i.e. capacitive, optical spectroscopy) that can be implemented in a flexible polymer substrate and how these may be used to advance fundamental scientific and clinical understanding of cochlear implantation outcomes, as well as to appreciate recent state-of-the-art experimental results showing sensor integration with CIs.

Desired Result: The audience will better understand the capabilities and feasibility of microfabricated sensors for integration with CI electrodes for real-time monitoring within the cochlea. We also aim for the audience to appreciate how such data can be used to refine clinical and fundamental science understanding of cochlear implantation.

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

Indicate IRB or IACUC : Exempt

NEUROTOLOGY FELLOW AWARD

Application of Spectral Domain Optical Coherence Tomography to Visualize Cochlear Microanatomy

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Timothy Holden, BSE; Chao Zhou, PhD
Craig A. Buchman, MD

Hypothesis: Our custom spectral domain optical coherence tomography (SD-OCT) platform can provide high resolution imaging of cochlear microanatomy.

Background: Current clinical imaging modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI), provide limited visualization of the human cochlea. Optical coherence tomography (OCT) is a non-invasive imaging modality that provides real-time three-dimensional (3D) visualization of tissue microstructure at higher spatial resolutions than that of clinical CT or MRI.

Methods: A customized SD-OCT system, operating at 1300 nm wavelength and providing 7 μm of transverse and 5 μm of axial resolution, was used to obtain 3D images of cochlear microanatomy before and after cochleostomy in cadaveric human temporal bones. The acquired OCT images were then directly compared with micro-CT library images of the human cochlea.

Results: High-resolution OCT images of the cochlea were obtained through both an intact and opened round-window membrane (RWM). Through an intact RWM, the scala tympani (ST) and basilar membrane (BM) were identified. Following cochleostomy, the scala vestibuli (SV), ST, and BM were visualized. OCT images were also obtained of a dummy cochlear implant electrode through the RWM. Importantly, our SD-OCT platform captured highly detailed and accurate 3D images of cochlear microanatomy and orientation that correlated with anatomical landmarks from a micro-CT human cochlea library.

Conclusion: Our custom SD-OCT platform can generate high-resolution real-time 3D visualization and orientation of cochlear microanatomy. This technology has the potential to further understanding of cochlear pathophysiology and to serve as a real-time surgical 3D image guidance tool for accessing the inner ear.

Professional Practice Gap & Educational Need: Intraoperative real-time visualization of cochlear orientation and anatomy remains limited. SD-OCT offers the potential to serve as a real-time surgical image guidance tool.

Learning Objective: To obtain high-resolution images of cochlear microanatomy using a custom SD-OCT system.

Desired Result: A custom SD-OCT platform can be used to generate real-time 3D images of the cochlear microanatomy and potentially serve as an intraoperative surgical guidance tool.

Level of Evidence: V

Indicate IRB or IACUC: Exempt

The Local Relationship between Acute Insertion Trauma and Chronic Intracochlear Ossification and Fibrosis after Cochlear Implantation: A Human Temporal Bone Study

Alexander R. Geerardyn, MD; MengYu Zhu, MS; Joseph B. Nadol Jr., MD
Nicolas Verhaert, MD, PhD; Alicia M. Quesnel, MD

Hypothesis: Trauma to the osseous spiral lamina (OSL) or spiral ligament (SL) during cochlear implant (CI) insertion induces localized intracochlear ossification and fibrosis.

Background: The goal of atraumatic insertion of the CI electrode is to preserve intracochlear structures in order to limit reactive intracochlear tissue formation and preserve residual hearing. Previous studies on individual 2D histological sections or the total cochlear volume reported conflicting results on the relationship between acute insertional trauma and chronic intracochlear ossification or fibrosis. This study evaluates the localized effect of insertional trauma on intracochlear tissue formation by virtually re-sectioning 3D reconstructions.

Methods: 3D reconstructions were generated based on digitized histological sections of a representative selection of twenty-one post-mortem human temporal bones with a CI. The reconstructions were virtually re-sectioned perpendicular to the cochlear spiral at high resolution. The percentage of the cochlear volume occupied by ossification or fibrosis was determined at the center, 30° proximal, and 30° distal to the trauma.

Results: Seven cases showed an OSL fracture. Significantly more intracochlear ossification was observed at the center of the OSL fracture, compared to 30° proximal or distal (paired t-test; $p=0.04$ and $p=0.02$, respectively). No such pattern was observed for fibrous tissue (paired t-test; $p>0.05$). In the twelve cases with a perforation of the SL no localized pattern of ossification, nor fibrosis was observed around these perforations.

Conclusions: A fracture of the OSL during CI insertion may serve as a nidus for localized intracochlear neo-ossification while perforation of the SL does not seem to have such a localized effect.

Professional Practice Gap & Educational Need: There is incomplete knowledge about the relationship between acute insertional trauma and chronic intracochlear tissue formation. This tissue formation may potentially cause a loss of residual hearing and limit the hearing performance with the cochlear implant.

Learning Objective: To understand the localized relationship between trauma to the osseous spiral lamina or spiral ligament and intracochlear tissue formation.

Desired Result: The participants become aware of the potential local consequences of an OSL fracture during cochlear implantation and further increase their effort to limit acute insertional trauma.

Level of Evidence – Level IV

Indicate IRB or IACUC : IRB 2021P001593, Mass General Brigham

Incidence Of Electrode Contacts in The Functional Acoustic Region for Cochlear Implant Recipients with Hearing Preservation

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Margaret T. Dillon, AuD, PhD; Matthew M. Dedmon, MD, PhD
A. Morgan Selleck, MD; Kevin D. Brown, MD, PhD

Objective: To investigate the incidence of electrode contacts within the functional acoustic hearing region in adults with post-operative hearing preservation following cochlear implantation.

Study Design: Retrospective review

Setting: Tertiary referral center

Patients: 142 cochlear implant recipients with functional acoustic hearing preservation as defined by an unaided hearing threshold of 80 dB or better at 250 Hz at their initial post-operative evaluation.

Interventions: Subjects underwent cochlear implantation with a 24-, 28-, or 31.5-mm lateral wall electrode array. The angular insertion depth (AID) of individual electrode contacts was calculated from post-operative imaging. Unaided acoustic thresholds and AID values were used to determine whether electrode contacts were within the subject's functional acoustic hearing region.

Main Outcome Measures: The presence and number of electrode contacts within the functional acoustic hearing region.

Results: Preliminary data demonstrate that 64% of subjects had one or more electrode contacts within the functional acoustic hearing region. For those with electrode contacts within the functional acoustic hearing region, 66% had one contact, 19% had two contacts, 9% had three contacts, and 6% had four or more contacts.

Conclusion: There is a high incidence of electrode contacts within the functional acoustic hearing region for adults with preserved acoustic hearing following cochlear implantation, which is not accounted for with default mapping procedures. Presenting electric stimulation within the functional acoustic hearing region could cause electric-on-acoustic masking, which could negatively impact speech recognition when listening with electric and acoustic stimulation in the same ear.

Professional Practice Gap & Educational Need: Hearing preservation following cochlear implantation with electrode contact placement within the functional acoustic hearing region was previously thought to be a rarity. Retrospective data quantifying the number of electrode contacts within the functional acoustic hearing region has yet to be reported.

Desired Result: Attendees will have a better understanding of the relationship between electrode angular insertion depth and post-operative hearing preservation outcomes.

Level of Evidence - Level V

Indicate IRB or IACUC: Approved

Factors Affecting Performance in Adults with Cochlear Implants: A Role for Cognition and Residual Cochlear Function

Amit Walia, MD; Matthew A. Shew, MD; Amanda Ortmann, PhD
Jordan Varghese, MD; Shannon Lefler, AuD
Jacques A. Herzog, MD; Craig A. Buchman, MD

Objective: To evaluate the impact of pre- and peri-operative factors on postlinguistic adult cochlear implant (CI) performance and design a multivariate prediction model.

Study Design: Prospective cohort study

Setting: Tertiary referral center

Patients: 192 postlinguistic adult CI recipients

Main Outcome Measures: Speech-perception testing (CNC, AzBio in noise +10-dB SNR) at 3-months postoperatively; Electrocochleography-total response (ECochG-TR), a measure of residual cochlear function, at the round window before electrode insertion

Results: There was a strong linear correlation between ECochG-TR and CNC word score at 3-months (r=0.66, p<0.0001). A multivariable linear regression model including age, pure tone average, Montreal Cognitive Assessment Score (MoCA), duration of hearing loss, angular insertion depth, and ECochG-TR did not perform significantly better than ECochG-TR alone in explaining the variability in CNC. There were also moderate linear correlations for AzBio in noise with MoCA (r=0.52, p<0.0001) and ECochG-TR (r=0.60, p<0.0001). Multivariate modeling using ECochG-TR and MoCA and the interaction between ECochG-TR*MoCA explained 59.8% of the variability in AzBio in noise scores.

Conclusions: This study uses the most comprehensive dataset to date to validate ECochG-TR as a measure of cochlear health as it relates to suitability for CI stimulation, and it further underlies the importance of the cochlear neural substrate as the main driver in speech perception performance. Performance in noise is more complex and requires both good residual cochlear function (ECochG-TR) and cognition (MoCA). Other demographic and audiologic variables are poorly correlated with CI performance suggesting that these are poor surrogates for the integrity of the auditory substrate.

Professional Practice Gap & Educational Need: Recognizing factors that affect CI performance has critical implications on counseling, post-CI aural rehabilitation, surgical technique, device choice and design and fitting. Prior studies consistently have shown that demographic, surgical, and audiologic variables account for less than 25% of the variability in speech-perception scores in quiet, making them poor indicators of performance. Recent work has highlighted the importance of residual cochlear function (as measured by ECochG-TR) and cognition in understanding the variability in CI performance. However, these studies have been underpowered to assess a comprehensive set of variables in addition to ECochG-TR.

Learning Objective: To understand the impact of demographic, audiologic, surgical, cognitive, and ECochG-TR measures on CI speech perception performance in adults.

Desired Result: Practitioners and researchers will further realize the value of using a peripheral measure of cochlear health (ECochG-TR) and a cognitive measures to understand much of the observed variability in performance among CI patients.

Level of Evidence - IV

Indicate IRB or IACUC : Washington University in St. Louis IRB #202007087.

Early Datalogging Predicts Cochlear Implant Performance: Building a Recommendation for Daily Device Usage

Nathan R. Lindquist, MD; Mary S. Dietrich, PhD, MS
Ankita Patro, MD, MS; René H. Gifford, PhD; David S. Haynes, MD
Elizabeth L. Perkins, MD; Jourdan T. Holder, AuD, PhD

Objective: We aim to elucidate the relationship between early device datalogging and speech recognition outcomes for cochlear implant (CI) recipients to better inform patient and clinician counseling regarding recommended daily wear time.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 337 adult patients with datalogging and speech outcomes data were implanted between August 2015 and August 2020.

Main Outcome Measures: Processor datalogging, speech recognition, achievement of 'benchmark speech recognition performance' defined as 80% of the median score for one year speech recognition outcomes at our institution.

Results: The one-month datalogging measure demonstrated a positive correlation to CNC and AzBio scores at one, three, six, and twelve-months post-activation. Compared to age and preoperative performance, datalogging was the largest predictive factor of benchmark achievement on multivariate analysis. Each hour/day increase of device usage at 1-month resulted in a higher likelihood of achieve benchmark CNC or AzBio score within the first year (OR 1.21, p <0.001). Receiver operator characteristic (ROC) analysis demonstrates benefit beyond 10 hours/day daily usage time.

Conclusions: Early CI device usage as measured by 1-month datalogging predicts ultimate speech outcomes and benchmark speech recognition achievement in adults. Datalogging is likely the most important predictor of CI performance within the first-year post-implantation. Patients should utilize their devices a minimum of 10 hours/day, as potential benefit exists beyond this cut-off.

Professional Practice Gap & Educational Need: Our understanding of the role between daily device usage and speech recognition outcomes are in the early stages. Further investigations into this potential counseling point and intervention are necessary.

Learning Objective:

1. Quantify and characterize the relationship between early daily device usage and speech recognition outcomes.
2. Understand the rationale for the 'benchmark speech recognition performance' metric in data analysis.
3. Recognize early data logging as an inexpensive, easily accessible, and post-implantation intervention that requires minimal clinician bandwidth besides counseling and follow-up.

Desired Result: Viewers will be able to quantify and characterize the relationship between early daily device usage and speech recognition outcomes. In addition, we hope that exposure to this information solidifies data logging as an inexpensive, easily accessible, and post-implantation intervention that requires minimal clinician bandwidth.

Level of Evidence - Level III

Indicate IRB or IACUC : Vanderbilt University Medical Center IRB# 220255

Responsible Imputation of Missing Speech Perception Testing Data

Cole Pavelchek, BS; David S. Lee, MD; Amit Walia, MD
Amanda Ortmann, PhD; Jacques A. Herzog, MD
Craig A. Buchman, MD; Matthew A. Shew, MD

Objective: To address outcome heterogeneity in cochlear implant (CI) research, we built imputation models using multiple imputation by chained equations (MICE) and K-nearest neighbors (KNN) to convert between four common open-set testing scenarios: Consonant-Nucleus-Consonant word (CNCw), Arizona Biomedical (AzBio) in quiet, AzBio +5dB SNR, and AzBio +10dB SNR. We then analyzed raw and imputed datasets to evaluate factors affecting CI outcome variability.

Study Design: Retrospective cohort study of a national CI database (HERMES) and a non-overlapping single-institution CI database.

Setting: Multi-institutional (32 CI centers)

Patients: Adult CI recipients (n=4,046 patients).

Main Outcome Measure: Mean absolute error (MAE) between imputed and observed speech perception scores

Results: Imputation models of preoperative speech perception measures demonstrate an MAE of less than 10% for feature triplets of CNCw/AzBio in quiet/AzBio +10dB SNR (MICE: MAE=9.52%, 95%CI=9.40–9.64; KNN: MAE=8.93%, 95%CI=8.83–9.03) and AzBio in quiet/AzBio +5dB SNR/AzBio +10dB SNR (MICE: MAE=8.85%, 95%CI=8.68–9.02; KNN: MAE=8.95%, 95%CI=8.74–9.16) with one feature missing. Postoperative imputation can be safely performed with up to 4 of 6 features missing in a set of CNCw and AzBio in quiet at 3, 6, and 12 months post-cochlear implantation using MICE (MAE=9.69%, 95%CI=9.63–9.76). For multivariable analysis of CI performance prediction, imputation increased sample size by 72%, from 2,756 to 4,739, with marginal change in adjusted R^2 (0.13 raw, 0.14 imputed).

Conclusions: Missing data across certain sets of common speech perception tests may be safely imputed, enabling multivariate analysis of one of the largest CI outcomes datasets to date.

***Professional Practice Gap & Educational Need:** A major challenge to studying CI outcomes is that there are multiple heterogeneous speech perception measures with no clear standard across practices. This prevents meaningful aggregation of data within and between institutions, limiting CI outcome research to predominantly single-institution studies and small sample sizes. Developing methods for converting one speech performance measure to another would facilitate analyses of multi-institutional databases for CI research with greater power, generalizability, and impact.

***Learning Objective:** To develop imputation models for converting between commonly used speech perception tests using a large multi-institutional database. To perform a proof-of-concept analysis on preoperative factors associated with postoperative hearing outcomes before and after imputation.

***Desired Result:** Empower attendees to use the proposed imputation models on their own CI outcome databases to increase sample size and generalizability of their studies.

***Level of Evidence -** III

***Indicate IRB or IACUC:** Washington University in St. Louis IRB #201911036

Age of Cochlear Implantation within the Pediatric Population with Congenital Sensorineural Hearing Loss

Ashley M. Nassiri, MD, MBA; John P. Marinelli, MD
Christine M. Lohse, MS; Matthew L. Carlson, MD

Objectives: The current study evaluates changes in the number of cochlear implant (CI) surgeries performed and the age of implantation among the pediatric population with congenital sensorineural hearing loss (SNHL) in the U.S.

Study Design: Deidentified CI data were acquired from prospectively collected patient registries from two CI manufacturers (Cochlear Americas and Advanced Bionics), which supply an estimated 85% of CIs in the U.S. Children ≤36 months old were assumed to have bilateral congenital SNHL.

Setting: U.S. CI centers.

Patients: Children ≤36 months old who received CIs.

Interventions: Cochlear implantation.

Main Outcome Measures: Annual implantation rates, age at implantation.

Results: A total of 4,311 children ≤36 months old received CIs between 2015 and 2019. The annual number of recipients increased from 787 in 2015 to 940 in 2019. The median age at implantation was 16 months (IQR 12-24), which did not change significantly during the 5-year study period ($p=0.09$). Age of implantation was not significantly associated with urban or rural residence ($p=0.5$) or distance traveled to CI center ($p=0.05$). Bilateral simultaneous implantation increased from 38% to 52% of CIs in 2015 and 2019, respectively ($p<0.001$). Children who received bilateral simultaneous implants were younger compared to those receiving unilateral or bilateral sequential implants (14 vs 18 months, $p<0.001$). Higher volume CI centers (>10 pediatric CIs per year) implanted children at a younger age compared to lower volume centers (15 vs 16 months, $p=0.009$), although this difference may not be clinically significant.

Conclusions: Though the number of pediatric CI recipients and the frequency of bilateral simultaneous implantation increased over the studied interval, age at time of implantation did not change and far exceeds current FDA (9 months) and AAOHNS position statement (6-12 months) guidelines. Timely implantation improves auditory and language outcomes and should be more prioritized in children with congenital SNHL.

Professional Practice Gap & Educational Need: While FDA labeling and indications for cochlear implantation have expanded in recent years, the level of success in clinical implementation within the pediatric CI candidate population has not been measured. Detailed metrics evaluating rates of CI, age at implantation, and rates of simultaneous implantation are critical in understanding current practices, which may lag behind recommendations.

Learning Objectives: Describe the rates of cochlear implantation and changes over time within the pediatric population with congenital sensorineural hearing loss. Understand factors associated with age of implantation within the pediatric population with congenital sensorineural hearing loss. Understand current practices and shortcomings of implementation of expanded cochlear implant criteria.

Desired Result: Physicians, audiologists, and researchers would better understand current cochlear implantation practices within the pediatric population with congenital sensorineural hearing loss and identify areas for improvement.

Level of Evidence: III

Indicate IRB or IACUC: Exempt

Pre-Surgical MRI Radiomics Data Predicts Post-Implantation Electrocochleography Thresholds in Radiographically Normal Pediatric Cochleae

Nicholas A. George-Jones, MD; Christine Etler, AuD
Tanya Van Vorst, AuD; Camille C. Dunn, PhD
Bruce J. Gantz, MD; Marlan R. Hansen, MD

Objective: Radiomics involves extracting higher-order relationships of voxel intensity and position from an image that that cannot be appreciated by the human eye. These features correlate with differences in underlying tissue composition and can provide predictive models of disease outcomes. Here, we investigated whether radiomics data from pre-implantation imaging can predict electrically evoked compound action potential (eCAP) thresholds in pediatric cochlear implant (CI) recipients.

Study Design: Retrospective study.

Setting: Tertiary care center

Patients: Children that had normal cochleae on pre-operative MRI and eCAP measures available for a slim perimodiolar array.

Interventions: Radiomics data were extracted from segmented T2 SPACE images and a predictive model of eCAP thresholds was constructed using a support vector machine regressor. Leave-one-out cross validation was used, in which a prediction was generated for each patient using a model trained on the other patients' radiomics features. A logarithmic transformation was used to scale model output.

Main Outcome Measures: Model performance was assessed using the regression coefficient p-value, least squares (R^2), and root mean square error (RMSE) of the predicted eCAP versus actual eCAP.

Results: 26 patients were included of which 14 had bilateral CI's for a total of 40 ears. Model performance on the apical ($p < 0.001$, R^2=0.665, RMSE = 9.438) , middle ($p < 0.001$, $R^2 = 0.6805$, RMSE = 15.47), and basal ($p < 0.001$, R^2=0.5864, RMSE = 14.85) portions of the electrode array each demonstrated strong correlation.

Conclusions: Pre-operative cochlear radiomics data may predict post-implantation eCAPs and provide information about individual cochlear physiologic characteristics.

Professional Practice Gap & Educational Need: Methods in machine learning and artificial intelligence are increasingly being applied to medical data and have important implications for individualizing care and patient expectations. It is important for providers to be aware of the growing importance of these methods, and their utility for use in studying other lateral skull base pathologies.

Learning Objective: To understand that new techniques and data analysis may be useful in offering previously unknown information about the state of health of the cochlea that may be important to better predict patient outcomes.

Desired Result: Providers will have a new understanding that certain types of radiomics data may offer a new way to characterize the physiology of the cochlea using established, routine medical imaging. This understanding may provide a new avenue for investigations in predicting outcomes for patients receiving surgery.

Level of Evidence - IV

Indicate IRB or IACUC : University of Iowa IRB #201110703

ANS TRAINEE AWARD

Machine Learning Approach for Screening Cochlear Implant Candidates: Comparing with the 60/60 Guideline

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Carlos Ortega, BS; Nathan R. Lindquist, MD; René H. Gifford, PhD
David S. Haynes, MD; Naweed Chowdhury, MD, MPH

Objective: To develop a machine learning-based referral guideline for patients undergoing cochlear implant candidacy evaluation (CICE) and to compare with the widely used 60/60 guideline.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 772 adults undergoing CICE from 2015—2020.

Interventions: Variables included demographics, unaided thresholds, and word recognition score (WRS). A random forest classification model was trained on patients undergoing CICE, and bootstrap cross-validation was used to assess the modeling approach's performance.

Main Outcome Measures: The machine learning-based referral tool was evaluated against the 60/60 guideline based on ability to identify CI candidates under traditional and expanded criteria.

Results: Of 587 patients with complete data, 563 (96%) met candidacy at our center, and the 60/60 guideline identified 512 (87%) patients. In the random forest model, WRS; thresholds at 3000, 2000, and 125; and age at CICE had the largest impact on candidacy (mean decrease in Gini coefficient: 2.8, 1.6, 1.2, 1.2, and 1.2, respectively). The 60/60 guideline had sensitivity of 0.91, specificity of 0.42, and accuracy of 0.89 (95% CI: 0.86—0.91). The random forest model obtained higher sensitivity (0.96), specificity (1.00), and accuracy (0.96; 95% CI: 0.95—0.98). Across 1000 bootstrapped iterations, the model yielded a median sensitivity of 0.92 (IQR 0.85—0.98), specificity of 1.00 (IQR 0.88—1.00), accuracy of 0.93 (IQR 0.85—0.97), and area under the curve of 0.96 (IQR 0.93—0.98).

Conclusions: A novel machine learning-based screening model predicts CI candidacy with notably higher sensitivity, specificity, and accuracy than the 60/60 guideline. Bootstrapping confirmed that this approach is likely generalizable with consistent results.

Professional Practice Gap & Educational Need: With less than 10% of adult candidates receiving CIs, several screening tools, including the 60/60 guideline, have been developed to help streamline referrals. Recent literature, however, highlights that these screening tools are only modestly successful at identifying potential CI candidates. Novel methods to improve referrals and access to implantation are needed.

Learning Objective: To identify how machine learning methods can aid in the development of superior screening tools for CICE.

Desired Result: Providers will have additional knowledge about this machine learning-based algorithm, which can more accurately refer patients for CICE than currently practiced guidelines. These results can be utilized to support increased awareness of CI candidacy and timely referrals, in turn, decreasing the burden associated with hearing loss.

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

Indicate IRB or IACUC: IRB Exempt (221833, Vanderbilt University).

The Impact of Musical Rehabilitation on Complex Sound Perception in Cochlear Implant Users: A Systematic Review

Hasan Abdulbaki, BA; Jonathan Mo, BS, BM; Charles J. Limb, MD; Nicole T. Jiam, MD

Objective: To evaluate the efficacy of music rehabilitation in controlled experimental studies on cochlear implant (CI) user speech and music perception.

Data sources: PubMed, Embase, Web of Science, PsycARTICLES, and PsycINFO databases were queried using the search terms "cochlear implant," "music rehabilitation," and "music therapy" for English-language articles through July 2022.

Study selection: Randomized controlled trials and prospective studies were included if they compared pretest and posttest data and excluded hearing aid-only users.

Data extraction: PRISMA guidelines were used to extract data from 11 included studies with a total of 206 pediatric and adult participants. Interventions included group music therapy, melodic contour identification (MCI) training, auditory-motor instruction, or structured digital music training. Risk of bias was assessed regarding confounding, timeframe, and rate of follow up among other parameters using the NIH Quality Assessment Tool.

Data synthesis: A total of 735 studies were screened and 11 met inclusion criteria. Studies employed heterogeneous outcome measures evaluating speech and music perception. Six trials reported both speech and music outcomes while 5 reported only music outcomes following intervention relative to control. For music perception outcomes, significant findings included improvements in MCI (5 studies, $p<0.05$), timbre recognition (3 studies, $p<0.05$), and song appraisal (3 studies, $p<0.05$) in their respective trials. For speech prosody outcomes, only vocal emotion identification demonstrated significant improvements (3 studies, $p<0.05$).

Conclusions: Music rehabilitation improves performance on multiple measures of music perception, as well as tone-based characteristics of speech (i.e., emotional prosody). This suggests that rehabilitation may facilitate improvements in the discrimination of spectrally complex signals.

Professional Practice Gap & Educational Need: While music training has been studied as a potential mode of aural rehabilitation for CI users, no standardized music intervention protocol has been developed for routine clinical application. As a result, providers rarely employ music as a rehabilitative strategy due to uncertainty in clinical outcomes. The lack of literature synthesizing music rehabilitation's impact on CI user complex sound processing represents a barrier to practice standardization and thus further contributes to uncertainty in clinical applicability despite existing evidence of efficacy.

Learning Objective: To review the various modes of music-based aural rehabilitation and improve current understanding regarding their impact on music and speech perception in cochlear implant users.

Desired Result: Encourage providers to adopt music-based interventions for CI user auditory rehabilitation by consolidating the wide base of evidence on their clinical efficacy for complex sound hearing improvement.

Level of Evidence - II

Indicate IRB or IACUC: Exempt.

Vestibular Weakness in Cochlear Implant Candidates

Allison Reeder, MD; Rema Shah, BS; John F. Kveton, MD
Eugenia Vining, MD; Hannah Dunn, AuD
Nofrat Schwartz, MD

Background: Cochlear implantation (CI) has been associated with postoperative vestibular dysfunction in the implanted ear, however, baseline vestibular function in this population is not well known

Objective: Describe preoperative prevalence of vestibular weakness/ identify correlated audiologic findings in the profoundly deaf

Study Design: Retrospective cohort study (2012-2022) of the CI candidate population. All patients evaluated for CI underwent routine preoperative vestibular evaluation, irrespective of symptoms.

Results: Of 180 CI patients, 39.4% had preoperative vestibular weakness as determined on caloric testing. Of these, 26.8% had bilateral weakness, 60.5% had unilateral weakness ipsilateral to planned implant ear and 12.7% had contralateral weakness. There was no difference in age between patients with vestibular weakness (65.4±14.8 years) and those without (65.6±15.9 years) or gender (%female 52.1% vs. 60.6%, p=0.263). Patients with vestibular weakness were more likely to have poorer low-tone hearing than those with normal vestibular function (250 Hz: 79.7dB±23.5 vs. 64.4dB±24.0, p<0.001 and 500 Hz: 86.1dB±23.3 vs. 73.8dB±23.8, p <0.001) as well as lower pure tone average (88.8dB±18.7 vs. 83.1dB±18.1, p=0.046). WRS were also lower in weak patients but did not reach significance (17.8%±20.9% vs. 20.6±20.1%, p=0.185).

Conclusions: CI candidates have a high prevalence of preoperative vestibular weakness both unilateral and bilateral. Previous studies have suggested increased postoperative dizziness in patients with abnormal VNG. This raises concerns prior to CI, especially in patients with bilateral/ contralateral vestibular weakness. Our data suggests that decreased low-tone hearing may be a predictor for abnormal vestibular function and further investigation with VNG may be useful in guiding decision making/ counseling prior to CI.

Professional Practice Gap & Educational Need: Preoperative VNG testing in CI candidates is not routinely done, however we suggest there are certain audiologic findings that may be indicative of preoperative vestibular dysfunction in this population.

Learning Objective: Understand prevalence of vestibular weakness in CI candidates and correlate this with audiogram findings that may be predictive of vestibular system dysfunction

Desired Result: Educate about preoperative prevalence of vestibular weakness in CI candidates and consider VNG testing in patients with poor low tone hearing on audiogram.

Level of Evidence - IV

Indicate IRB or IACUC: Yale School of Medicine, IRB ID: 2000031399

Estimation of Cochlear Implant Insertion Depth Using 2D-3D Image Registration of Postoperative X-Ray and Preoperative CT Images

George S. Liu, MD; Shayna P. Cooperman, MD
Caio A. Neves, MD; Nikolas H. Blevins, MD

Objective: To evaluate cochlear implant (CI) insertion depth using fused 2D and 3D spatial information from postoperative x-rays and preoperative CTs.

Study Design: Retrospective cohort.

Patients: 10 adult cochlear implant recipients with pre- and postoperative temporal bone CT and postoperative skull x-ray imaging.

Interventions: Postoperative x-rays and digitally reconstructed radiographs (DRR) from preoperative CTs were registered using 3D Slicer and MATLAB to enhance localization of the round window and modiolus. Angular insertion depth (AID) was estimated in original and registration-enhanced x-rays and DRRs in the cochlear view. Linear insertion depth (LID) was estimated in registered images by two methods that localized the proximal CI electrode or segmented the cochlea. Ground truth assessments were made in postoperative CTs.

Main Outcome Measure(s): Errors of insertion depth estimates were calculated relative to ground truth measurements and compared with paired t-tests. Pearson correlation coefficient was used to assess inter-rater reliability of two reviewer's measurements of AID in original x-rays.

Results: In postoperative x-rays, AID estimation errors were similar with and without registration enhancement (-1.3 ± 20.7° and -4.8 ± 24.9°, respectively; mean ± SD; $p=0.6$). AID estimation in original x-rays demonstrated strong inter-rater agreement ($\rho=0.79$, $p<0.05$) and inter-rater differences (-15.0 ± 35.3°) comparable to estimate errors. In the cochlear view, AID estimation errors were 14.6 ± 30.6°. Estimation errors of LID were similar between proximal electrode localization and cochlear segmentation methods (-0.9 ± 2.2 mm and -2.1 ± 2.7 mm, respectively; $p=0.3$).

Conclusions: 2D-3D image registration is a promising approach to measure angular and linear insertion depths of CIs without postoperative CT imaging.

Professional Practice Gap & Educational Need: Final cochlear implant position is an important determinant of audiologic outcomes but is not readily assessed in 3-dimensional space from a single postoperative skull radiograph. With advances in digital image technology, developing systems to enhance the assessment of cochlear implant positioning in radiographs using patient-specific anatomical image data from preoperative CT imaging is important.

Learning Objective: Review existing and new potential applications of image analysis technology to quantitatively assess cochlear implant insertion depth.

Desired Result: Discuss the opportunities and limitations of applying digital image analysis technology to aid in the assessment of postoperative CI positioning and outcomes.

Level of Evidence: IV

Indicate IRB or IACUC: Stanford University IRB #48036 approved 11/9/2018

Comparison of Cochlear Implant Outcomes in Vestibular Schwannoma between Sporadic and Neurofibromatosis Type 2 Populations

James R. Dornhoffer, MD; Travis Haller, MD; Brian A. Neff, MD
Colin L.W. Driscoll, MD; Matthew L. Carlson, MD

Objective: To compare cochlear implant outcomes between patients with sporadic vs neurofibromatosis type 2 (NF2)-related vestibular schwannoma.

Study Design: Retrospective review

Setting: Tertiary academic center

Patients: 60 patients (64 ears) undergoing cochlear implantation for moderate-to-profound hearing loss in the setting of vestibular schwannoma. Of these, 27 presented with sporadic disease, and 33 with NF2.

Interventions: Cochlear implantation ipsilateral to vestibular schwannoma

Main Outcome Measures: Consonant-Nucleus-Consonant phoneme (CNCp), CNC word (CNCw), and AzBio sentences in quiet.

Results: Average speech perception scores after cochlear implantation were 39.0±29.8% CNCw, 51.8±33.0% CNCp, 50.9±35.2% Azbio Quiet at an average of 18.7±16.6 months after implantation. Overall, patients with sporadic disease performed better than their NF2 counterparts in CNCw (47.1±26.2% vs 32.8±31.3%, p=0.038), CNCp (59.6 ±27.3% vs 44.7±36.6%, p=0.066), and AzBio Quiet (55.7±33.0% vs 46.9±37.0%, p=0.184). When comparing patients with observation or radiosurgery, there was no significant difference in cochlear implant outcomes between the NF2 or sporadic groups. In patients who had microsurgery, those with sporadic disease had significantly better outcomes than those with NF2: CNCw (37.1±28.0% vs 7.0±12.5%, p=0.006), CNCp (48.9±32.5% vs 5.9±16.6%, p=0.002), and AzBio Quiet scores (44.2±34.9% vs 18.1±28.2%, p=0.037). In patients with surgery, 6 out of 14 with NF2 failed to achieve open-set speech recognition, compared to 2 out of 11 with sporadic disease. All patients treated with radiosurgery or observation achieved open-set speech recognition.

Conclusions: Patients with hearing loss relate to vestibular schwannoma may benefit from cochlear implantation. However, patients with NF2 may have worse speech recognition with an implant than those with sporadic disease, specifically those with a history of microsurgical resection.

REQUIRED:
Professional Practice Gap & Educational Need: Cochlear implantation is an appropriate modality of salvage and/ or preservation of functional hearing in patients with vestibular schwannoma. However, most data on implantation with vestibular schwannoma comes from the NF2 population, despite the fact that the majority of all schwannomas are sporadic. As such, we must understand differences in cochlear implant outcomes between these two populations to most appropriately counsel patients and further research on such care.

Learning Objective: To explore differences in cochlear implant outcomes between vestibular schwannoma patients with and without a history of NF2.

Desired Result: Practitioners and researchers will recognize important differences in cochlear implant outcomes between patients with sporadic and NF2-associated vestibular schwannoma, and use this to inform research goals and counselling of patients considering cochlear implantation in the setting of vestibular schwannoma.

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

Indicate IRB or IACUC : 22-000183

Metformin Reduces Tumor Growth in a Murine Flank Schwannoma Model

Sudhir Manickavel, MD; Yolanda Hartman, BS; Andrew Burns, BS
Manuel A. Lora Gonzalez, MD; Jason Warram, PhD
Erika M. Walsh, MD; Daniel E. Killeen, MD

Hypothesis: Metformin reduces schwannoma growth.

Background: Patients with vestibular schwannomas prescribed metformin had decreased tumor volumetric growth compared to non-users in retrospective studies. Aspirin has also been found to reduce schwannoma growth in animal studies**.**

Methods: Rat schwannoma cell lines were grown and implanted into 50 athymic nude mice. Tumors were allowed to grow to 5mm and then injected with either low or high dose metformin, aspirin, or saline daily. Tumors were measured until mice demonstrated symptoms or 14 days had elapsed.

Results: There were no significant differences in day 0 tumor sizes between the control and treatment groups ($p = 0.7271$). In the low dose but not high dose groups, day 7 volumes were significantly different for both metformin ($p = 0.0437$) and aspirin ($p = 0.02$) compared to placebo. Mean tumor growth rates were 126.6 +/- 65.57 mm^3 for saline compared to 73.67 +/- 29.51 mm^3 for low dose metformin ($p=0.0315$) and 68.66 +/- 34.76 mm^3 for low dose aspirin ($p=0.0164$). There were no significant differences in tumor sizes ($p = 0.5913$) or growth rates ($p = 0.7459$) between low dose metformin and aspirin groups. Low dose groups had treatment stopped at 14 days and continued monitoring demonstrated significant increases in tumor growth off treatment for both aspirin ($p=0.0057$) and metformin ($p=0.0483$).

Conclusions: In the first study, to our knowledge, to investigate the effect of metformin on schwannomas in an animal model, metformin treatment significantly reduced schwannoma growth to a similar level as aspirin. Furthermore, when removing metformin treatment, tumor growth significantly increased.

***Professional Practice Gap & Educational Need:** Patients with vestibular schwannomas are currently offered observation, radiosurgery, or microsurgical approaches for management. Data regarding the treatment of vestibular schwannomas with aspirin and metformin can help provide additional treatment options for patients in the future.

***Learning Objective:** Attendees will understand the effect of metformin and aspirin on vestibular schwannomas tumor growth in a murine model

***Desired Result:** Attendees will note that there are decreased tumor size and growth rates in mice treated with metformin in this preliminary study, though further animal studies and eventually prospective clinical trials are needed with regard to dosing and efficacy to determine if metformin would be an effective treatment for vestibular schwannoma.

***Level of Evidence –** N/A (basic science lab research)

***Indicate IRB or IACUC :** University of Alabama Medical Center, IACUC #22466

ANS TRAINEE AWARD

Identifying Tumor Microenvironment Biomarkers in Adherent and Cystic Vestibular Schwannomas

Lisa Zhang, MD; Hsuan-Chih Kuo; Jose Otero, MD, PhD
Yin Ren, MD, PhD

Objective: A subset of vestibular schwannomas (VS) exhibit cystic degeneration resulting in adherence of the tumor capsule to the brainstem and facial nerve. We aim to identify tumor microenvironment (TME) biomarkers to better classify these tumors.

Study Design: Retrospective case series

Setting: Tertiary academic skull base referral center

Methods: Adult patients with sporadic cystic VS and patients with solid VS matched in tumor size who underwent microsurgical resection between February 2010 and August 2021 were included. TME biomarkers including matrix metalloproteinases (MMP-2, MMP-9, MMP-14), pan-leukocyte (CD45), tumor-associated macrophages (CD80, CD163) and endothelial cells (CD31) were quantified via immunohistochemical staining. The distribution of CD45+ cells was evaluated in both intratumoral and perivascular regions. Degree of tumor adherence was categorized as none, adherent to facial nerve, or adherent to both facial nerve and brainstem.

Results: Twenty-eight patients were included (50% female, mean age 56 +/- 15 years). Cystic VS were significantly more adherent to the facial nerve and brainstem than solid VS ($p=0.02$). Linear discriminant analyses demonstrate MMP-14, CD80, CD163, and perivascular CD45 to be individually predictive of the degree of tumor adherence (all $p<0.04$), with perivascular CD45 being the best performing independent predictor ($p=0.005$). A linear discriminant model including these biomarkers demonstrated 100% accurate discrimination of all three levels of tumor capsule adherence ($p=0.003$).

Conclusions: Cystic VS tend to be more adherent to critical neurovasculature structures and negatively affecting surgical outcomes. Adherent tumors have a distinct TME characterized by elevated MMP-14 expression, enrichment of tumor-associated macrophages, and perivascular immune cell infiltration.

Professional Practice Gap & Educational Need: A subset of sporadic VS exhibit uniquely aggressive cystic degeneration and increased tumor adherence to the facial nerve and brainstem, making tumor resection extremely challenging and could lead to significant postoperative morbidity. Currently, there are no well-established biomarkers to classify these tumors or provide mechanistic insight into how cystic VS develop.

Learning Objective: We provide initial insights into the role of the VS tumor microenvironment in highly adherent tumors. We identify several novel biomarkers that classify adherent tumors, including a matrix metalloproteinase, tumor-associated macrophages, and the degree of perivascular immune cell infiltration.

Desired Result: To describe the unique tumor microenvironment of cystic VS that are adherent to the facial nerve and brainstem.

Level of Evidence – Level IV

IRB: The Ohio State University, IRB #1994H0241, Approved 6/2/2022

A Mouse Model of Neurofibromatosis Type 2 Demonstrates Glial Cell Proliferation and Neuronal Loss

Judith S. Kempfle, MD; Andrea Zhang, BS; Richard Kuang, BS
Sina Schwinn, BS; Konstantina Stankovic, MD, PhD
D. Bradley Welling, MD, PhD; David H. Jung, MD, PhD

Objective: Neurofibromatosis type 2 (NF2) is associated with loss of *NF2*/Merlin, which leads to schwannomas of the vestibular nerve and varying degrees of sensorineural hearing loss (SNHL). The etiology of the hearing loss remains to be elucidated, although leading current theories implicate the secretion of pro-inflammatory and potentially neurotoxic factors. In this study, we examined the auditory and vestibular nerves in a mouse model for NF2 to further investigate the underlying cochlear NF2 phenotype.

Study Design: Basic Science study

Setting: Animal model

Patients: N/A

Interventions: NF2 mice or controls were aged up to 11 months. Animals underwent serial measurements of auditory brainstem responses (ABR) and 5-Ethynyl-2′-deoxyuridine (EdU) injections.

Main Outcome Measures: Inner ear histology was performed for glial and neuronal markers at 11 months. Proliferation was assessed after EdU labeling. Schwann cells and neurons were quantified on serial sections. Cochlear whole mounts were stained and quantified for synaptic markers. Glial cells at early and late time points were isolated using fluorescence-activated cell sorting (FACS), and microRNA and mRNA were isolated for quantitative PCR.

Results: At 10-11 months of age, and compared to controls, ABR demonstrated significant hearing loss in all NF2 animals. EdU increased proliferation of glial cells within the cochlea that was associated with increased loss of ribbon synapses, followed by neuronal loss.

Conclusions: NF2 mice display a cochlear phenotype that associated with dysregulation of glial cell proliferation after loss of *NF2*/Merlin. This proliferation is further associated with a loss of auditory synapses and neurons. These findings may in part explain the sensorineural hearing loss in patients with vestibular schwannomas.

Professional Practice Gap & Educational Need: To date, there is no conclusive explanation for the SNHL developed by patients with NF2. In order to treat NF2 related hearing loss, we need to understand the underlying pathophysiology of the disease.

Learning Objective: Animal models for NF2, pathophysiology of NF2

Desired Result: Become familiar with theories regarding SNHL in NF2

Level of Evidence – N/A

Indicate IRB or IACUC : IACUC 2021N000080

Automated Radiomic Analysis of Vestibular Schwannomas and Inner Ears using Contrast-enhanced T1-weighted and T2-weighted MRI Sequences and Artificial Intelligence

Caio A. Neves, MD; George S. Liu, MD; Trishia El Chemaly, MS
Isaac A. Bernstein, BS; Nikolas H. Blevins, MD

Objective: To objectively evaluate vestibular schwannomas (VS) and their spatial relationships with the ipsilateral inner ear (IE) in MRI scans using deep learning.

Study Design: Cross-sectional study.

Patients: 490 adults with VS, high resolution MRI scans, and no prior neurotologic surgery.

Interventions: The VS patient cohort was split into training (390 patients) and test (100 patients) sets. A 3-dimensional convolutional neural network model was trained to segment VS and IE structures using contrast-enhanced T1-weighted and T2-weighted MRI sequences, respectively. Manual segmentations were used as ground truths. Model performance was evaluated on the test set and on an external set of 100 VS patients in a public dataset (Vestibular-Schwannoma-SEG).

Main Outcome Measure(s): Dice score, relative volume error (RVE), average symmetric surface distance (ASSD), 95th-percentile Hausdorff distance (HD95), and centroid locations.

Results: Dice scores for VS and IE volume segmentations in the test set were 0.91 and 0.90, respectively. On the public dataset, the model segmented VS tumors with a Dice score of 0.89 ± 0.06 (mean ± SD), VRE of 9.8 ± 9.6%, ASSD of 0.31 ± 0.22 mm, and HD95 of 1.26 ± 0.76 mm. Predicted VS segmentations overlapped with ground truth segmentations in all test subjects. Mean errors of predicted VS volume, VS centroid location, and IE centroid location were 0.05 cm^3, 0.52 mm, and 0.85 mm, respectively.

Conclusions: A deep learning system can segment VS and IE structures in high resolution MRI scans with excellent accuracy. This technology offers promise to improve the clinical workflow for assessing VS radiomics and enhance the management of VS patients.

Professional Practice Gap & Educational Need: Volumetric measurement is the gold standard for detecting subtle growth of VS tumors but is cumbersome to implement in clinical practice. With advances in artificial intelligence technology, developing systems to improve the workflow for measuring VS volumes is potentially both important and achievable.

Learning Objective: Review technological advances in artificial intelligence and their application to quantitatively assessing radiomic features of VS tumors.

Desired Result: Discuss the opportunities and limitations of applying deep learning technology to aid in the volumetric assessment of VS tumors and neighboring inner ear anatomy.

Level of Evidence: IV

Indicate IRB or IACUC: Stanford University IRB #61070

Stratifying Risk of Future Growth Among Growing Sporadic Vestibular Schwannomas

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Jacob B. Hunter, MD; Douglas Kondziolka, MD
J. Thomas Roland Jr., MD; Matthew L. Carlson, MD

Objective: Whether considering upfront treatment or toleration of growth during observation management, stratification of patients at increased risk for future growth is critical. The aim of the current work was to determine if patients with growing sporadic vestibular schwannomas could be stratified by likelihood of subsequent growth based on prior growth behavior.

Study Design: Slice-by-slice volumetric tumor measurements from 3,505 serial MRI studies were analyzed from 952 consecutively treated patients.

Setting: Three tertiary-referral centers.

Patients: Adults with sporadic vestibular schwannoma.

Interventions: Wait-and-scan.

Main Outcome Measures: Composite endpoint of subsequent growth- or treatment-free survival rates (where growth is defined as ≥20% increase in tumor volume from size at time of initial growth).

Results: Among 405 patients who elected continued observation despite documented growth, stratification by volumetric growth rate into <25% (reference), 25 to <50% (HR 1.39, p=0.06), 50 to <100% (HR 1.71, p=0.002), and ≥100% (HR 2.01, p<0.001) change per year predicted likelihood of future growth. Subsequent growth or treatment-free survival rates (95% CI) at 1 and 5 years following detection of initial growth were 80% (73-88) and 31% (21-44); 65% (56-76) and 18% (10-32); 57% (49-68) and 15% (9-26); and 51% (41-62) and 6% (2-16), respectively, for the four stratification groups.

Conclusions: At time of diagnosis, clinical features cannot predict which tumors will ultimately display aggressive behavior. Stratification by volumetric growth rate at time of initial growth results in a stepwise progression of increasing likelihood of subsequent growth. When considering toleration of growth during observation management, almost 95% of patients with ≥100% change in tumor volume between diagnosis and first detection of growth demonstrate further tumor growth or undergo treatment within 5 years.

Professional Practice Gap & Educational Need: When considering tolerating some growth during observation management, stratifying which patients are at highest risk for future growth or requiring treatment is paramount. However, due to the historical paradigm where growing tumors undergo treatment, little data currently characterizes future growth behavior of growing sporadic vestibular schwannomas.

Learning Objective: Describe the survival rates and associated risk for future growth or treatment by the volumetric growth rate stratification grouping for patients with sporadic vestibular schwannoma.

Desired Result: In patients undergoing a Threshold Observation approach where some growth during observation is tolerated, practitioners would be able to stratify those patients with greatest risk of future growth or requiring definitive management with either radiosurgery or microsurgery.

Level of Evidence – IV

Indicate IRB or IACUC: IRB approval was obtained from each participating center before data collection (IRB numbers 15-008224, 112016-040, and S13-00063, respectively).

Limitations of Linear Tumor Measurement in Vestibular Schwannoma

Michael H. Freeman, MD; Nathan R. Lindquist, MD
Robert J. Dambrino IV, MD; Nathan D. Cass, MD
Peter J. Morone, MD; Kareem O. Tawfik, MD

Objective: Characterize the relationship between tumor length and tumor volume in vestibular schwannomas (VS) to better understand the role of volumetric analysis.

Study Design: Retrospective review

Setting: Single tertiary care center from 2000-2020

Patients: 382 patients with diagnosis of VS undergoing a total of 652 MRIs

Interventions: Imaging analysis including volumetric segmentation

Main Outcome Measures: VS length, VS volume

Results: Mean tumor length was 2.3cm with a mean volume of 4.3cm^3. The variability of tumor volumes as a function of length increased exponentially as tumor size increased. For tumors greater than or equal to 2 centimeters in maximal linear dimension, the variance in volume was as much as 300% for equivalently long tumors. Tumor volumes increased at about half the rate expected for a spheroid object based on tumor maximal length (slope ratio 0.44, $p<0.01$).

Conclusions: Although VS are spheroid, their most obvious linear dimension, maximal length, is a poor surrogate for tumor volume. This is especially true in larger tumors – as tumor length increases, variability in actual tumor size as measured by volume increases accordingly. In larger tumors, volumetric analysis should be employed to ensure accurate analysis of tumor growth.

Professional Practice Gap & Educational Need: A number of measuring schemes have been utilized in an attempt to standardize the measurement of VS. These typically rely on linear dimensions. Accurate measurements of tumor size are important, as management paradigms often center around observation of nongrowing tumors. Volumetric analysis has been popularized in the evaluation of other tumors, and the role for volumetric analysis in monitoring VS is developing.

Learning Objective: To understand that tumor length is a relatively poor predictor of tumor volume, especially in larger tumors.

Desired Result: Attendees will: (1) Understand the relationship between VS length and volume; and (2) Appreciate the limitations of linear measurement and role for volumetric analysis in surveillance of VS.

Level of Evidence – Level V

Indicate IRB or IACUC : VUMC IRB #220712

Contribution of Endoplasmic Reticulum Stress to Noise-induced Hearing Loss in the Mouse Cochlea

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Alicia M. Frank, MPPM; Abigail Sanders BS
Christopher L. Cunningham, PhD
**These authors contributed equally*

Hypothesis: Endoplasmic reticulum stress (ERS) and the unfolded protein response (UPR) contribute to noise-induced cochlear pathology.

Background: Noise exposure is the most common cause of acquired hearing loss and can lead to temporary and permanent hearing threshold shifts termed noise-induced hearing loss (NIHL). Recent work has implicated ERS/UPR in NIHL, but little is known about cochlear ERS/UPR. Furthermore, the molecular details of cochlear ERS/UPR in NIHL are unclear. This project examined the dynamics of cochlear ERS/UPR-linked RNA and protein expression after pathologic noise exposure.

Methods: Awake 8-week-old C57BL/6 mice were exposed to 105dB noise (8-16 kHZ) for 2 hours. Auditory brainstem responses (ABRs) were obtained 1 day prior and 1, 7, and 14 days post treatment. At each time point, cochleae from noise-exposed and sham mice were extracted and processed to examine cell-type-specific ERS/UPR protein dynamics with immunohistochemistry and cochlea-wide and cell-type-specific ERS/UPR RNA dynamics with quantitative PCR and fluorescent in situ hybridization respectively.

Results: Noise exposures at 105 dB led to temporary and permanent shifts in ABR thresholds. RNA expression of multiple canonical ERS/UPR genes were dynamically altered cochlea-wide, while others were unchanged. Major cochlear cell types expressed distinct subsets of ERS/UPR genes and unique responses to noise exposure.

Conclusions: We characterized cochlear ERS/UPR-associated RNA and protein expression dynamics associated with NIHL. We identified subsets of ERS/UPR-associated genes that exhibit altered expression after noise exposure, supporting the hypothesis that ERS/UPR contribute to the cochlear response in NIHL. Future experiments will examine whether genetic or pharmacological manipulation of key cochlear ERS/UPR molecules has potential to mitigate NIHL.

Professional Practice Gap & Educational Need: Noise exposure commonly encountered in occupational and recreational settings can lead to temporary and permanent hearing threshold shifts due to myriad cellular effects in the cochlea, called noise-induced hearing loss (NIHL). There are no biological treatments to prevent or mitigate NIHL.

Learning Objective: Understanding the contribution of ERS/UPR to noise-induced cochlear pathology

Desired Result: Uncovering molecular ERS/UPR cochlear targets to prevent or mitigate NIHL

Level of Evidence – Level III

Indicate IRB or IACUC : University of Pittsburgh IACUC Protocol# 21049152

Use of Observational Camera in Rotary Chair Test for Young Children: Clinical Experience and Outcomes

Guangwei Zhou, ScD; Stephanie Walsh, BA; Jacob Brodsky, MD

Objective: To explore the usefulness of observational camera during rotary chair testing for young children when video-goggles can't be used.

Study Design: Retrospective cohort study.

Setting: Tertiary referral center.

Patients: Young pediatric patients (≤3 years) with suspected vestibular impairment.

Interventions: Rotary chair test was conducted using observational camera vs binaural video goggles to determine the functional status of vestibulo-ocular reflex (VOR).

Main Outcome Measures: Normal vs abnormal results of rotary chair test

Results: A total of 221 young children, averaged age = 1.8 years (SD = 0.8) underwent rotary chair test. Overall, 129 patients (58%) had abnormal VOR outcome. Observational camera was used in 196 patients and 105 of them (54%) had abnormal VOR findings. In comparison, 24 of 28 patients (86%) who were able to wear video goggles for rotary chair test had abnormal VOR findings. Probable causes of abnormal VOR included inner ear malformations, infection diseases and genetic mutations, etc. There were 33 patients who returned for follow-up testing and 28 of them had no change in their VOR responses, including 5 patients who underwent the second rotary chair test using video goggles.

Conclusions: Observational camera is useful for young children who needs assessment of VOR function when video-goggles is not an option. The outcomes of VOR obtained by this method seem reliable and consistent. Although clinical protocol may be needed to establish initially, experienced clinicians can interpret the VOR responses accurately base on recorded video clips, which can be replayed off-line for analysis and training.

Professional Practice Gap & Educational Need: Due to practical reasons, rotary chair test for young children ≤ 3 years is unavailable in most of vestibular specialty clinics. Lack of published study on this subject should be addressed. Providers of vestibular services should recognize the importance of early diagnosis of VOR loss in young children.

Learning Objective: To demonstrate the value of observational camera as an alternative method during rotary chair testing for young children.

Desired Result: Recognition of observational camera in rotary chair test being effective in identification of VOR loss among young children.

Level of Evidence - Level IV

Indicate IRB or IACUC : IRB of Boston Children's Hospital (#P00005505 and #P00014654).

Nortriptyline *vs.* Migraine Lifestyle Modifications on Vestibular Migraine

Karen Tawk, MD; Joshua K. Kim, BS; Abdula Al-Seraji, BS
Khodayar Goshtasbi, MD; Mehdi Abouzari, MD, PhD; Hamid R. Djalilian, MD

Objective: To compare the effectiveness of nortriptyline regimen *vs.* migraine dietary/lifestyle modifications on symptoms of dizziness and stress level in patients diagnosed with vestibular migraine.

Methods: Thirty-five patients diagnosed with definite vestibular migraine based on the International Classification of Headache Disorders (ICHD-3) were enrolled. The patients received either a nortriptyline regimen alone without instruction on lifestyle/dietary changes (escalating dosage starting at 10 mg to 40 mg daily) (Group A, n=17) or migraine dietary/lifestyle modifications (Group B, n=18). Group B patients were instructed to avoid starvation and certain food triggers, stay hydrated, get regular sleep, and were asked to take vitamin B2 and magnesium supplements. The primary outcomes were the severity of dizziness and the stress level measured by the visual analog scale (VAS).

Results: The mean age was 54.7±8.7 and 62.3±17.6 (p=0.11) and 58% and 72% were women (p=0.42) in groups A and B, respectively. At 4-week point post treatment, the VAS score for dizziness decreased from 6.0±2.5 to 4.2±3.4 (p=0.069) and from 8.7±1.5 to 3.6±3.0 (p<0.001) and the VAS score for stress decreased from 5.5±1.3 to 5.4±2.9 (p=0.93) and from 6.9±3.2 to 5.0±2.7 (p=0.025) in groups A and B, respectively. The δ value (i.e., pre-treatment minus post-treatment) of the VAS score for dizziness was 1.8±3.7 and 5.1±3.1 (p=0.008) and the δ value of the VAS score for stress was 0.06±2.9 and 1.9±3.3 (p=0.09) in groups A and B, respectively. Quality of life improved in 15 (88%) patients in group A and 17 (94%) patients in group B (p=0.53).

Conclusions: This study suggests that nortriptyline alone, while helpful in alleviating the patients' symptoms is less effective than migraine diet and lifestyle modifications in treating vertiginous symptoms and reducing the stress level in vestibular migraine patients. However, both interventions are equally effective in ameliorating the quality of life of patients.

REQUIRED:
Define Professional Practice Gap & Educational Need: The pathophysiology and management of vestibular migraine have remained subject of debate. Further investigation into discovering new and improved management solutions for better treating vestibular migraine has been called. For this reason, a need to educate otolaryngologists on appropriate pharmacological and non-pharmacological treatments for vestibular migraine is warranted.

Learning Objective: To propose a treatment option in vestibular migraine patients to ANS members which can relate this entity with other complex disorders such as migraine. This can help in creating an improved treatment algorithm using our results, as well as results from other clinical trials of high quality.

Desired Result: Informing neurotologists of a possible effective treatment option in patients with vestibular migraine.

Level of Evidence - III

Indicate IRB or IACUC: The study has IRB approval from UC Irvine under the PI name of Hamid R. Djalilian.

The Natural History of Observed *Sdhx*-Related Head and Neck Paragangliomas Using 3D Volumetric Tumor Analysis

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Anne Naumer, MS; Luke O. Buchmann, MD
Samantha E. Greenberg, MS; Neil S. Patel, MD

Objective: Characterize the natural history and clinical behavior of head and neck paragangliomas (HNPGL) in patients with *SDHx* pathogenic variants (PV) using volumetric tumor measurements.

Study Design: Using a prospectively maintained database of individuals with *SDHx* PV HNPGL, a retrospective review of all patients with serial (≥2) imaging (MRI or CT) between 2004 and 2022 was performed. Age at diagnosis, sex, laterality, type of tumor, *SDHx* PV, clinical symptoms at time of diagnosis, clinical symptoms that developed during period of observation, type of treatment, and cranial nerve (CN) outcome data were obtained. Serial tumor MRI and CT volumes were generated using a slice-by-slice, non-interpolative method and reviewed by a senior neuroradiologist.

Setting: Tertiary referral academic medical center.

Patients: Individuals aged 13-75 years with confirmed *SDHx* PV HNPGL tumors and serial (≥2) imaging (MRI or CT) between 2004 and 2022 were included.

Interventions: Diagnostic interventions included next generation sequencing (NGS), MRI, and CT imaging. Tumors were treated using microsurgical resection, stereotactic radiosurgery (SRS), or multimodality therapy.

Main Outcome Measures: Radiographic progression and rapid radiographic progression were defined as a ≥15% and ≥50% increase in volume, respectively. Cranial nerve functional outcomes were assessed using clinical documentation of facial, laryngeal, tongue, and shoulder function.

Results: Thirty-two HNPGL comprising carotid body tumor (CBT) (n=17), vagal paraganglioma (VP) (n=10), and jugular paraganglioma (JP) (n=5) were radiographically observed for a median duration of 2.08 years, 2.58 years, and 0.75 years, respectively. The median volumetric increase per year was 15% for CBT, 21% for VP, and 44% for JP. Kaplan-Meier estimated rates of survival free of radiographic progression (n= number still at risk) at 1, 2, and 3 years were as follows: CBT (93%, n=14; 62%, n=7; 31%, n=5), VP (89%, n=8; 78%, n=7; 33%, n=3), and JP (60%, n=2; 60%, n=2; 30%, n=1). Survival free of rapid (≥50%) radiographic progression at 1, 2, and 3 years were as follows: CBT (100%, n=14; 83%, n=9; 50%, n=5), VP (100%, n=8; 100%, n=7; 57%, n=3), and JP (100%, n=2; 100%, n=2; 50%, n=1). Among HNPGLs, 12% (n=2) of CBT, 30% (n=3) VP, and 80% (n=4) of JP presented with tumor related symptoms at the time of diagnosis. No tumors developed new CN palsies during the period of observation. No CBT or VP became symptomatic during observation while 40% (n=2) of JP developed new symptoms, prompting intervention. No CBT or JP developed iatrogenic CN deficits while 40% (n=4) of VP developed vagal neuropathy, of which 3 were permanent.

Conclusions: This is the first study to characterize the natural history of observed *SDHx*-related HNPGLs. Over short to intermediate term follow up, observation did not result in new cranial neuropathy, even when including tumors that grew rapidly during the interval. Expectedly, VP had the highest rates of iatrogenic lower cranial nerve palsy, suggesting that the decision to intervene should be primarily based on CN status and not necessarily growth rate. Patients with observed JP that underwent intentional subtotal resection did not suffer a new lower CN palsy. Given the rate of multicentricity of *SDHx*-related HNPGLs, these data may aid in determining the optimal treatment strategy for cranial nerve functional preservation.

Professional Practice Gap & Educational Need: At present, the natural history of head and neck paragangliomas as it relates to cranial nerve involvement, development of new symptoms, and tumor growth remains unknown.

Learning Objective: Understand the natural history of observed *SDHx*-related head and neck paragangliomas

Desired Result: Characterize the natural history of observed *SDHx*-related head and neck paragangliomas

Level of Evidence – Level V **Indicate IRB or IACUC:** Approved

The Role of Lumbar Drains in the Perioperative Management of Primary Spontaneous Temporal Lobe Encephaloceles and Cerebrospinal Fluid Leaks

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Objective: To determine the role of postoperative lumbar drains (LDs) in managing spontaneous temporal bone cerebrospinal fluid (CSF) leaks.

Study Design: Retrospective cohort study.

Setting: Tertiary neurotology practice.

Patients: Those with primary spontaneous temporal encephaloceles and CSF leaks undergoing surgical correction.

Interventions: Transmastoid (TM), middle fossa craniotomy (MFC), or combined approach with or without perioperative LD.

Main Outcome Measures: Complication rate, ICU stay, length of stay (LOS), readmission, treatment failure.

Results: 62 patients were identified between 2017-2022, with mean age 58.7 years and mean BMI 33.4. Bony defect width was a mean 6.29mm on coronal CT. Mean follow-up was 10.5 months. TM/MFC approach was used in 79.0%, TM alone in 19.4%, and isolated MFC in 1.6%. The most common reconstructive grafts were fat (77.4%), temporalis fascia (93.5%), split calvarial bone (21.0%), and cartilage (45.2%). Overall complication rate was 14.5%, and the treatment failure rate was 4.8%. A lumbar drain was placed in 71.0% and when present, was kept for a median of 2.0 days. Length of stay (LOS) was significantly longer for those with a LD (mean 3.4 versus 1.6 days, p=.005). Presence of a LD was associated with higher ICU admission rates amongst TM/MCF and MCF patients (p=.020) but not physical therapy needs or rates of readmission, overall complications, or treatment failures (p=.470). There was no correlation between bony defect size, age, graft type, or BMI and placement of LD.

Conclusions: LD placement is associated with higher LOS without lower treatment failure rates.

Professional Practice Gap & Educational Need: To recognize the role of lumbar drains in the perioperative management of patients with temporal encephaloceles and spontaneous CSF leaks.

Learning Objective: To critically examine the factors that go into LD placement and whether perioperative LD affect patient outcomes for this indication.

Desired Result: To show a significant or non-significant difference in the rates of treatment failure, complications, or admission-level variables as they relate to LD placement.

Level of Evidence - IV

Indicate IRB or IACUC : Icahn School of Medicine at Mount Sinai, #21-01768

NICHOLAS TOROK VESTIBULAR AWARD

Mindfulness-Based Stress Reduction for the Treatment of Vestibular Migraine: A Prospective Trial

Eric J. Formeister, MD, MS; James Mitchell, PhD
Roseanne Krauter, FN-P; Ricky Chae, BS; Adam Gardi, BS
Maxwell Hum, BS; Jeffrey D. Sharon, MD

Objective: To describe the implementation and efficacy of mindfulness based stress reduction (MBSR) therapy for treating dizziness symptoms in subjects with vestibular migraine (VM).

Study Design: Prospective cohort study.

Setting: Tertiary referral center; virtual platform for guided MBSR classes.

Patients: Twenty adult, English-speaking patients with a diagnosis of VM.

Interventions: Subjects participated in an eight-week long virtual MBSR course with required reading materials and weekly, 2.5 hour guided meditation and instructional sessions.

Main Outcome Measures: Pre- and post-MBSR scores on the Dizziness Handicap Index (DHI), Cognitive Failures Questionnaire (CFQ), Patient Health Questionnaire-9 (PHQ-9), General Anxiety Disorder-7 (GAD-7), VM Patient Assessment Tool and Handicap Inventory (VM-PATHI), Patient Reported Outcome Measure Information System (PROMIS) Global Physical and Mental Health Forms, and daily vertigo severity scores.

Results: Twenty participants (100.0% female, 70.0% White; avg. age, 46.7 years) completed the study. The DHI, CFQ, PHQ-9, GAD-7, VM-PATHI, and PROMIS scores all improved significantly after MBSR treatment compared to prior to treatment (all questionnaires, $p<0.01$ except for CFQ ($p=0.02$)). Mean daily vertigo scores did not change significantly over time in the 24 day lead-in period (adjusted $r^2 = 0.03$; $p=0.54$) but decreased significantly over the 8 week MBSR treatment period (adjusted $r^2 = 0.32$, $p<0.001$).

Conclusions: In this prospective pilot study, MBSR was highly effective for decreasing dizziness burden and improving measures of quality of life in subjects with VM. Future randomized controlled trials are warranted and forthcoming.

Professional Practice Gap & Educational Need:

Despite being the second most common cause of dizziness in the U.S., the data surrounding treatment for vestibular migraine (VM) is lacking. In particular, treatments are borrowed by analogy from treating migraine headaches, and all carry substantial side effects that lead to a high rate of medication non-adherence. Those with VM might have symptoms attributable to catastrophization, a concept that can be broken through time-honored mindfulness based stress reduction and medication techniques. More research is needed to investigate non-pharmacologic treatment option for vestibular migraineurs.

Learning Objective:

To discuss the efficacy of non-pharmacologic, mindfulness based stress reduction and meditation techniques for treating dizziness symptoms in patients with VM.

Desired Result:

At the end of this presentation, the participant will learn 1) about the techniques of mindfulness-based stress reduction, and 2) how application can effectively reduce dizziness burden and improve quality of life metrics for patients with VM.

Level of Evidence: Level III.

Indicate IRB or IACUC : This study was approved by the University of California – San Francisco's Institutional Review Board (IRB #18-25365).