PROGRAM, ABSTRACTS and MORE

One Hundred Fifty Seventh Annual Meeting

of the

AMERICAN OTOLOGICAL SOCIETY

May 17-18, 2024
Hyatt Regency
Chicago, IL

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AMERICAN OTOLOGICAL SOCIETY

MISSION STATEMENT

Purpose
The American Otological Society, created in 1868, is dedicated to fostering a dialogue on and dissemination of, information pertaining to advances in evidence based diagnosis and management of otologic and neurotologic disorders. The focus on otologic and neurotologic disorders and scientific advances are translated to the provision of quality care that is consistent with the ACGME general competency areas and the Institute of Medicine competencies.

Target Audience
The primary target audience for the educational efforts of the American Otological Society is the current and potential members of the society. These members are physicians, physicians-in-training, audiologists and researchers in the fields of otology and neurotology. Educational activities are also open to other healthcare professionals who are involved in the care of patients with otologic and neurotologic conditions.

Activities
The primary activity of the American Otological Society is the Annual Meeting that focuses on the advancement of the scientific and clinical evidence that supports advances in otologic and neurotologic care to patients. Additionally, non certified educational support and resources include the publication and dissemination of peer reviewed and evidence-based content through *Otology & Neurotology* Journal and support for research in otology/neurotology and lateral skull base surgery and related disciplines.

Content
The content for the Annual Meeting and other related educational efforts are focused on otologic and neurotologic evidence based science, clinical standards of care, effects on communication, and other topics to the specialty.

Expected Results
The expected results are focused on enhancing knowledge translation and promoting competence for the membership and other identified target audiences. The Annual Meeting, the CME certified annual activity of the society, and the other scholarly activities such as the publication of the Journal and support for research provide a rich and robust environment for self assessment and reflection, access to resources for lifelong learning and opportunities for discussion and re-evaluation.

Resolution on Diversity of Meeting Presenters and Participation for the American Otological Society and the American Neurotology Society

- Whereas the councils of the American Neurotology Society and American Otological Society desire to promote inclusivity within the membership of both organizations.

- Whereas it is recognized that diverse leadership and diversity of presenters allows for cross pollination of knowledge, perspective and experiences enabling a stronger and more robust educational experience for our members.

- Whereas the Councils of the organizations recognize the importance of acknowledging diversity among our patients, our trainees, and our colleagues.

- Whereas the purpose of the education programs of both organizations is to disseminate information designed to improve physician knowledge, patient care and outcomes, and advance the respective specialties.

- Whereas valuable scientific contributions to Otology and Neurotology by colleagues (regardless of gender, race, or other attributes) should be presented at the society's respective meetings.

- Be it resolved that the Scientific Program Committees of the American Neurotology Society and American Otological Society will select speakers and panel members endeavoring to balance educational goals while promoting the diversity of our respective Societies' memberships and educational offerings.

- Be it resolved the Executive Councils of the ANS and AOS will select participation at all levels of the organizations endeavoring to reflect diversity of our respective Societies' memberships.

CONTINUING MEDICAL EDUCATION CREDIT INFORMATION

CONTINUING MEDICAL EDUCATION CREDIT INFORMATION

Accreditation

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of American College of Surgeons and American Otological Society. The American College of Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

AMA PRA Category 1 Credits™

The American College of Surgeons designates this live activity for a maximum of 9.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACS AMERICAN COLLEGE OF SURGEONS

ACCME ACCREDITED WITH COMMENDATION

ADDITIONAL CME INFORMATION

Award of CME credits by ACS is based on compliance of the program with the ACCME accreditation requirements and does not imply endorsement by ACS of the content, the faculty, or the sponsor of the program.

AND

Successful completion of this CME activity, which includes participation in the evaluation component, enables the learner to earn credit toward the CME of the American Board of Surgery's Continuous Certification program.

Program Objectives Educational Activity Details

What are the practice or patient care problems being addressed by this activity?

1. Intraoperative injury to cochlear and vestibular nerves
2. Chronic ear disease management
3. Diagnosis and management of congenital CMV
4. Prevention of inner ear damage by ototoxic substances and noise
5. Sudden sensorineural hearing loss
6. Dizziness
7. Disease of the external ear
8. Auditory implant surgery and outcomes

Why do these issues exist? Is there a deficit in provider's knowledge or skill? Is there a deficit in health care system process or outcomes?
Deficiency of knowledge of new advances including emerging surgical technologies, diagnostic tests, new drugs and advances in imaging. Deficiency of knowledge of new applications of currently available treatments for otologic disease

How will this activity improve the learners' competence (knowledge in action), performance (skill set) and/or patient outcomes (impact of care)?

- **Competence**:
  Increased knowledge of fluorescein labeling to improve intraoperative visualization.
  Increased knowledge of MRI techniques to diagnose cholesteatoma.
  Increased knowledge of current and emerging approaches to otoprotection and tinnitus.
  Increased knowledge of otologic problems including sudden SNHL, dizziness, external ear diseases.
  Increased understanding of congenital CMV diagnosis and its impact on children and families.
- **Performance**:
  Knowledge gained will improve patient counseling which will improve compliance and satisfaction with recommended interventions.
- **Patient Outcomes**:
  Knowledge gained from this educational activity will improve diagnosis and treatment of otologic disorders and therefore patient outcome.

How do you anticipate this activity improving health care systems?
The knowledge provided will increase the ability of physicians and surgeons to engage patients and health systems about the importance of otologic diseases as well as provide effective means of addressing hearing loss and dizziness to improve public health.
If applicable, **how do you anticipate this activity impacting the health of patients and their communities?**
An understanding of otological health care disparities will identify those areas within underserved communities that require medical attention.
State the learning objectives for this activity:

1. Discuss the advantages of newborn testing for congenital CMV.
2. Describe the use and purpose of fluorescein during otologic surgery.
3. Evaluate dizziness and discuss role of mental health specialist in management.
4. Discuss emerging treatments for tinnitus, sudden sensorineural hearing loss and otoprotection.
5. Interpret MRI scans to diagnose cholesteatoma.
6. Recognize diseases of the external ear.
7. Discuss chronic ear disease management.

Explain why the selected educational format(s) is considered appropriate for the setting, objectives and desired results of this activity.

This program's educational formats have been successful in the past in achieving similar education objectives in similar settings based upon survey acquired feedback from attendees.

DISCLOSURE INFORMATION

In accordance with the ACCME Accreditation Criteria, the American College of Surgeons must ensure that anyone in a position to control the content of the educational activity (planners and speakers/authors/discussants/moderators) has disclosed all financial relationships with any commercial interest (termed by the ACCME as "ineligible companies", defined below) held in the last 24 months (see below for definitions). Please note that first authors were required to collect and submit disclosure information on behalf of all other authors/contributors, if applicable.

Ineligible Company: The ACCME defines an "ineligible company" as any entity producing, marketing, re-selling, or distributing health care goods or services used on or consumed by patients. Providers of clinical services directly to patients are NOT included in this definition.
Financial Relationships: Relationships in which the individual benefits by receiving a salary, royalty, intellectual property rights, consulting fee, honoraria, ownership interest (e.g., stocks, stock options or other ownership interest, excluding diversified mutual funds), or other financial benefit. Financial benefits are usually associated with roles such as employment, management position, independent contractor (including contracted research), consulting, speaking and teaching, membership on advisory committees or review panels, board membership, and other activities from which remuneration is received, or expected.
Conflict of Interest: Circumstances create a conflict of interest when an individual has an opportunity to affect CME content about products or services of a ineligible company with which he/she has a financial relationship.

The ACCME also requires that ACS manage any reported conflict and eliminate the potential for bias during the educational activity. Any conflicts noted below have been managed to our satisfaction. The disclosure information is intended to identify any commercial relationships and allow learners to form their own judgments. However, if you perceive a bias during the educational activity, please report it on the evaluation.

Disclosure Information
In accordance with the ACCME Accreditation Criteria, the American College of Surgeons must ensure that anyone in a position to control the content of the educational activity (planners and speakers/authors/discussants/moderators) has disclosed all financial relationships with any ineligible company held in the last 24 months. Please note that first authors were required to collect and submit disclosure information on behalf all other authors/contributors, if applicable.

A complete list of disclosures is available at the AOS registration table.

THE AMERICAN OTOLOGICAL SOCIETY WOULD LIKE TO THANK THE FOLLOWING MEMBERS FOR THEIR CONTRIBUTION TO THE 2024 AOS SCIENTIFIC PROGRAM

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OTOLOGY & NEUROTOLOGY JOURNAL REQUIREMENTS

Publication Statement: The material in this abstract must not have been published or presented previously at another national or international meeting and may not be under consideration for presentation at another national or international meeting including another COSM society. The study detailed in this abstract *may be submitted* for consideration for publication to *Otology & Neurotology* at any time after this call for papers begins. However, should the abstract be selected as a poster or an oral presentation, publication of the manuscript will be delayed until after the 2024 COSM meeting takes place. If this policy is violated, the AOS will prohibit presentation at the COSM meeting and the manuscript will be withdrawn from publication in print or online. The penalty for any duplicate presentation/publication is prohibition of the author from presenting at a COSM society meeting for up to three years. **Duplicate submission to ANS or another participating COSM Society will disqualify your abstract immediately.**

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Manuscripts are required of ALL ORAL presentations. Manuscripts must be submitted online a minimum of four weeks prior to the annual meeting, via the journal's website. Instructions for registering, submitting a manuscript, and the author guidelines can be found on the Editorial Manager site: https://www.editorialmanager.com/on/

The Journals of *OTOLOGY & NEUROTOLOGY* or *ONO (O&N OPEN)* do not accept paper manuscripts. Manuscripts are reviewed prior to the Annual meeting for conflict of interest and resolution.

Failure to comply with the guidelines & requirements of the American Otological Society and the O&N Journal will result in the disqualification of your presentation.

FUTURE MEETING DATES

ANS 59th Annual Fall Meeting
"FAB FRIDAY"
Friday, September 27, 2024
Fontainebleau Miami Beach

The Abstract deadline for the AOS 158th Annual meeting is Tuesday, October 15, 2024.
Abstract Instructions and the submission form will be available on the AOS website September 1st.
Website - www.americanotologicalsociety.org

AOS 158th Annual Meeting
May 16-18, 2025
Hyatt Regency New Orleans
New Orleans, Louisiana

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AMERICAN OTOLOGICAL SOCIETY
PROGRAM
157th Annual Meeting
May 17-18, 2024
Chicago, IL

FRIDAY, MAY 17, 2024

1:00 BUSINESS MEETING and **NEW MEMBER INTRODUCTION**
(Open to registered Members and Non-members - Badge required for admittance)

1:25 SCIENTIFIC PROGRAM

1:25 WELCOME & OPENING REMARKS BY THE PRESIDENT
Sujana S. Chandrasekhar, MD

1:27 PRESIDENTIAL CITATIONS
Karen Jo Enright, MD, PhD
Derald E. Brackmann, MD
Lisa Bell, AuD, CCC-A
Debara L. Tucci, MD, MS, MBA
Aziz Belal, MD

1:37 INTRODUCTION OF GUEST OF HONOR
Sujana S. Chandrasekhar, MD

1:39 GUEST OF HONOR LECTURE
Choices, Challenges and Opportunities in Auditory Implantation Surgery
Emma Stapleton, MBChB, FRCS (ORL-HNS), MFSTEd
Consultant Otolaryngologist and Auditory Implant Surgeon
Manchester Royal Infirmary, UK

2:14 Q&A

2:19 SESSION A - Basic and Applied Otologic Science
David R. Friedland, MD, PhD, Moderator - AOS Secretary/Treasurer

2:20 PODIUM PRESENTATIONS - Of Mice and Men
Joni K. Doherty, MD, PhD & Kenneth H. Lee, MD, PhD, Moderators

2:21 Deep Phenotyping of a Mouse Model for Hearing Instability Disorders
J. Dixon Johns, MD
Samuel Adadey, PhD
Rafal Olszewski, PhD
Michael Hoa, MD

2:27 Inositol trisphosphate (IP3) and Ryanodine receptor (RyR) Signaling Are Essential and Have Distinct Roles in Regulating Neurite Pathfinding in Response to Micropatterned Growth Cues
Joseph T. Vecchi
Madeline Rhomberg
C. Allan Guymon, PhD
Marlan R. Hansen, MD

2:33 Western Blot Characterization of Human Serum Prestin, an Outer Hair Cell Biomarker
Heather M. McClure, BS
Mohsin Mirza, BS
Patrick Adamczyk, BS
Ashley Parker, PhD
Erika Skoe, PhD
Kourosh Parham, MD, PhD

2:39 Otoprotection and Effects on Cochlear Synaptopathy by Angiotensin Receptor Blockade in a Murine Model of Noise Induced Hearing Loss
Peter Eckard
Tanner Kempton
Carolina Chu
Rhong Zhuo Hua
Bryce Hunger
Miles J. Klimara, MD
Marlan R. Hansen, MD
Douglas M. Bennion, MD, PhD

2:45 Q&A

2:49 EXPERT PRESENTATION
Introduction by Moderator, Michael J. Ruckenstein, MD, MSc
Fluorescence Imaging of Cochlear and Vestibular Nerves during Surgery
Quyen Nguyen, MD, PhD

3:00 DISCUSSION with MODERATOR and Q&A

3:05 BREAK WITH EXHIBITORS

3:30 SESSION B - Otologic Public Health and Chronic Ear Disease
Nikolas H. Blevins, MD, Moderator - AOS Council Member-At-Large

3:31 ANNOUNCEMENT OF AOS and ANS POSTER PRESENTATION WINNERS
Yuri Agrawal, MD - ANS Education Director
Nancy Young, MD - AOS Education Director

3:33 PODIUM PRESENTATIONS - Systemic & Systematic Factors and The Ear
Sharon L. Cushing, MD, MSc & James E. Saunders, MD, Moderators

3:34 Effects of Smoking on Acute Postoperative Outcomes in Otologic Surgery
Pablo Llerena, BS
Bryce Hambach, BS
Kathryn Nunes, BA
Joseph Lu, BS
Praneet Kaki, BS
Jena Patel, MD
Jacob B. Hunter, MD

3:40 Statins and Their Effect on Hearing: An All of Us Database Study
Benjamin J. Homer, ScB
Rishubh Jain, AB
Alexander S. Homer, AB
Viknesh S. Kasthuri, AB
Emily Gall, MD
Kathryn Y. Noonan, MD

3:46 Blast Exposure, Tinnitus, Hearing Loss, and Post-Deployment Quality of Life in U.S. Veterans: Longitudinal Analysis
Hoda AO. Mohammed, MPH
Charlotte K. Hughes, MD (presenter)
Kelly M. Reavis, PhD, MPH
Samrita Thapa, MPH
Emily Thielman, MS
Wendy Helt, MA
Kathleen F. Carlson, PhD, MPH

3:52 Analysis of Adherence to AAO-HNSF Clinical Practice Guidelines for Sudden Hearing Loss
Bao Y. Sciscent, BS
F. Jeffrey Lorenz, MD
Hanel W. Eberly, BS
Andrew Rothka, BS
Mark E. Whitaker, MD
Neerav Goyal, MD, MPH

3:58 Contemporary, Individual and Community-Level Social Determinant Associations with Acoustic Neuroma Disparities in the US
David J. Fei-Zhang, BA
Rishabh Sethia, MD
Cyrus W. Abrahamson, BA
Daniel C. Chelius, MD
Jill N. D'Souza, MD
Anthony M. Sheyn, MD
Jeffrey C. Rastatter, MD, MS

4:04 Q&A

4:09 EXPERT PRESENTATION
Introduction by Moderator, John Greinwald, MD
Congenital Cytomegalovirus: Science and Social Policy
Stephanie A. Moody-Antonio, MD

4:20 DISCUSSION with MODERATOR and Q&A

4:25 PANEL
Chronic Ear Disease: How do we Improve Outcomes?
Dennis S. Poe, MD, PhD, Moderator - AOS Council Member-At-Large
Maura E. Ryan, MD
Aaron K. Remenschneider, MD, MPH
Michael Hoa, MD

5:10 CLOSING REMARKS/ADJOURNMENT
Sujana S. Chandrasekhar, MD

5:20 AOS MEMBER PHOTOGRAPH

5:30 MEET THE AUTHORS POSTER RECEPTION
AOS, ANS, ABEA, ALA, TRIO, ASPO

6:00 WIN (WOMEN IN NEUROTOLOGY) RECEPTION

SATURDAY, MAY 18, 2024

7:00 BUSINESS MEETING *including Committee Reports and launch of AOS Development Plan*
(All welcome – Coffee, tea and continental breakfast for all registered AOS attendees)

7:30 SCIENTIFIC PROGRAM
(Open to registered Members and Non-members – Badge required for admittance)

7:30 WELCOME & OPENING REMARKS BY THE PRESIDENT
Sujana S. Chandrasekhar, MD

7:31 SESSION C - Cochlear Implants and Inner Ear Biology
Nancy M. Young, MD, Moderator - AOS Education Director

7:32 PODIUM PRESENTATIONS - COCHLEAR IMPLANTS
Christina L. Runge, PhD & Abraham Jacob, MD, Moderators

ADULT COCHLEAR IMPLANTS

7:33 Early Use of Computer-based Auditory Training Yields Greater Speech Recognition and Quality-of- life Benefits in New Adult Cochlear Implant Recipients
James R. Dornhoffer, MD
Christian Shannon, BS
Kara C. Schvartz-Leyzac, AuD, PhD

Judy R. Dubno, PhD
Theodore R. McRackan, MD, MSCR

7:39 Preoperative Factors Predicting Electroacoustic Stimulation Usage in Adults following Cochlear Implantation
Ankita Patro, MD, MS
Connie Ma, MD
Natalie Schauwecker, MD
Nathan R. Lindquist, MD
Michael H. Freeman, MD
David S. Haynes, MD, MMHC
Elizabeth L. Perkins, MD

7:45 Impact of Implantable Hearing Devices on Delirium Risk in Patients with Hearing Loss: A National Database Study
Bryce Hambach, BS
Elliott M. Sina, BA
Kathryn Nunez, BS
Jena Patel, MD
Jacob B. Hunter, MD

7:51 Q&A

PEDIATRIC COCHLEAR IMPLANTS

7:54 Early Auditory Development of Cochlear Implanted Children with Sensorineural Hearing Loss following Congenital CMV Infection
Piotr H. Skarzynski, Prof
Anita Obrycka, PhD
Aleksandra Kolodziejak, MSc
Elzbieta Gos, PhD
Rita Zdanowicz, MSc
Artur Lorens, Prof
Henryk Skarzynski, Prof

8:00 Cochlear Implantation (CI) Outcomes in Children Under 5 Years of Age with Single-Sided Deafness (SSD): A Systematic Review and Meta-analysis
Corinne Pittman, MD
Nadia Samaha, BS
Myra Zaheer, BA
Luke Llaurado, BA
Xue Geng, MS
Michael Hoa, MD

8:06 A Systematic Review and Meta-Analysis Examining Outcomes of Cochlear Implantation in Children with Bilateral Cochlear Nerve Deficiency
Jay Maturi, BS
Kimberley S. Noij, MD, PhD

Vidya Babu, BS
Carolyn M. Jenks, MD

8:12 Q&A

8:15 EXPERT PRESENTATION
Introduction by Moderator, Hung Jeffrey Kim, MD
Getting Closer to Serene Silence: Tinnitus Update 2024
Konstantina M. Stankovic, MD, PhD

8:30 DISCUSSION with MODERATOR and Q&A

8:35 INTRODUCTION OF SAUMIL N. MERCHANT MEMORIAL LECTURE
Sujana S. Chandrasekhar, MD

8:36 SAUMIL N. MERCHANT MEMORIAL LECTURE
An Omics Path to Otoprotection
Ronna Hertzano, MD, PhD
Senior Investigator and Neurotology Branch Chief
National Institute on Deafness and Other Communication Disorders
National Institute of Health, Bethesda, MD
Adjunct Clinical Professor, Department of Otolaryngology Head and Neck Surgery
University of Maryland School of Medicine, Baltimore, MD

9:06 Q&A

9:11 SESSION D - MIDDLE EAR PATHOLOGY
Lawrence R. Lustig, MD, Moderator - AOS Immediate Past President

9:12 PODIUM PRESENTATIONS - CHRONIC OTITIS MEDIA
Darius Kohan, MD & Huseyn Isildak, MD, Moderators

9:13 Tympanic Membrane Regeneration Therapy for Pediatric Tympanic Membrane Perforation
Shin-ichiro Kita, MD
Shin-ichi Kanemaru, MD, PhD
Rie Kanai, MD
Tomoya Yamaguchi, MD
Akiko Kumazawa, MD
Ryohei Yuki, MD
Toshiki Maetani, MD, PhD

9:19 Unique Cell-Type Specific Signaling Patterns Define Cholesteatoma
Christopher M. Welch, MD, PhD
Shuze Wang, PhD
Joerg Waldhaus, PhD

9:25 The NLRP3 Inflammasome in Macrophages Causes Sensory Hearing Loss in Chronic Suppurative Otitis Media (CSOM)
Viktoria Schiel, MD, PhD
Anping Xia, MD, PhD
Ritwija Bhattacharya, PhD
Ankur Gupta, MD
Kourosh Efthekarian, MD
Peter Santa Maria, MD, PhD

9:31 RESIDENT RESEARCH TRAVEL AWARD
Outcomes after Exoscopic versus Microscopic Ossicular Chain Reconstruction
Caleb J. Fan, MD
Jacob C. Lucas, MD
Robert M. Conway, DO
Masanari G. Kato, MD
Seilesh C. Babu, MD

9:37 Q&A

9:41 BREAK WITH EXHIBITORS

10:06 SESSION E - Sudden Hearing Loss and Vestibular Disease
Michael E. Seidman, MD, Moderator

10:07 INVITED PRESENTATION
Hearing Science Accelerator – SSNHL
William H. Slattery III MD - AOS Council President-Elect
Andrea Vambutas, MD - AOS Research Advisory Board, Executive Secretary
Seth Schwartz, MD
Nicholas S. Andresen, MD

10:22 Q&A

10:25 EXPERT PRESENTATION: Dizziness, We Mean Business
Introduction by Moderator, Michael E. Seidman, MD
Seeing the Whole Patient – A Practical Approach to Detecting Functional and Psychiatric Disorders in Patients with Dizziness
Jeffrey P. Staab, MD
PPPD: Persistent Postural-Perceptual Dizziness – It's Not All in Their Head
Maja Svrakic, MD, MSEd

10:52 DISCUSSION with MODERATOR and Q&A

10:56 SESSION F - ARTIFICIAL INTELLIGENCE, MIGRAINE AND EXTERNAL EAR DISEASE
Marlan R. Hansen, MD, Moderator - AOS Past President

10:57 PODIUM PRESENTATIONS - ARTIFICIAL INTELLIGENCE AND THE BRAIN
THE TAMING OF THE SHREW?
Jack Shohet, MD, Moderator

10:58 Temporal Integration of Multisensory Stimuli in Migraine
Timothy E. Hullar, MD
Jwala Rejimon, BS
Michelle E. Hungerford, AuD
Robert J. Peterka, PhD
Angela C. Garinis, PhD
Yonghee Oh, PhD
Richard F. Lewis, MD

11:04 Artificial Intelligence for Diagnostic and Treatment Planning: Is It Ready to Be Your Doctor?
Camryn Marshall, BS
Jessica Forbes, MS
Luis Roldan, MD
Jim Atkins, MD
Michael D. Seidman, MD

11:10 RESIDENT RESEARCH TRAVEL AWARD
Artificial Intelligence Tracking of Otologic Instruments in Mastoidectomy Videos
George S. Liu, MD
Sharad Parulekar
Trishia El Chemaly, MS
Melissa C. Lee, BS
Mohamed Diop, MD
Roy Park, MD
Nikolas H. Blevins, MD

11:16 Q&A

11:20 PANEL
EarWise: Spotlight on External Ear Disease
Erika A. Woodson, MD, Moderator
Matthew B. Hanson, MD
Emma Stapleton, MBChB, FRCS (ORL-HNS)
Alan G. Micco, MD

12:00 INTRODUCTION OF INCOMING PRESIDENT
William H. Slattery, III, MD

12:03 CLOSING REMARKS/ADJOURNMENT
Sujana S. Chandrasekhar, MD

SELECTED ABSTRACTS

ORAL PRESENTATIONS

IN ORDER OF PRESENTATION

157th Annual Meeting
AMERICAN OTOLOGICAL SOCIETY

May 17-18, 2024
Hyatt Regency Chicago
Chicago, IL

Deep Phenotyping of a Mouse Model for Hearing Instability Disorders

J. Dixon Johns, MD; Samuel Adadey, PhD; Rafal Olszewski, PhD
Michael Hoa, MD

Hypothesis: Hearing instability in *Slc26a4*-insufficiency mice may be due to differential expression of genes related to ion homeostasis and activated macrophages.

Background: Hearing instability (HI) disorders, defined by either hearing fluctuation or sudden loss, remain incompletely understood. Recent studies have described a *Slc26a4* (pendrin)-insufficiency mouse model (DE17.5) that offers a genetically-driven model for HI, although deep audiometric and immunohistologic phenotyping of this model remains poorly characterized.

Methods: Homozygous DE17.5 mice with (F) and without (NF) HI were delineated by serial auditory brainstem response (ABR) between postnasal day 30 and 60 and compared to adult *Slc26a4*-heterozygous controls (Het). HI was defined as a change in threshold of at least 15dB in at least two frequencies or at least 20dB in at least one frequency from the prior week. Analysis of stria vascularis (SV) cell type-specific gene expression, endolymphatic hydrops (EH), endocochlear potential (EP), and macrophage activation was compared between the cohorts.

Results: F mice demonstrated significant reductions in the expression of cell-type specific genes related to ion homeostasis and increased macrophage activation within the SV compared to NF and Het cohorts, respectively. Both F and NF DE17.5 mice demonstrated reductions in EP and increased EH compared to the Het cohort.

Conclusions: Deep phenotyping of DE17.5 mice demonstrates changes in EP and EH compared to control, however, the HI phenotype was associated with differential ion homeostasis gene expression and increased macrophage activation in the SV. This provides potential further insights into the underlying pathogenesis and possible immunologic contributions of HI in humans.

Professional Practice Gap & Educational Need: To date, there is a lack of an animal model that adequately replicates disorders of hearing instability in humans. This study utilizes the *Slc26a4*-insufficiency mouse model (DE17.5) to perform deep phenotyping of a hearing instability cohort to investigate potential changes in audiometric and immunohistologic parameters.

Learning Objective: To 1) review current gaps in our understanding of the pathogenesis of disorders of hearing instability and 2) provide novel investigations into potential mechanisms hearing instability in a mouse model

Desired Result: This study supports the potential role of differential expression of genes related to ionic homeostasis and macrophage activation in the pathogenesis of disorders of hearing instability. Furthermore, an immunologic “second hit” may contribute to differential phenotypic expression of hearing instability within the DE17.5 cohort, although further studies are needed to elucidate this association.

Level of Evidence: III

Indicate IRB or IACUC: 1379

Inositol trisphosphate (IP3) and Ryanodine receptor (RyR) Signaling Are Essential and Have Distinct Roles in Regulating Neurite Pathfinding in Response to Micropatterned Growth Cues

Joseph T. Vecchi; Madeline Rhomberg; C. Allan Guymon, PhD
Marlan R. Hansen, MD

Hypothesis: RyR and IP3 signaling are activated by and required for spiral ganglion neurons (SGNs) to sense and pathfind in response to topographical and biochemical substrate cues.

Background: Micro-scale patterning of surface features and biochemical cues has emerged as a promising approach to direct neurite growth into close proximity with next-generation cochlear implant electrodes. However, the underlying signaling events governing the ability of growth cones to respond to these features and cues remain unclear. Increasing evidence highlights the pivotal role of Ca^{2+} signaling in growth cone sensing and response to diverse cues.

Methods: We investigated the role of IP3 and RyR signaling in cultured mouse SGNs and dorsal root ganglion neurons as they pathfind in response to wide varieties of engineered micropatterned substrates.

Results: Stable, complex micropatterned surfaces were produced by photopolymerization using methacrylate systems. Inhibition of IP3 and RyR signaling disrupts real time Ca^{2+} transients in growth cones and neurite pathfinding in response to these biophysical features. Additionally, IP3 and RyR signaling are necessary for SGN guidance to both chemo-permissive and chemo-repulsive patterns. In exploring the roles of this signaling in pathfinding to complex cues, RyR signaling is essential for halting growth in response to a repulsive cue. Conversely, IP3 signaling is necessary for growth cone turning in response to guidance cues.

Conclusions: IP3 and RyR, fundamental Ca^{2+} signaling elements, are essential for SGNs to effectively pathfind in response to diverse biophysical and biochemical cues. Importantly, they exhibit distinct and complementary roles in the pathfinding process, shedding light on the intricate mechanisms governing neurite guidance.

Professional Practice Gap & Educational Need: Understanding how neurites sense and respond to cues informs fundamental neural development as well as offers insights into translating these principles into applications such as guiding SGN neurite growth for improved neural prostheses, including cochlear implants.

Learning Objective: Inform how the tip of SGN neurites, i.e. the growth cone, sense and turn in response to various environmental cues as the neurite grows towards a target.

Desired Result: Knowledge of the signaling pathways that enable SGN neurites to turn in response to biophysical and biochemical substrate cues and, in particular, clarification of the role of Ca^{2+} release from internal stores via RyR and IP3 in this process.

Level of Evidence - Level N/A

Indicate IRB or IACUC: IACUC 1101569, University of Iowa

Western Blot Characterization of Human Serum Prestin, an Outer Hair Cell Biomarker

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Erika Skoe, PhD; Kourosh Parham, MD, PhD

Hypothesis: Western blot analysis of human prestin in the blood reveals multiple bands, rather than a single band.

Background: Previously, using the ELISA method, prestin was shown to be a good biomarker of outer hair cell (OHC) health and sensorineural hearing loss that could be measured in the blood. Recently, we found that a western blot approach in guinea pigs demonstrates three prestin bands providing greater insights into prestin in the blood and its origins. This approach has not yet been explored in humans.

Methods: Serum samples from 25 healthy human subjects were analyzed. Automated western blot for each sample was generated and the bands were analyzed and compared with transient evoked otoacoustic emission levels (TEOAE).

Results: There were five bands at ~32, ~50, ~94, ~139, and ~171 kDa, respectively. Notably, the second band consistently had the largest area and height. When the subjects were divided based on TEOAE level, those with high emission levels had a significantly larger 94 kDa band than those with low emission levels ($p=0.015$).

Conclusions: Western blot characterization of OHC biomarker prestin in humans shows that the band closest to the previously estimated molecular weight of prestin (81 kDa) is related to a functional measure of OHCs. This finding increases confidence in the value of serum prestin as a biomarker. The western blot method appears to offer higher resolution information on serum prestin. Future work will be carried out under pathological conditions to inform on the application of this quantitative method in the clinical setting.

Professional Practice Gap & Educational Need: Hearing loss is currently diagnosed by audiometric testing which has limitations in the diagnosis of sensorineural hearing loss before it has occurred. The search for meaningful biomarkers of inner ear health that could be measured via blood analysis is imperative to pre-emptive and early interventions.

Learning Objective: To understand the role of prestin as a serum biomarker for sensorineural hearing loss.

Desired Result: To develop a biomarker for sensorineural hearing loss to supplement current audiometric techniques.

Level of Evidence – Level III

Indicate IRB or IACUC: UConn IRB Protocol H14-214.

Otoprotection and Effects on Cochlear Synaptopathy by Angiotensin Receptor Blockade in a Murine Model of Noise Induced Hearing Loss

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Hypothesis: Angiotensin receptor blockade provides otoprotection from noise induced hearing loss.

Background: Noise overexposure causes progressive damage to cochlear hair cells, stria vascularis, and spiral ganglia causing hearing loss. Losartan is an angiotensin receptor antagonist that has systemic vascular modulating and anti-inflammatory effects with unknown cochlear microvascular effects.

Methods: 9–10-week-old CBA/J mice received either standard chow (n=7) or losartan-infused chow (n=6; 20mg/kg/day, comparable to 100mg daily dose in humans) for three days prior and two weeks after exposure to two hours of 8-16k octave band noise at 102.5dB for males and 105dB for females. ABR and DPOAE measurements and losartan serum samples were taken on -1, 1, 7, and 14 days after noise exposure (dANE). Cochleae were collected at 14dANE for whole mount and immunofluorescent staining for CtBP2 (C-terminal binding protein 2), PSD-95 (post-synaptic density protein 95), and myosin VIIA. Synapses per inner hair cell were quantified after confocal microscopy using IMARIS software.

Results: Treatment with losartan reduced ABR temporary threshold shifts (TTS) at 16kHz (5dB vs 16dB; p=0.009) and 32kHz (1dB vs 18dB; p=0.028) 1dANE. Return to baseline thresholds occurred by day 7 in both groups. There was no significant difference in DPOAE threshold at any timepoint. There was a trend toward more synapses per hair cell in Losartan-treatment compared to control (p=0.12).

Conclusions: Losartan provided otoprotection against noise induced as measured by ABR TTS in a murine model. The lack of significant difference in the synaptopathy of cochlear inner hair cells may be due to the low dose of noise exposure.

Professional Practice Gap & Educational Need: No current treatments target the pathophysiologic mechanisms of noise induced hearing loss. Further, the mechanisms of cochlear synaptopathy are incompletely described. The electrophysiologic and immunohistologic data can help provide additional treatment options for noise induced hearing loss and help describe the mechanism of synaptopathy in noise induced hearing loss.

Learning Objective: To explore cellular mechanisms of noise induced hearing loss in murine cochleae and to evaluate losartan as a potential otoprotective treatment for noise induced hearing loss.

Desired Result: Researchers and clinicians will (note) have a new understanding that losartan offers otoprotection from noise induced hearing loss in mice in this preliminary study. Additional animal and human studies are needed to determine if losartan is an effective treatment for noise induced hearing loss.

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

Indicate IRB or IACUC: University of Iowa, IACUC # 3022519

Effects of Smoking on Acute Postoperative Outcomes in Otologic Surgery- A Multi-National Database Study

Pablo Llerena, BS; Bryce Hambach, BS; Kathryn Nunes, BA; Joseph Lu, BS
Praneet Kaki, BS; Jena Patel, MD; Jacob B. Hunter, MD

Objective: To investigate the impact of smoking on 30-day postoperative outcomes in patients undergoing otologic surgery

Study Design: A retrospective cohort database study with propensity-score matching (PSM) utilizing TriNetX clinical database

Setting: TriNetX is a global research database which includes about 110-million patients.

Patients: Included patients had a history of surgical procedures involving the external ear, middle ear, inner ear, and temporal bone (CPT 1010116, CPT 010417, CPT 1010223, and CPT 1010242). Patients were stratified into two cohorts based on smoking status. We then did a subgroup analysis of smokers based on if they continued smoking vs quit smoking after surgery.

Interventions: Observational

Main Outcome Measures: We assessed 30-day postoperative complications in patients after otologic surgery based on smoking status. PSM was used to control for 43 patient characteristics.

Results: After PSM, smokers had an increased risk of tympanic membrane perforation (OR 1.2, 95% CI: 1.0-1.5), CSF leak (OR 1.8, 95% CI: 1.0-3.1), and wound dehiscence (OR 1.8, 95% CI: 1.1-3.0) when compared to non-smokers. Patients who continued smoking postoperatively had an increased risk of hematoma (OR 2.2, 95% CI: 1.2-3.9), myocardial infarction (OR 3.9, 95% CI: 2.6-5.9), and deep vein thrombosis (OR 3.9, 95% CI: 2.5-5.9). Comparatively, patients who quit smoking postoperatively had a decreased risk for developing sensorineural hearing loss (OR 0.3, 95% CI: 0.2-0.3), cholesteatoma (OR 0.6, 95% CI: 0.4-0.9), and tinnitus (OR 0.3, 95% CI: 0.2-0.6).

Conclusion: Patients with a smoking history are more likely to experience postoperative complications compared to non-smokers; smoking cessation after surgery decreased the risk of certain complications.

Professional Practice Gap & Educational Need: While previous literature has shown an association between smoking history and poorer otologic surgery outcomes, there are few studies that account for other confounding variables that may also impact these outcomes. By propensity-score matching, our population-level cohort-control study informs surgeons that despite controlling for other risk factors, smoking still contributes to poorer surgical outcomes. Understanding this relationship can help educate surgeons on the potential risks smoking has on patient outcomes and highlights the importance of smoking cessation in practice.

Learning Objective: 1) Identify that smoking is a risk factor for postoperative complications. 2) Understand the effects of perioperative smoking status on outcomes after otologic surgery.

Desired Result: Provide knowledge and educate healthcare providers on smoking as a risk factor for postoperative complications and enhance our understanding of how perioperative smoking status impacts outcomes following otologic surgery.

Level of Evidence – III

Indicate IRB or IACUC: Exempt.

Statins and Their Effect on Hearing: An All of Us Database Study

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Objective and Background: Hearing loss affects approximately 23% of Americans and is associated with medical comorbidities including hyperlipidemia. Statins, commonly used for dyslipidemia, may protect against hearing loss in animal models, but human studies show mixed results. This study aims to investigate statins and their effect on hearing loss and tinnitus.

Study Design: Retrospective cohort study.

Setting: All of Us is a NIH-funded research database representing more than 710,000 participants in the United States.

Patients: Participants with hyperlipidemia.

Methods: Patients with hyperlipidemia were labeled based on their exposure to at least one statin and additionally labeled for diagnoses of sensorineural hearing loss and/or tinnitus. Logistic regressions were performed with independent variables of statin use, aspirin use, age, race, and sex at birth and dependent variables of hearing loss and tinnitus.

Results: 90,271 patients were included in this study. The analysis showed an association between the use of statins and sensorineural hearing loss (OR=1.62, $p<0.01$) as well as tinnitus (OR=1.37, $p<0.01$). In the individual statin analysis, simvastatin was associated with the strongest correlation with hearing loss (OR=1.57, $p<0.01$) and tinnitus (OR=1.50, $p<0.01$) while fluvastatin was the least associated both hearing loss (OR: 1.15, $p<0.01$) and tinnitus (OR=1.02, $p<0.01$). Atorvastatin, the most used statin, was also associated with hearing loss (OR=1.28, $p<0.01$) and tinnitus (OR=1.212, $p<0.01$).
Conclusions: In this study, the All of Us database was used to investigate the relationship between statins and hearing loss/tinnitus. Results indicate a potential ototoxic association of statins on hearing and tinnitus.

Professional Practice Gap & Educational Need: Statins, commonly used for dyslipidemia, may protect against hearing loss in animal models, but human studies show mixed results.

Learning Objective: To evaluate if there is an association between statin use and sensorineural hearing loss or tinnitus, while accounting for race, age, sex, and hyperlipidemia.

Desired Result: To inform discussion around statin use and future research into statin side effects.

Level of Evidence – Level IV

Indicate IRB or IACUC: Exempt

Blast Exposure, Tinnitus, Hearing Loss, and Post-Deployment Quality of Life in U.S. Veterans: A Longitudinal Analysis

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Objective: Examine the association between military blast exposure on the quality of life (QoL) in Veterans and to determine if this association is modified by hearing loss.

Study Design: Longitudinal.

Setting: Tertiary care center.

Patients: 545 Veterans.

Interventions: Self-reported blast exposure, tinnitus (yes/no) immediately following the blast, and high-frequency hearing loss (puretone hearing threshold average 3000-8000 Hz > 20 dBHL) near the time-of-service separation.

Main Outcome Measures: WHO Disability Assessment Schedule 2.0 questionnaires at baseline and annually over 5 years. Group-based trajectory modeling was used to classify QoL of Veterans into three trajectories: (1) consistently high-QoL; (2) consistently moderate-QoL; (3), consistently low-QoL.

Results: The probability of having consistently high-QoL after military service is approximately 60% if there was no exposure to a blast or presence of hearing loss. The probability of consistently high QoL drops precipitously to approximately 20% with a self-reported military blast exposure accompanied by tinnitus and hearing loss. The probability of having consistently moderate-QoL is approximately 70% if there was a self- reported history of military blast exposure accompanied by tinnitus and hearing loss. Self-reported blast exposure increases the odds of being in the moderate-QoL group compared to the high-QoL, OR 1.58 (95% CI 0.97, 2.59). Self-reported blast exposure associated with tinnitus further increases the odds, OR 3.61 (95% CI 2.12, 6.14). Hearing loss further increases the odds of a lower QoL trajectory group.

Conclusions: Blast exposure negatively affects the quality of life of Veterans especially when compounded with tinnitus and hearing loss.

Professional Practice Gap & Educational Need: Blast exposure likely negatively affects quality of life. This effect is stronger when the blast exposure is compounded with tinnitus and hearing loss.

Learning Objective: Understand the association of blast exposure with and without tinnitus and hearing loss on quality of life.

Desired Result: Highlight the importance of exploring treatment options for hearing loss in Veterans who have been exposed to blasts to improve quality of life.

Level of Evidence – III

Indicate IRB or IACUC : #3159/9495 Joint VA Portland Health Care System (VAPORHCS) Oregon Health and Science University (OHSU)

Analysis of Adherence to AAO-HNSF Clinical Practice Guidelines for Sudden Hearing Loss

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Andrew Rothka, BS; Mark E. Whitaker, MD; Neerav Goyal, MD, MPH

Objective: Sudden hearing loss (SHL) necessitates prompt evaluation. In 2019, the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNSF) released guidelines for the diagnosis and management of SHL and sudden sensorineural hearing loss (SSNHL). The objective of this study is to assess adherence to these guidelines on a national scale.

Study Design: Retrospective Cohort

Setting: TriNetX, a de-identified healthcare database was retrospectively queried to identify patients with SHL.

Patients: Adults with SHL

Main Outcome Measures: Adherence to guidelines was measured by the percentage of patients undergoing proper workup and treatment.

Results: 26,626 patients with unilateral SHL were identified. Guidelines for SHL include undergoing an audiogram within 2 weeks of presentation to distinguish SSNHL from conductive hearing loss (CHL). In our cohort, less than half of all patients (48.0%, n=12,784) underwent subsequent audiogram testing, and just 30.2% (n=8,065) completed it within 2 weeks. 460 patients had testing within 2 weeks-1-month, 427 patients within 1-3 months, and 161 patients between 3-6 months of SHL. Overall, 2,749 patients were diagnosed with unilateral SSNHL and 96 patients were diagnosed with unilateral conductive hearing loss (CHL). The remainder had mixed conductive and sensorineural hearing loss (n=110) or were lost to follow-up (n =9829).

For SSNHL patients, guidelines recommend MRI or ABR to evaluate for retrocochlear pathology. Among 2,749 patients with SSNHL in our cohort, just 24.7% (n=680) obtained an MRI or ABR within 1 month. The median time from diagnosis of SSNHL to MRI was 16 days. 3.7% of patients (n=101) with SSNHL were diagnosed with a vestibular schwannoma. Of these patients, <9.9% (n<10) underwent stereotactic radiosurgery (SRS) and 13.9% (n = 14) underwent surgical resection. Additionally, the guidelines emphasize the option of steroids within 2 weeks as initial therapy for SSNHL, which was the case for 49.7% (n=1,365). Less than 0.5% of patients (n<10) underwent CT scan, or were prescribed vasodilators or thrombolytics, in accordance with strong recommendations against these diagnostics and treatments. 91 (n=3.3%) patients were on antivirals despite insufficient evidence to support their effectiveness. No patients were prescribed hyperbaric oxygen although it is an optional recommendation.

Conclusions: There is significant opportunity for improvement in evaluating patients with SHL, specifically SSNHL. Proper adherence to guidelines for SSNHL may improve screening, detection, and management of neurotologic pathologies including vestibular schwannoma, and result in expedited hearing recovery and QOL in patients.

Professional Practice Gap & Educational Need: SHL is common, but missed or late diagnosis and treatment can lead to poor and costly outcomes. The AAO-HNSF guidelines were established to ensure adequate workup and determine optimal therapy. No study has assessed the adherence to clinical practice guidelines for SHL.

Learning Objective: To evaluate the adherence to the AAO-HNSF Clinical Practice Guidelines for SHL

Desired Result: To recognize and improve awareness of adherence to guidelines for SHL

Level of Evidence – Level III

Indicate IRB or IACUC: Exempt

Contemporary, Individual and Community-Level Social Determinant Associations with Acoustic Neuroma Disparities in the US

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Jill N. D'Souza, MD; Anthony M. Sheyn, MD; Jeffrey C. Rastatter, MD, MS

Objective: Using multivariate, social determinants of health (SDoH)-models featuring census-level Yost-Index-socioeconomic status (SES) measures, to determine whether community-level SDoH-factors quantifiably influence Acoustic Neuroma care-prognostic disparities nationally more than individual-level SDoH-factors

Study Design: Observational-Retrospective Cohort

Setting: Specially Authorized Head-Neck SEER 2020 Dataset

Patients: 23,330 adult (20+ years) patients diagnosed with Acoustic Neuroma from 2010-2018

Main Outcome Measures: Age-adjusted multivariate regressions and cox-proportional hazard models with individual-level (sex, race-ethnicity) and census-level covariate factors (Yost-Index-SES [aggregate measure of 7-measures of income, education, housing], Rurality-Urbanicity) assessing outcomes of delay-of-interventional treatment (3 months or more after diagnosis), treatment receipt, and overall survival.

Results: Increases in all-cause mortality showed markedly positive and independent associations with poor Yost-SES (HR, 1.55; 95%CI, 1.41-1.71) and Male-Sex (HR, 1.30; 95% CI, 1.19-1.43) (all $p<0.001$). Stereotactic radiotherapy receipt showed significantly negative and independent associations with poor Yost-SES (OR, 0.93; 95%CI, 0.86-0.99; $p=0.040$). Surgical resection receipt showed significantly positive and independent associations with poor Yost-SES (OR, 1.13; 95%CI, 1.07-1.20; $p<0.001$) and non-statistically significant positive associations with increasing rurality (OR, 1.10; 95%CI, 1.00-1.20; $p=0.057$). Having a delay-of-interventional treatment showed significantly negative and independent associations with poor Yost-SES (OR, 0.91; 95%CI 0.85-0.97; $p=0.005$).

Conclusions: Comprehensive, multivariate models of individual- and community-level SDoH showcased detrimental care and prognostic disparities mainly contributed by community-level SES differences across a recent, national cohort of adults diagnosed with acoustic neuromas.

Professional Practice Gap & Educational Need: Nuanced analyses assessing wide varieties of SDoH-factors inform providers and policymakers of how to specifically target and allocate resources of prospective investigations and initiatives towards the most pertinent needs of patients and their surrounding communities.

Learning Objective: To understand how to conduct comprehensive, multivariate analyses encompassing a breadth of SDoH-factors affecting individuals and their surrounding communities; to navigate and work with modern large datasets; and to apply these methods towards understanding acoustic neuroma disparities affecting patients in the real world

Desired Result: Using these multivariate, interactional analyses across 12 SDoH-factors on the individual and community-levels, this investigation hypothesizes that community/census-level SES status, as measured by the Yost Index, would confer the highest-magnitude associations in detrimental survival and treatment outcomes of adults with acoustic neuromas.

Level of Evidence - III

Indicate IRB or IACUC : Exempt

Early Use of Computer-based Auditory Training Yields Greater Speech Recognition and Quality-of-life Benefits in New Adult Cochlear Implant Recipients

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Judy R. Dubno, PhD; Theodore R. McRackan, MD, MSCR

Objective: Computer-based auditory training (CBAT) has been shown to improve outcomes in adult CI users. This study evaluates whether early vs late CBAT intervention, post-activation, impacts the effect of CBAT on CI outcomes.

Study Design: Prospective natural experiment

Setting: Tertiary academic medical center

Patients: 65 new adult CI users

Interventions: CBAT use over the first-year post-activation

Main Outcome Measures: Speech recognition scores and CIQOL-35 Profile score improvements between CI recipients who used CBAT resources early (<3 months) vs late (3-12 month) post-activation.

Results: 43 CI recipients used CBAT within 3 months post-activation (early) and 22 after 3 months (late). Early CBAT users trended toward higher CNC (60.33-62.55% vs 45.35-54.22%;*d*-range=0.25-0.83) and AzBio Quiet (72.4-75.2% vs 49.8-65.6%;*d*-range=0.39-0.72) scores at 3-, 6-, and 12-months post-activation, compared to later CBAT users. Differences in speech recognition between early/late cohorts were greatest at 3 months (CNC:*d*=0.83 [0.22, 1.43] and Azbio:0.72 [0.14, 1.3]) and narrowed as the late cohort started using CBAT (CNC:*d*=0.25 [-0.35, 0.85] and Azbio:0.39 [-0.20, 0.98]).
Early CBAT users also had greater CIQOL-35 Profile global and all domain score improvement at all time points post-activation, compared to late users (*d*-range=0.014-0.67), with the largest difference for the communication (*d*-range=0.24-0.63) and listening effort domains (*d*-range=0.35-0.73). As with speech scores, differences in CIQOL scores were greatest at 3 months and narrowed as the late cohort started using CBAT resources, however less convergence was observed (*d*-range=0.07-0.73 vs 0.14-0.47, at 3- and 12-months respectively)

Conclusions: Auditory training with self-directed computer software (CBAT) may yield greater speech and quality-of-life benefits for new adult CI recipients if started within 3 months post-activation.

Professional Practice Gap & Educational Need: CBAT is a free and widely accessible form of auditory rehabilitation that has been shown to have a possible association with improved CI outcomes in new adult recipients. However, the most effective time-course or schedule of CBAT use after implantation is poorly understood.

Learning Objective: To explore the effectiveness of using CBAT if started early (<3 months) vs late (3-12 months) post-activation for new adult recipients.

Desired Result: Practitioners and researchers will learn that the use of CBAT starting early after activation by new adult CI recipients may offer improved outcomes as compared to training started later in the post-activation period. As such, clinicians should consider counselling on the early use of this widely accessible and effective form of auditory rehabilitation for newly implanted patients.

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

Indicate IRB or IACUC: Pro00077593

Preoperative Factors Predicting Electroacoustic Stimulation Usage in Adults Following Cochlear Implantation

Ankita Patro, MD MS; Connie Ma, MD; Natalie Schauwecker, MD; Nathan R. Lindquist, MD
Michael H. Freeman, MD; David S. Haynes, MD, MMHC; Elizabeth L. Perkins, MD

Objective: To identify preoperative clinical factors that impact electroacoustic stimulation (EAS) usage in adult cochlear implant (CI) recipients.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 339 adults (375 ears) with preoperative residual hearing who underwent CI from 2012 to 2021. Hearing preservation (HP) was defined as low-frequency pure-tone average (LFPTA) up to 65 dB HL.

Main Outcome Measures: Demographics; audiometry; CNC; Speech, Spatial, and Qualities (SSQ).

Results: Of 149 ears who had HP at 1 or 3 months, 114 (76.5%) were fit with EAS. Compared to non-users, EAS users had higher hearing aid usage at initial evaluation (76.3% vs. 48.6%, p=0.002) and less smoking history (26.3% vs. 51.4%, p=0.016). Preoperative CNC scores in the contralateral ear (40.0% vs. 25.6%, p=0.015) and bilateral listening condition (41.1% vs. 27.0%, p=0.004) were significantly higher for EAS users. Rates of EAS fitting improved from 40% in 2013 to 100% in 2021 (p=0.043). Preoperative LFPTA and CNC in the ear to be implanted, preoperative SSQ, age at implantation, duration of deafness, etiology of hearing loss, diabetes, functional health status, gender, race, and marital status were equivalent between EAS users and non-users (p>0.05). On multivariate analysis, only higher preoperative bilateral CNC scores significantly predicted EAS usage (OR 1.06, 95% CI 1.01—1.13, p=0.048).

Conclusions: Although rates of EAS fitting have improved in the last decade, patients who are non-smokers, are hearing aid users at initial evaluation, and have better preoperative contralateral hearing are more likely to use EAS after HP surgery. These findings can help with early identification and counseling of potential EAS non-users.

Professional Practice Gap & Educational Need: Despite the known benefits of HP and EAS in adult CI patients, EAS has been reported to be underutilized in this population. To our knowledge, a comprehensive analysis of predictive preoperative factors that can influence EAS usage has not been reported in the literature.

Learning Objective: To identify preoperative demographic and audiometric factors that can impact EAS usage in adult CI recipients.

Desired Result: Providers will have knowledge about the impact of hearing aid use, smoking status, and preoperative contralateral hearing on rates of EAS utilization. These findings can help counsel patients and identify those who may reject EAS early but may still perceive benefit.

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

Indicate IRB or IACUC: IRB Exempt (221833, Vanderbilt University, approved on 10/12/22).

Impact of Implantable Hearing Devices on Delirium Risk in Patients with Hearing Loss: A National Database Study

Bryce Hambach, BS; Elliott M. Sina, BA; Kathryn Nunez, BS
Jena Patel, MD; Jacob B. Hunter, MD

Objective: To test the hypothesis that utilization of implantable hearing rehabilitation devices is associated with a reduced likelihood of developing delirium in patients with hearing loss.

Study Design: A retrospective cohort database study with propensity-score matching (PSM) utilizing TriNetX clinical database.

Setting: The US Collaborative Network within the TriNetX database (100 million people).

Patients: Patients over 55-years old were selected based off of three categories: a non-hearing loss study control (ICD-10:H90-91), a hearing loss (HL without implantable device), and an implantable device cohort (ICD-10:Z96.21;Z96.29;09HD;09HE; CPT:69714;69930). Patients with prior dementia or memory loss diagnosis were excluded (F01-03, 27-29).

Interventions: Observational

Main Outcome Measures: Odds ratios with 95% confidence intervals for delirium diagnosis code (F0.5).

Results: The control cohort (n = 32.4 million) was 1:1 PSM for age and sex with the HL cohort (n = 1.55 million) in which 0.74% of patients developed delirium compared to 2.23% in the HL cohort (OR, 95% CI: 0.33, 0.32-0.34). When looking at the same PSM between HL and implantable device cohorts (n=18,463), 2.23% developed a delirium diagnosis compared to 1.45% in the implantable device cohort (OR, 95% CI: 1.54, 1.32-1.80). Further analysis accounting for 17 PSM covariates showed that 0.76% of the HL cohort developed delirium compared to 0.40% of the implantable device cohort (OR, 95% CI: 1.89, 1.43-2.50).

Conclusions: The present study supports the current literature in that patients with hearing loss were more likely to develop delirium than those with normal hearing. Importantly, patients with implantable hearing devices were significantly less likely to develop delirium compared to hearing loss patients without an implantable device. Our research highlights the importance of treating hearing loss to prevent delirium in a hospital setting.

Professional Practice Gap & Educational Need: Despite literature demonstrating a relationship between hearing loss and risk of delirium, there remains a notable gap in our understanding of clinical management strategies focused on mitigating the risk of developing delirium in hearing-impaired patients. It is critical for healthcare providers to know how hearing rehabilitation devices impact this relationship between hearing loss and delirium.

Learning Objective: 1) Identify that hearing impairment is a risk factor for delirium. 2) Understand the impact that implantable hearing devices may have on delirium compared to HL patients who may defer to hearing aids.

Desired Result: Provide knowledge and educate healthcare providers on 1) hearing loss as a risk factor for in-hospital delirium and 2) the role implantable hearing devices may play in delirium prevention.

Level of Evidence – III

Indicate IRB or IACUC: Exempt

Early Auditory Development of Cochlear Implanted Children with Sensorineural Hearing Loss following Congenital CMV Infection

Piotr H. Skarzynski, Prof; Anita Obrycka, PhD; Aleksandra Kolodziejak, MSc; Elzbieta Gos, PhD
Rita Zdanowicz, MSc; Artur Lorens, Prof; Henryk Skarzynski, Prof

Objective: The aim of the study was to assess early auditory development in CI children with CMV-related hearing loss.

Study Design: The retrospective study included children with congenital CMV who underwent cochlear implantation at an early age due to hearing loss caused by the infection.

Setting: Tertiary referral center.

Patients: 47 CI children with sensorineural hearing loss following congenital CMV infection with mean age 14 months.

Interventions: Minimally invasive cochlear implantation via round window.

Main Outcome Measures: All children underwent Auditory Brainstem Response test before operation. Early development was assessed with LittleEARS Auditory Questionnaire. The questionnaire was performed at CI activation assessing pre implant auditory development and at each follow up visit related to CI fitting to 14 months of CI use.

Results: In children with CMV-related hearing loss the mean LittleEARS total score was 5.2 pts. (SD=7.1) at CI activation, 16.7 pts. (SD=8.8) at 5 months of CI use, and 24,8 pts. (SD=8.4) at 14 months after implantation. In the reference group the mean results were as follow: 8.3 pts. (SD=7.6) at CI activation, 25.0 pts. (SD=5.6) after 5 months of CI use, and 32.3 pts. (SD=3.9) 14 months post activation.

Conclusions: Early cochlear implantation in children with sensorineural hearing loss following congenital CMV infection facilitates their early auditory development. Nevertheless in this group of children the level of auditory development is lower comparing to the level observed in children with no CMV-related hearing loss.

Professional Practice Gap & Educational Need: There are no clear guidelines on screening for CMV in children.

Learning Objective: Early detection of CMV infection in children, which causes many complications in addition to hearing impairment.

Desired Result: Introduction of newborn screening for congenital CMV infection.

Level of Evidence – III level

Indicate IRB or IACUC : The study was approved by Bioethics Committee of the Institute of Physiology and Pathology of Hearing (KB.IFPS/Statement 4/2022).

Cochlear Implantation (CI) Outcomes in Children Under 5 Years of Age with Single-Sided Deafness (SSD): A Systematic Review and Meta-analysis

Corinne Pittman, MD; Nadia Samaha, BS; Myra Zaheer, BA
Luke Llaurado, BA; Xue Geng, MS; Michael Hoa, MD

Objective: To ascertain the outcomes of CI in children under 5 years of age with SSD in the areas of speech discrimination, speech comprehension in various environments, and qualities of hearing experience.

Data Sources: Medline, Embase, Cochrane and Web of Science databases were searched using relevant MeSH terminology.

Study Selection: Inclusion criteria captured the following: 1) age ≤ 5 years, 2) diagnosis of SSD, 3) normal hearing in the contralateral ear, 4) numerical data regarding speech perception thresholds, sound localization, and patient-reported outcomes.

Data extraction: Our study was adherent to the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting guidelines. Data were pooled using a random-effects model.

Data Synthesis: Among 759 articles screened, 16 met inclusion criteria. The 204 children had a mean age at implantation of 60.41 months (95% CI, 40.37-80.57), and a mean 37.44 month duration of deafness (95% CI, 24.80-50.08). Speech discrimination improved significantly after CI (MD, -0.2906; 95% CI, -0.5596 to -0.0324) and there was significant heterogeneity between studies (p=0.028). Many children showed significant improvement on the spatial hearing domain of the Speech, Spatial and Qualities of Hearing Scale (SSQ) (MD, -2.1500; 95%, -3.7679, -0.5320; p=0.009).

Conclusions: Our findings demonstrate a clinically significant improvement in speech discrimination and spatial hearing outcomes among pediatric CI patients under the age of 5 years with SSD. Further studies investigating very young children with SSD following CI are needed to refine candidacy criteria, and appropriately counsel eligible patients and their families on treatment expectations.

Professional Practice Gap & Educational Need: In 2019, the FDA approved CI for SSD in children 5 years or older, however, earlier implantation may provide better hearing outcomes by impeding preference for the normal hearing (NH) ear and, possibly, reversing adaptive cortical reorganization patterns formed in favor of the NH ear.

Learning Objective: To understand the audiological and patient-reported outcomes of CI in children under 5 years of age with SSD in the areas of speech discrimination, speech comprehension, and qualities of hearing experience, and to assess their relationship to age at implantation and duration of deafness.

Desired Result: Treatment with cochlear implantation before the age of 5 years is associated with improvements in speech discrimination and spatial hearing among children with SSD.

Level of Evidence - Level I

Indicate IRB or IACUC: Exempt

A Systematic Review and Meta-Analysis Examining Outcomes of Cochlear Implantation in Children with Bilateral Cochlear Nerve Deficiency

Jay Maturi, BS; Kimberley S. Noij, MD, PhD; Vidya Babu, BS; Carolyn M. Jenks, MD

Objective: To characterize hearing and speech outcomes after cochlear implantation (CI) in pediatric patients with bilateral cochlear nerve deficiency (CND)

Data Sources: MEDLINE, Cochrane Library, Embase, and Web of Science databases were queried from conception to July 2023.

Study Selection: Studies that reported hearing and speech outcomes of pediatric patients with bilateral CND who underwent CI were included. 314 papers were screened, and 36 met inclusion criteria.

Data Extraction: Demographics, comorbidities, inner ear abnormalities, CND classification (aplasia or hypoplasia), details of diagnostic workup, and outcomes data were extracted from each paper. Patient outcomes were assessed with the four-level Auditory Performance Level (APL) scale. Meta-analysis was performed on patients with individual data to assess factors associated with performance.

Data Synthesis: A total of 295 patients with bilateral CND who underwent CI were included: 96 underwent unilateral CI in an ear with CN hypoplasia, 138 underwent unilateral CI in an ear with aplasia, 34 patients underwent bilateral CI (14 had bilateral hypoplasia, 18 had bilateral aplasia, 2 had mixed aplasia/hypoplasia), and the remainder were not classified. Among implanted ears, 91 had additional cochlear anomalies and 49 had vestibular anomalies. 52 patients had syndromic diagnoses, the most common being CHARGE. Among 256 patients for whom post-CI APL could be defined, 50 patients (20%) showed no improvement, 58 (23%) attained parent-perceived benefit, 68 (27%) attained closed-set speech perception, and 80 (31%) attained open-set speech perception.

Conclusions: Although most patients with bilateral CND benefited from CI, outcomes were heterogenous and one fifth of patients did not experience measurable benefit from CI.

Professional Practice Gap & Educational Need: Outcomes of CI in CND are variable and poorly defined, and there remains disagreement about whether patients with CND benefit from CI. This review provides valuable information regarding CI outcomes in patients with bilateral CND and will aid providers in preoperative discussions regarding outcome expectations for this patient population.

Learning Objective: To recognize the array of features that result in successful hearing and speech improvements following cochlear implantation in bilateral CND patients.

Desired Result: Improved patient selection and counseling for patients with bilateral CND undergoing CI.

Level of Evidence - Level III (systematic review and meta-analysis including case-control studies)

Indicate IRB or IACUC : Exempt (systematic review and meta-analysis)

Tympanic Membrane Regeneration Therapy for Pediatric Tympanic Membrane Perforation

Shin-ichiro Kita, MD; Shin-ichi Kanemaru, MD, PhD; Rie Kanai, MD
Tomoya Yamaguchi, MD; Akiko Kumazawa, MD; Ryohei Yuki, MD
Toshiki Maetani, MD, PhD

Objective: To evaluate tympanic membrane regenerative therapy (TMRT) for pediatric tympanic membrane perforations (TMPs)

Study Design: Intervention study

Setting: Research institute hospital

Patients: Twenty cases (M/F:13/7, 13/8 ears, 0-15 y.o.) in patients with chronic TMP were evaluated in this study. As comparison, twenty pediatric patients with chronic TMP who underwent myringoplasty/tympanoplasty were included.

Interventions: For the TM repair procedure, the edge of the TMP was disrupted mechanically, and gelatin sponge immersed in basic fibroblast growth factor were placed inside and outside the tympanic cavity and covered with fibrin glue. The TMP was examined 4 ± 1 weeks later. The protocol was repeated up to four times until closure was complete.

Main Outcome Measures: Closure of the TMP and hearing improvement were evaluated at 16 weeks after the final regenerative procedure. Adverse events were monitored.

Results: The mean follow-up period was 427.1 days. The TM regenerated in all cases, but pinhole reperforation occurred in two cases, and the final closure rate was 90.5% (19/21). Hearing improved to 24.9 ± 7.6 dB on average before surgery and to 13.8 ± 5.4 dB after surgery. The AB gap improved from 12.9 ± 8.0 dB to 5.2 ± 3.5 dB. The myringoplasty/tympanoplasty group had significantly lower AB gap improvement compared to the TMRT group. There were no adverse events.

Conclusions: TMRT can be expected to regenerate near-normal TMs with a high closure ratio, resulting in better hearing improvement compared to the myringoplasty/tympanoplasty group, and is an effective treatment for children with long life expectancy.

Professional Practice Gap & Educational Need: TMRT is a new treatment method that became covered by health insurance in Japan in November 2019. This treatment method is based on a tissue engineering concept that is fundamentally different from traditional tympanic membrane reconstruction. Therefore, it is important to fully understand this idea in order to regenerate the eardrum reliably. Appropriate treatment can regenerate a near-normal eardrum and provide good hearing with a very small AB gap. TMRT is gradually replacing most myringoplasty and some tympanoplasty in Japan. Although a tympanic membrane regeneration rate of over 90% has been reported in adults, there have been no reports only in children, so I would like to make this presentation and discuss some precautions.

Learning Objective: At the conclusion of this presentation, the participants should be able to know how to regenerate the tympanic membrane without conventional surgical therapy. This new tissue engineered treatment will change the former concept of the otologic surgery.

Desired Result: TMRT is currently undergoing Phase II clinical trials in the United States, and Phase III trials are planned for next year to obtain FDA approval. This treatment is expected to spread around the world because it is short, minimally invasive, low cost, and requires easy training for the surgeon. I hope that this announcement will be of some help.

Level of Evidence - Level III

Indicate IRB or IACUC : IRB No.2106006, Medical Research Institute Kitano Hospital. Initial approval 14/06/2021
TMRT became covered by health insurance in Japan in November 2019.

Unique Cell-Type Specific Signaling Patterns Define Cholesteatoma

Christopher M. Welch, MD, PhD; Shuze Wang, PhD; Joerg Waldhaus, PhD

Hypothesis: Cholesteatoma has a unique cellular composition and cell-type specific signaling pathways relative to normal tympanic membrane tissues that drive its behavior.

Background: Cholesteatoma is a complex, heterogeneous, expansile and destructive cystic epithelial lesion that occurs within the middle ear and temporal bone. It causes destruction of surrounding tissue, leading to significant otologic complications. Currently, the only treatment option is surgical removal of the disease, and despite surgical treatment, rates of recurrent or residual cholesteatoma following surgery approach 40-50% 10 years later. Extensive research has attempted to generate medical treatments by delineating signaling pathways that drive cholesteatoma behavior, with numerous pathways identified. This work has been hampered by the inherent heterogeneity of cholesteatoma, with cell-type specific behaviors obscured by bulk analysis of cholesteatoma.

Methods: Single-cell RNA (scRNA) sequencing was utilized to evaluate human cholesteatoma specimens, which were compared to available scRNA data for normal human tympanic membrane. Results were validated utilizing immunohistochemistry on human cholesteatoma specimens and in an *in vitro* model of cholesteatoma. The CellChat algorithm analyzed differential patterns in cell signaling pathways.

Results: Cholesteatoma cellular composition differs notably from normal tympanic membrane, with increased numbers of immune cells in cholesteatoma. A number of cell signaling pathways are also differentially regulated between cholesteatoma and normal tissues, including growth factor, Wnt, interleukin, cell adhesion, and tumor necrosis factor pathways, with unique cell-type specific patterns in cholesteatoma.

Conclusions: scRNA sequencing data defines the cellular composition and cell-type specific signaling pathways in cholesteatoma, demonstrating unique composition and signaling patterns relative to normal tympanic membrane.

Professional Practice Gap & Educational Need: The molecular understanding of cholesteatoma remains poor, resulting in a lack of medical treatments for this relatively common and troublesome condition.

Learning Objective: To define the cellular profile and cell-type specific signaling pathways of cholesteatoma relative to normal tympanic membrane.

Desired Result: To define the unique cell-type specific signaling pathways within cholesteatoma that may warrant further evaluation as potential therapeutic targets for medical treatment of cholesteatoma.

Level of Evidence – Not applicable, *in vitro* cellular study.

Indicate IRB or IACUC: IRB HUM00153531

The NLRP3 Inflammasome in Macrophages Causes Sensory Hearing Loss in Chronic Suppurative Otitis Media (CSOM)

Viktoria Schiel, MD, PhD; Anping Xia, MD, PhD; Ritwija Bhattacharya, PhD
Ankur Gupta, MD; Kourosh Efthekarian, MD; Peter Santa Maria, MD, PhD

Hypothesis: The NLRP3 inflammasome causes sensory hearing loss in CSOM.

Background: CSOM is a global disease and affects 300 million people worldwide. We previously showed that sensory hearing loss (SHL) in CSOM is associated with macrophages and not due to direct bacterial invasion or direct ototoxin exposure. We aimed to investigate the macrophage associated mechanism that drives hearing loss in CSOM. The NLRP3 inflammasome is an innate immune sensor and is expressed in monocytes and macrophages. It can be activated via multiple different pathways, including many direct pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs) that are toxic.

Methods: We investigated in our validated pseudomonas aeruginosa CSOM mouse model.

Results: We found that the relative mRNA levels of components of the NLRP3 pathway (NLRP3, PYCARD, Caspase 1, IL-1b) were significantly increased at 7 days in CSOM without depletion of cochlear macrophages. We then used a NLRP3 knockout mouse model (NLRP3 -/-) to study the inflammasome function in CSOM. We found that the knockout condition was protective for HC loss in the cochlea and showed significantly better outer hair cell (OHC) survival at 14 days compared to the WT control ($p = 0.0393$). The protein levels of NLRP3 ($p = 0.0018$) and its downstream cytokines IL-1b ($p = 0.0004$) and IL-18 ($p = 0.0129$) were significantly increased at 7 days in CSOM compared to the non CSOM control.

Conclusion: The NLRP3 inflammasome in macrophages causes SHL in CSOM and could be a potential target for future therapeutics development to prevent NLRP3 associated hearing loss.

Professional Practice Gap & Educational Need: CSOM is a global disease and the most common cause for permanent hearing loss in children in the developing world. There is currently no effective medical cure due to the lack of understanding what drives the sensory hearing loss in CSOM. There is a need to understand the mechanism to be able to develop therapeutics to prevent sensory hearing loss in CSOM.

Learning Objective: To study the role of the NLRP3 inflammasome in macrophages towards sensory hearing loss in CSOM.

Desired Result: NLRP3 activation causes sensory hearing loss in CSOM and sensory hearing loss can be prevented in a knockout mouse model.

Level of Evidence – III

Indicate IRB or IACUC: Approved by Stanford IACUC (APLAC) 32833

RESIDENT RESEARCH TRAVEL AWARD

Outcomes after Exoscopic versus Microscopic Ossicular Chain Reconstruction

Caleb J. Fan, MD; Jacob C. Lucas, MD; Robert M. Conway, DO
Masanari G. Kato, MD; *Seilesh C. Babu, MD*

Objective: To analyze the outcomes of exoscopic versus microscopic ossicular chain reconstruction (OCR)

Study Design: Retrospective chart review

Setting: Tertiary care otology-neurotology practice

Patients: Adult subjects with a diagnosis of ossicular discontinuity from 2018-2022

Interventions: Exoscopic or microscopic primary OCR (without mastoidectomy) with a partial ossicular replacement prosthesis (PORP) or total ossicular replacement prosthesis (TORP)

Main Outcome Measures: Audiometric outcomes at 1 year post-operatively including: bone and air pure tone averages (PTA), air-bone gap (ABG), change in ABG, speech reception threshold (SRT), and word recognition score (WRS). Secondary outcomes included operative time and complication rates of primary and delayed graft failure, tympanic membrane lateralization, cerebrospinal fluid leak, facial nerve injury, profound hearing loss, persistent tinnitus, and persistent vertigo.

Results: Sixty ears underwent primary OCR and were subdivided based on prosthesis type (PORP and TORP) and surgical approach (exoscope versus microscope). Exoscopic OCR was performed on 30 ears (21 PORP, 9 TORP) and microsocpic OCR was performed on 30 ears (19 PORP, 11 TORP). Controlling for prosthesis type and surgical approach, there were no significant differences in 1) demographics; 2) intraoperative findings including post-auricular approach, cartilage use, chronic otitis media, and cholesteatoma; 3) audiometric outcomes of bone and air PTA, ABG, change in ABG, SRT, and WRS. Operative time was 64.7 minutes and 59.6 minutes for the exoscopic and microsocpic group, respectively (p=0.4, 95% CI [-16.4, 6.1], Cohen's D =0.2). There was 1 case of delayed graft failure in the exoscopic group and 1 case in the microscopic group.

Conclusions: Audiometric and surgical outcomes after exoscopic and microscopic OCR are comparable.

Professional Practice Gap & Educational Need: The current standard of care is that otologic surgery is performed with a microscope. Newer technologies such as the endoscope and exoscope have become more popular in recent years, which requires a comparison of patient outcomes to uphold standards in otologic surgery.

Learning Objective: The outcomes after exoscopic OCR are comparable to those after microscopic OCR.

Desired Result: For otologic surgeons and patients to understand that newer technologies such as the exoscope do not sacrifice outcomes in OCR surgery.

Level of Evidence – IV

Indicate IRB or IACUC: Exempt

Temporal Integration of Multisensory Stimuli in Migraine

Timothy E. Hullar, MD; Jwala Rejimon, BS; Michelle E. Hungerford, AuD; Robert J. Peterka, PhD
Angela C. Garinis, PhD; Yonghee Oh, PhD; Richard F. Lewis, MD

Hypothesis: Patients with migraine have difficulties accurately merging multisensory integration in the temporal domain, helping explain their symptoms of dizziness and motion sensitivity.

Background: Multisensory cues generated by a single event arrive at the brain asynchronously due to variable delays in transmission, encoding, and processing. The brain must accommodate for these discrepancies to form a maximally useful, unified impression of the environment. The time offset over which multiple sensory inputs are interpreted as "synchronous" is known as the temporal binding window (TBW). We hypothesized migraine patients might have abnormal (widened) TBWs, causing sensory confusion and processing difficulties. Widened TBWs are known to occur in autism, schizophrenia, dyslexia, Parkinson's, and other neurologic disorders.

Methods: Stimuli were a 10 ms flash, a 10 ms beep, and a sinusoidal yaw rotation in the dark, presented pairwise at varying temporal offsets. The TBW was defined as the time interval over which subjects were less than 75% accurate which came first. TBWs for visual-auditory, auditory-vestibular, and visual-vestibular stimuli were characterized in 34 normal controls and 17 migraine patients.

Results: Pairwise t-tests showed TBW was longer among migraine patients than normal controls for the visual-vestibular pairing (261 vs 171 ms, $p = 0.036$). Visual-auditory and auditory-vestibular pairings were not different between participant groups ($p=0.125$ and 0.384 respectively). Vestibular response thresholds were correlated with TBW but independent of participant group.

Conclusions: Prolonged TBW may relate to imbalance and motion sensitivity in migraine patients. Narrowing the TBW with specific training techniques may help improve these symptoms.

Professional Practice Gap & Educational Need: Patients with migraine often present with generalized symptoms of imbalance and related motion sensitivity, but our inadequate understanding of its pathophysiology limits the development and implementation of effective treatment options.

Learning Objective: To describe important characteristics of multisensory balance-related sensory information in patients with imbalance and motion sensitivity.

Desired Result: To demonstrate the relationship between multisensory integration in the temporal domain and migraine.

Level of Evidence: 3

Indicate IRB or IACUC: [1635600-4] VAPORHCS/OHSU J (7/1/2020)

Artificial Intelligence for Diagnostic and Treatment Planning:
Is It Ready to Be Your Doctor?

Camryn Marshall, BS; Jessica Forbes, MS; Luis Roldan, MD
Jim Atkins, MD; Michael D. Seidman, MD

Objective: Investigate the precision of language-model artificial intelligence (AI) in diagnosing conditions by contrasting its predictions with diagnoses made by board-certified otologic/neurotologic surgeons, using patient-described symptoms.

Study Design: Prospective Correlational Study.

Setting: Tertiary Care Center

Patients: 100 adults participated in the study. These included new patients or established patients returning with new symptoms. Individuals were excluded if they could not provide a written description of their symptoms.

Interventions: Summaries of the patients' current illnesses were supplied to three publicly available AI platforms: Chat GPT 4.0, Google Bard, and WebMD "Symptom Tracker" licensed by DXplain.

Main Outcome Measures: This study evaluates the accuracy of three distinct AI platforms in diagnosing otologic conditions by comparing AI results to diagnoses provided by three different otologic/neurotologic surgeons.

Results: AI-generated diagnoses were broad, non-specific, and often unrelated to diagnoses provided by physicians after thorough history-taking. As it stands, AI is not yet ready to be your doctor.

Conclusions: Contemporary language-model AI platforms can generate extensive differential diagnoses with limited data input. However, doctors are able to refine these diagnoses through focused history-taking, physical examinations, and clinical experience – skills that current AI platforms lack.

Professional Practice Gap & Educational Need: Recognizing the existing and prospective roles of AI in patient care is imperative for medical professionals, especially considering the large number of individuals who research medical details online, including potential diagnoses from their symptoms, before seeing a healthcare professional. Currently, AI does not possess the capability to fine-tune a differential diagnosis using patient-centric history-

Learning Objective: Clarify the accuracy and, consequently, the present role of AI as a diagnostic tool in medicine.

Desired Result: Physicians will cultivate an understanding of the role, benefits, and risks that AI can inadvertently present in diagnosis and patient care.

Level of Evidence: Level III

Indicate IRB: IRB 2079755, Advent Health, Orlando, Initial approval 10/10/2023

RESIDENT RESEARCH TRAVEL AWARD

Artificial Intelligence Tracking of Otologic Instruments in Mastoidectomy Videos

George S. Liu, MD; Sharad Parulekar; Trishia El Chemaly, MS; Melissa C. Lee, BS
Mohamed Diop, MD; Roy Park, MD; Nikolas H. Blevins, MD

Objective: Develop an artificial intelligence (AI) model to track otologic instruments in mastoidectomy videos.

Study Design: Retrospective case series.

Setting: Tertiary care center.

Subjects: 6 otolaryngology residents (PGY 3-5) and one senior neurotology attending with >25 years of experience.

Interventions: Thirteen 30-minute videos of cadaveric mastoidectomies were recorded by residents. The suction irrigator and drill were manually annotated. Videos were split into training (N=8), validation (N=3), and test (N=2) sets, and used to develop an AI model by adapting YOLOv8, a state-of-the-art object tracking model, to track the drill and suction irrigator.

Main Outcome Measure(s): Precision, recall, and mean average precision using an intersection over union cutoff of 50% (mAP50). Differential patterns of motion between resident and attending surgeon in two prospectively collected live mastoidectomy videos.

Results: The model achieved excellent accuracy for tracking the drill (precision 0.93, recall 0.89, and mAP50 0.93) and suction irrigator (precision 0.67; recall 0.61; and mAP50 0.62) in hold-out test videos. Prediction speed was fast (~100 ms per image) and included detection of when instruments were absent. Predictions on prospective videos revealed accurate tracking in attending and resident-performed surgeries and faster drill speed in the former (8.6 ± 5.7 mm/s versus 7.6 ± 7.4 mm/s, respectively; mean ± SD; $p<0.01$).

Conclusions: Our AI model can accurately track otologic instruments in mastoidectomy videos with high accuracy and near real time processing speed. Automated tracking opens the door to the automated analysis of objective metrics of surgical skill without the need for manual annotation and will provide valuable data for future navigation and augmented reality surgical environments.

Professional Practice Gap & Educational Need: Objective analysis of otologic surgical technique based on instrument tracks in recorded videos is limited by the time needed to manually annotate videos. With advances in AI technology, developing systems to automate the assessment of surgical techniques using computer analysis of surgical video recordings is feasible.

Learning Objective: Review existing and new applications of computer vision technology to quantitatively track and analyze otologic instrument motion in recorded videos.

Desired Result: Discuss the opportunities and limitations of applying computer vision technology to aid in the assessment of otologic surgical technique in recorded mastoidectomy videos.

Level of Evidence: IV

Indicate IRB or IACUC: Stanford University IRB #40945 approved 5/14/2019

SELECTED ABSTRACTS

POSTER PRESENTATIONS

IN ORDER OF PRESENTATION

157th Annual Meeting
AMERICAN OTOLOGICAL SOCIETY

May 17-18, 2024
Hyatt Regency Chicago
Chicago, IL

The Effect of Ventriculoperitoneal Shunts on Hearing: A Systematic Review

Emily Goodman, BA; Soroush Farsi, BS; Anna Bareiss, MD
Andrew Mangan, BS; John Dornhoffer, MD; Robert Saadi, MD

Objective: To review hearing outcomes following ventriculoperitoneal shunt (VPS) placement in the literature and to assess potential risk factors for hearing loss.

Data sources: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocol, PubMed was queried for articles published between January 1980 to January 2023 describing hearing outcomes related to ventriculoperitoneal shunts.

Study selection: Search terms used were "ventriculoperitoneal shunt", "hearing loss", and "hydrocephalus" in the title/abstract. Abstracts were screened with subsequent full-text reviews of relevant publications.

Data extraction: Extracted data was divided into two categories: VPS resulting in hearing loss, and VPS relieving hearing loss.

Data synthesis: Of 246 abstracts initially identified, 23 met inclusion criteria. 11 articles reported VPS causing hearing loss. 7 of these were case reports with 4 immediate and 3 delayed presentations of hearing loss after VPS. Two prospective cohort studies showed rates of hearing loss following VPS to be 38.9% and 64.5%. One cross-sectional study showed that 10/12 (83%) children with hydrocephalus and VPS had ipsilateral hearing loss. One retrospective study showed higher rates of hearing loss in children with medulloblastoma who received chemotherapy and VPS 13/13 (100%) as compared to chemotherapy alone 14/20 (70%). Conversely, 6 articles reported VPS relieving hearing loss in patients with hydrocephalus, with one prospective study showing 14/20 (70%) had improved hearing.

Conclusions: VPS has the potential to impact hearing, positively or negatively. Pre-operative audiograms should be considered. There should be a low threshold for audiology referral for postoperative hearing concerns. Further studies are needed to fully understand anatomic and physiologic factors impacting this delicate balance between CSF pressure and inner ear fluid homeostasis.

Professional Practice Gap & Educational Need: There is no comprehensive review of current literature that addresses hearing outcomes after ventriculoperitoneal shunt placement.

Learning Objective: To understand how cerebrospinal fluid pressures alter the inner ear homeostasis and how hearing is impacted by placement of a VPS.

Desired Result: Our goal is to educate practitioners on the potential consequences of VPS placement, allowing them to better counsel their patients and assess for post-operative hearing loss.

Level of Evidence – Level 3

Indicate IRB or IACUC: Exempt

Assessment of Modes of Anesthesia for Cochlear Implant Surgery

Phuong H. Bao, BS; David R. Friedland, MD, PhD; Jazzmyne Adams, MPH
Julie K. Freed, MD, PhD; Masoud Khani, BS; Jake Luo, PhD

Objective: Otologic surgery has specific anesthetic requirements such as avoiding nitrous oxide and permitting facial nerve monitoring. However, little evidence exists for selecting the best anesthetic agent and it is often left to anesthesiologist preference.

Study Design: Retrospective review of 600 primary cochlear implant surgeries and associated anesthetic variables.

Setting: Tertiary academic medical center.

Patients: Adult patients undergoing cochlear implant surgery over 10 years by a single surgeon.

Interventions: Anesthesia regimen: Balanced, Gas, TIVA (total intravenous anesthesia).

Main Outcome Measures: 1) Emergence Time, 2) Time in Phases of Recovery, 3) Anesthetic agents

Results: Among 600 cochlear implant surgeries, a balanced regimen was most commonly used (84.3%) with less often use of gas (13.5%) or TIVA (2.2%) alone. Average surgical time was 72.1±18.5 minutes. Emergence from anesthesia averaged 13.7±5.4 minutes and was shortest with the use of TIVA (11.9±4.6 minutes) and longest with only gas (14.2±5.3 minutes). Univariate analyses demonstrated no statistically significant correlation between anesthesia regimen and emergence time, time in recovery, and time in phase II. Multivariate linear regression showed significantly shorter emergence times with TIVA anesthetic regimen versus gas alone (coeff: -5.29, p=.0027). No difference was noted by sex, race, or ASA class. Interestingly, N20 was administered in 18.8% of cases at an average of 8.3±18.3% without effect on emergence time.

Conclusions: TIVA anesthetic regimen is associated with shorter emergence time than gas alone. These findings may inform best practice for anesthesia in otologic surgical cases.

Professional Practice Gap & Educational Need: Balanced, gas, and TIVA are currently administered in cochlear implant surgery. A gap exists in the understanding of the relative efficacy of each anesthesia regimen relating to patient recovery.

Learning Objective: Understand recovery rates for cochlear implant surgery in different age demographics, anesthetics, anesthesia staffing, and anesthetic regimen.

Desired Result: For physicians to use evidence-based information when administering anesthesia during cochlear implant surgery.

Level of Evidence - IV

Indicate IRB or IACUC: PRO00045896

Do Patients Treated with Teprotumumab Meet American Speech-Language-Hearing Association (ASHA) Criteria for Ototoxicity?

Oliwia W. Mlodawska, BS; Molly M. Murray, MD; Mami K. Sow, MD; Adam Thompson-Harvey, MD
Erin A. Harvey, MD; Gerald J. Harris, MD; Michael S. Harris, MD

Objective: To determine if patients receiving teprotumumab (TEPEZZA®) therapy for thyroid eye disease (TED) demonstrate hearing loss consistent with American Speech-Language-Hearing Association (ASHA) criteria for ototoxicity.

Study Design: Retrospective Cohort Study

Setting: Tertiary Care Academic Medical Center

Patients: Adult patients receiving infusions of teprotumumab for TED between January 1, 2020 and June 1, 2023.

Interventions: Baseline, intra-treatment, and post-treatment audiograms when available.

Main Outcome Measures: 1) Hearing loss consistent with ASHA criteria for ototoxicity after receiving teprotumumab treatment; 2) Effect of teprotumumab on low-frequency, high-frequency, or overall pure-tone averages; 3) Association of age, BMI, previously identified hearing loss, and prior exposure to ototoxic medication with post-treatment audiologic outcomes.

Results: Out of 79 patients treated with teprotumumab for TED at our institution during the study period, 18 patients completed a baseline and intra- or post-treatment audiogram sufficient for analysis. Seven of these 18 patients (38.9%) met ASHA criteria (>20 dB pure-tone threshold increase at one frequency or >10 dB at two consecutive frequencies from baseline) for ototoxicity. Median composite data showed statistically significant differences in high frequency ($p=0.036$) and overall ($p=0.018$) pure-tone average between baseline and post-treatment audiograms. The change in overall frequency between pre- and post-treatment was significant when considering age <65 or ≥65 years ($p=0.047$) and pre-existing hearing loss ($p=0.023$).

Conclusions: Seven patients undergoing teprotumumab treatment in our study with sufficient audiologic evaluation met ASHA ototoxicity criteria, suggesting that teprotumumab may contribute to sensorineural hearing loss. Scheduled audiometric testing during treatment is necessary to monitor symptoms and prevent hearing loss.

Professional Practice Gap & Educational Need: Teprotumumab is the first and only Food and Drug Administration (FDA)-approved drug for the treatment of TED, making it an attractive option to avoid surgical intervention. Despite earlier reports raising concern for treatment-associated hearing loss, currently no recommendations exist for audiologic ototoxicity monitoring for patients receiving teprotumumab treatment.

Learning Objective: To understand the potential of teprotumumab-induced ototoxicity in patients undergoing this route of intervention and to recognize the need for ototoxicity surveillance to avoid hearing loss.

Desired Result: For physicians to provide an evidence basis for patient counseling regarding risks associated with teprotumumab and support for consistent ototoxicity monitoring alongside teprotumumab therapy for TED.

Level of Evidence - IV

Indicate IRB or IACUC: Medical College of Wisconsin IRB #1538127

Round Window Electrocochleography in Genetic Causes of Hearing Loss: Pediatric Case Series

Vivian F. Kaul, MD; Meghan Hiss, AuD; William J. Rigss, AuD, PhD
Oliver F. Adunka, MD, MBA

Objective: To describe a case series of patients with common genetic mutations which result in severe-profound hearing loss leading to cochlear implantation.

Study Design: Case series

Setting: Tertiary care free-standing pediatric hospital

Patients: 4 pediatric patients

Interventions: Genetic testing for hearing loss, round window electrocochleography (EcoG), and cochlear implantation

Main Outcome Measures: Cochlear microphonic responses

Results: Case 1 is a GJB2 homozygous mutation of c.35DelG who's EcoG total response (TR) was 17.7 decibel (dB). Case 2 is also a GJB2 homozygous of c.35DelG but did not have enough responses recorded intraoperatively for a TR. There were responses bilaterally at both 500 and 1000 Hz at 90 dB but not at 70 dB. Case 3 is a TMPRSS3 homozygous mutation of c.208delC. Her EcoG findings revealed an EcoG-TR of 17.3 dB with most cochlear microphonic responses composed of 250-1000 Hz. Case 4 is a Pendred compound heterozygous of 707T>C (p.L236P) and c.1-5A>G. Her EcoG findings revealed an EcoG-TR of 14.7 dB. All 4 cases resulted in cochlear implantation with good hearing results.

Conclusions: All four cases suggest some degree of poor development of the cochlear hair cells. When compared to previous levels, EcoG-TR responses for auditory neuropathy and normal hearing reach 40-50 dB. The four cases suggest significant hair cell loss compared to patients with auditory neuropathy spectrum disorder and those with normal hearing, yet reasonable evidence of hair cell activity that could be amenable to potential future gene therapies.

Professional Practice Gap & Educational Need: Practicing cochlear implant surgeons should be aware that while the current therapy for pediatric severe to profound sensorineural hearing loss is cochlear implantation, that may not be the case going forward. It is imperative to get genetic testing on patients, and moreover, the utility of electrocochleography can showcase the function and status of existing hair cells.

Learning Objective: To understand that routine ABR or behavioral audiometry do not always reflect intactness of residual hair cells in the cochlea. Objective near-field recordings of cochlear activity (i.e., electrocochleography) can be utilized in patients with severe to profound hearing loss due to genetic forms of hearing loss, to determine the level of the residual hair cells remaining. This approach is likely to be critical for clinicians as developments in potential advanced therapies such as gene therapies continue to emerge in clinical trials.

Desired Result: Education for cochlear implant surgeons to pursue genetic testing on their pediatric patients with severe to profound sensorineural hearing loss and to also evaluate the status of the residual cochlear hair cells.

Level of Evidence - Level V

Indicate IRB or IACUC: Ohio State University Wexner Medical Center Institutional Review Board approved protocol number 2015H0045.

All That Jazz: Emotional Responses to Music Among Unilateral Cochlear Implant Users

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Meghan A. Despotidis, AuD; Scott Kelly, BS; Tiffany Hwa, MD
Anil K. Lalwani, MD

Objective: Emotional response to music following cochlear implantation, though central to music listening/enjoyment, remains poorly studied. In this study, we investigate emotional experience in single-sided deafness (SSD) and bimodal cochlear implant (CI) users.

Study Design: Cross-sectional analysis.

Setting: Tertiary academic center and community hearing loss groups.

Patients: SSD (N=13) and bimodal (N=23) cochlear implantees

Interventions: Participants listened (via an online survey) to ten previously validated 15-second musical clips representing multiple genres and wide range of valence (happiness vs. sadness) and arousal (excitement vs. calm) and rated the musical clips on validated nine-point visual analog scales of valence and arousal. Participants listened to each clip through implanted ear only, through non-implanted ear only, and through both ears simultaneously.

Main Outcome Measures: Range and error of valence and arousal.

Results: SSD participants demonstrated increased error in identifying each clip's valence (2.20 vs 1.46, p=0.01) and arousal (1.61 vs. 1.46, p=0.04) through their CI. Additionally, they experienced decreased range of valence (4.83 vs. 5.86, p=0.03) and decreased appreciation of low arousal (minimum arousal 2.18 vs. 1.63, p=0.04) when listening through their CI only compared to both ears together. Among bimodal participants, their error for valence and arousal was not significantly different across conditions. However, valence range was significantly lower when listening through CI only (4.59 vs. 5.77, p<0.001) compared with the both-ears condition, while arousal range was lowest in the hearing aid ear alone (4.89 vs. 5.81, p=0.01).

Conclusions: Unilateral cochlear implantees experience significantly different emotional response when listening through CI compared to NH or hearing-aided ear. This deficit likely contributes to reduced music enjoyment and represents a critical target for improvement.

Professional Practice Gap & Educational Need: While discrepancies in music perception and enjoyment are well-described among CI recipients, there is extremely limited research into emotional responses to music, and none that have included SSD participants. Given the centrality of emotion in music enjoyment, understanding this aspect of music listening could identify targets for improvement of music listening in CI users.

Learning Objective: To understand the effects of cochlear implantation on the ability to identify emotional content of a musical stimulus, and identify differences in emotional range in response to music between implanted and non-implanted ears.

Desired Result: To better illuminate potential deficits in a crucial aspect of music listening among CI users, paving the way for improved music enjoyment among this population.

Level of Evidence – Level III

Indicate IRB or IACUC: Columbia University Irving Medical Center Institutional Review Board (AAA43559).

Exploring the Association Between Secondhand Smoke Exposure and Hearing Loss Among U.S. Nonsmokers

Aashish Batheja, MPH; Daniel H. Coelho, MD

Hypothesis: Increased secondhand smoke exposure is associated with elevated hearing thresholds and greater odds for hearing loss in adult nonsmokers.

Background: Although tobacco usage is a well-established risk factor for hearing loss, secondhand smoke (SHS) exposure may also be implicated. However, there is a relative paucity of inconsistent findings with limited frequency-specific details. This study investigates the relationship between SHS exposure and hearing loss in adult nonsmokers in the U.S.

Methods: 1644 nonsmokers between ages 20 and 69 and without diabetes, stroke, or heart disease were isolated from the 2015-2016 National Health and Nutrition Examination Survey cycle. Serum cotinine level was used as a marker of SHS exposure. Outcomes included hearing thresholds at low-, mid-, and high-frequencies and hearing loss as defined by World Health Organization guidelines. Linear regression analyses between hearing thresholds and SHS exposure stratified by Body Mass Index (BMI) category and controlled for age, gender, race, income, and noise exposure. Logistic regression modeling hearing loss by SHS exposure controlled for the same.

Results: SHS exposure was associated with elevated hearing thresholds at low-frequencies ($p = 0.0329$) and mid-frequencies ($p = 0.012$), and only in the obese (BMI ≥ 30) population. SHS exposure was associated with greater risk of hearing loss (Odds Ratio: 1.163, 95% Confidence Interval: 1.053 – 1.285).

Conclusions: Although SHS exposure was associated with hearing loss overall, its relationship with hearing thresholds was not demonstrated across all hearing frequencies or BMI categories. Notably, SHS exposure was positively correlated with hearing thresholds at low- and mid-frequencies, and only in the obese population.

Professional Practice Gap & Educational Need: While published literature suggests there is a link between SHS exposure and hearing loss, an association is not consistently demonstrated across all frequencies and sample subgroups. There is a need to better understand the strength of this association and its clinical impact on patients. Additionally, the role of BMI in modulating the relationship between SHS exposure and hearing loss remains unclear and must be evaluated.

Learning Objective:

1. Characterize the relationship between SHS exposure and hearing loss among U.S. nonsmokers.
2. Discuss the potential for factors to modulate the relationship between SHS exposure and hearing loss.

Desired Result: Providers and researchers will better understand how SHS exposure may be related to hearing loss. Fostering discussion on this topic will encourage future studies that may further improve understanding in this area.

Level of Evidence - V

Indicate IRB or IACUC: Exempt

Correlation between Tinnitus and Life Stress

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Masoud Khani, BS; Jake Luo, PhD; Kristina Osinski, BS

Objective: To identify correlates of tinnitus severity including the characteristics of the tinnitus percept, measures of life stress, and auditory function.

Study Design: Retrospective cohort study

Setting: Tertiary Academic Center

Patients: Patients undergoing tinnitus evaluation at an academic Tinnitus Clinic between 2011 and 2022.

Interventions: None

Main Outcome Measures: 1) HR Stress inventory score, 2) THI/TRQ scores, 3) DPOAEs

Results: There were 785 patients (mean age 53.9±15.4, 52.6% male) undergoing tinnitus evaluation. Within this patient cohort, 76% reported having constant tinnitus. Whether the tinnitus was constant or intermittent as reported by patients had no correlation with HR stress scores or THI/ TRQ. Ringing was the most noted tinnitus sound in 52% of patients, followed by other (39%), buzzing (25%), tonal (11%), humming (10%), and static (9%). Patients that reported other tinnitus sounds had a higher HR stress level than those with more typical perceptions ($p=0.0009$). There was no correlation between the tinnitus sound and THI or TRQ. Normal high frequency right and left DPOAE's were statistically more likely to have a higher THI/ TRQ than DPOAEs that were absent/abnormal/uncertain ($p<0.05$). Ordinary Least Squares regression showed a statistically significant positive correlation of tinnitus awareness, TRQ, and THI scores with HR risk score. This score is a subcategorization of the overall HR stress score and predicts the risk of health issues from stress.

Conclusions: Validated measures of stress-related health risk correlate with tinnitus severity.

Professional Practice Gap & Educational Need: Tinnitus treatment is often associated with stress relief methods though the correlation between level of life stress and tinnitus severity is uncertain.

Learning Objective: Understand the importance of evaluating life stress in treating patients with complaints of tinnitus.

Desired Result: To increase the use of stress assessment tools in the treatment of patients with tinnitus.

Level of Evidence: IV

Indicate IRB or IACUC: IRB# 1538127; approved July 23rd, 2020

Age-Related Variations in Tinnitus Patient Profiles and Characteristics

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Objective: The diversity of tinnitus patient profiles often complicates tinnitus research and hinders result interpretation. This study investigates age-related factors among tinnitus patients' characteristics.

Study Design: Retrospective Case Review

Setting: Analysis of medical records at XXX National University Hospital

Patients: From January 2018 to March 2020, we conducted a screening of 421 consecutive patients (570 tinnitus ears) who had previously undergone Pure Tone Audiometry (PTA) up to 16kHz, psychoacoustic testing of tinnitus characteristics, including tinnitus frequency, loudness matching, minimum masking level, and residual inhibition after acoustic masking. In addition, we administered the Tinnitus Handicap Inventory (THI) and Visual Analog Scale (VAS) questionnaires, along with a supplementary questionnaire aimed at assessing associated factors such as subjective hyperacusis, headache, dizziness, neck or jaw pain, and psychiatric symptoms. Subsequently, we categorized these 421 tinnitus patients into three age groups: <30 years (n=111), 30-49 years (n=182), and ≥50 years (n=277).

Interventions: N/A

Main Outcome Measures: We compared PTA thresholds, psychoacoustic characteristics of tinnitus, THI scores, and VAS scores for subjective loudness, daily duration of awareness, annoyance, and impact on daily life in each age group. We also explored differences in the incidence of non-auditory factors, such as headaches, dizziness, neck or jaw disorders (potential somatosensory causes of tinnitus), psychiatric symptoms, and hyperacusis.

Results: The youngest group displayed the lowest pure-tone hearing thresholds and reported the lowest annoyance level, tinnitus loudness, and THI scores. Hyperacusis was most prevalent in the youngest group, with headaches and dizziness also frequently reported in this age category.

Conclusions: Our research highlights a notable disparity among tinnitus patients based on age, with those under 30 years old demonstrating significantly better hearing function and a higher prevalence of comorbid factors compared to their older counterparts. These findings underscore the potential benefits of implementing more comprehensive audiological assessments and exploring non-auditory factors in the management of tinnitus, particularly for younger patients.

Professional Practice Gap & Educational Need: Analyzing tinnitus patient characteristics across different age groups can help tailor management approaches based on age.

Learning Objective: Recognize distinct characteristics of tinnitus patients within different age groups.

Desired Result: Identify significant age-related factors for improved, individualized tinnitus management.

Level of Evidence: Level IV

Indicate IRB or IACUC: Institutional Review Board of Kangwon National University Hospital approved the study (IRB Approval: KNUH-2019-04-013-005).

Factors Driving Patient Selection of Cochlear Implant Brand

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David S. Haynes, MD, MMHC; Marc L. Bennett, MD, MMHC

Objective: To assess the factors that drive a patient's selection of cochlear implant (CI) brand.

Study Design: Prospective survey study.

Setting: Tertiary referral center.

Patients: 104 adult patients undergoing primary CI in 2023.

Interventions: Survey administered in the preoperative area.

Main Outcome Measures: Sources of information regarding CI brand offerings, factors that were most important in deciding on a brand, brand ultimately selected.

Results: 104 patients were included (average age 63 years, 96% White race). The most popular sources of information to help patients choose a device were their audiologist (80.7%), company promotional materials (28.8%), Google search (26.9%), and their surgeon (20.19%). When asked their #1 reason for choosing their CI brand, the three most commonly cited reasons were technology (50.5%), cosmetics of the wearable portion (14.5%), and audiologist recommendation of that brand (13.6%). Audiologist recommendation of a specific brand was a top 3 deciding factor for 32.7% of patients, while surgeon recommendation was for 10.6% of patients. Of the 15 patients who cited cosmetics as their most important factor, 13 of them selected Cochlear Americas. When analyzing aspects of technology that patients found important, iPhone compatibility was popular among Cochlear Americas recipients and hearing aid pairing was popular among Advanced Bionics recipients. No dominant motivating factor was noted for Med El recipients. 10.6% of patients were not aware of which brand of implant they were receiving.

Conclusions: Although patients access multiple sources of information to choose their CI brand, their audiologist is influential in this decision. CI manufacturers should be aware of patient priorities in designing and marketing their devices.

Professional Practice Gap & Educational Need: Better understanding of the CI brand choice decision can help deliver patient-centered care.

Learning Objective: To identify factors of importance to patients in choosing a CI brand.

Desired Result: Providers will have improved understanding of the factors that patients prioritize as they choose a device company. This can help in counseling patients in an unbiased and informed fashion.

Level of Evidence: Level IV – cross section study.

Indicate IRB or IACUC: IRB 221926 (Vanderbilt University).

Antioxidant Therapies in the Treatment of Aminoglycoside-Induced Ototoxicity: A Systematic Review

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Vivian F. Kaul, MD

Objective: To examine the effectiveness of antioxidant therapies in the treatment of aminoglycoside-induced ototoxicity in clinical trials.

Data sources: The databases Pubmed, Embase, Web of Science, and ClinicalTrials.gov were browsed for English-language articles published before July 2023.

Study Selection: This review sought randomized controlled trials conducted in humans discussing outcomes in aminoglycoside-induced ototoxicity following administration of antioxidants or medications intended to reduce oxidative stress.

Data Extraction: Each study was assessed for bias using the Cochrane risk of bias tool for randomized trials. Six criteria were assessed for each study.

Data Synthesis: NA

Conclusions: A literature search produced 1959 results, from which seven studies met our inclusion criteria. N-acetylcysteine was investigated in four studies, aspirin in two studies, and vitamin E in one study. Six studies examined the benefit of antioxidant treatments up to eight weeks after administration, while one study tested subjects' hearing after one year. In six of the seven studies, antioxidant therapy resulted in significant reduction of ototoxicity after administration of aminoglycosides. However, aspirin and N-acetylcysteine were much more effective at reducing ototoxicity than was vitamin E, which showed no prevention of aminoglycoside-induced ototoxicity compared to the placebo. The studies reviewed suggested that antioxidant therapies provide a promising therapeutic option for aminoglycoside-induced ototoxicity. Further study is necessary to examine whether aspirin and N-acetylcysteine provide long-term benefit.

Professional Practice Gap & Educational Need: Previous studies using animal models have suggested that myriad therapies targeting oxidative stress may prevent ototoxicity due to aminoglycosides. However, few clinical studies have evaluated treatments with this mechanism, and no studies have collectively evaluated these therapies in aminoglycoside-induced ototoxicity.

Learning Objective: To evaluate whether clinical benefits exist in the use of antioxidants for aminoglycoside-induced ototoxicity.

Desired Result: Encourage additional clinical and basic science research on therapies with a promising mechanism of action in treating aminoglycoside-induced hearing loss.

Level of Evidence – Level I

Indicate IRB or IACUC: Exempt

Levels of Inner Ear Biomarker, Otolin-1, are Related to Serum Calcium Levels

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Objective: We hypothesize that levels of the inner ear biomarker, otolin-1, are influenced by serum calcium levels.

Background: Otolin-1 is an otoconia scaffolding protein expressed exclusively in the inner ear. Previous studies demonstrated high blood levels of otolin-1 in patients with benign paroxysmal positional vertigo (BPPV), suggesting that otolin-1 may serve as an inner ear biomarker for otoconia disorders. Prior work suggests that calcium carbonate and endolymphatic calcium levels influence otoconia.

Study Design: Case series.

Setting: Tertiary Care Center.

Patients: Patients with primary hyperparathyroidism (PHPT), the epitome of calcium disorders, were recruited. A total of 32 PHPT subjects consisting of 24 females and 8 males were enrolled with age ranging from 18 to 86 years, with a mean and median of 56 and 59 years, respectively.

Results: Subjects had a mean otolin-1 level of 600.92 ± 427.37 pg/mL. Otolin-1 was weakly associated with ionized calcium (r^2=0.21). With vitamin-D as a covariate, otolin-1 was moderately associated with corrected calcium (r^2=0.44) and ionized calcium (r^2=0.35). There was no significant correlation between otolin-1 and parathyroid hormone.

Conclusions: Otolin-1 is elevated in the setting of high serum calcium levels, implying that systemic calcium metabolism may influence otoconia health. Further research is needed to identify factors that influence otoconia health and determine their potential role in the pathogenesis of BPPV. This research may aid in developing new management options to supplement traditional canalith repositioning.

Professional Practice Gap & Educational Need: BPPV is a common disorder with a lifetime prevalence of 2.4% and recurrence rate between 13-65%. The mechanism of pathogenesis is not understood.

Learning Objective: Understand how systemic calcium metabolism can potentially influence otoconia.

Desired Result: Further elucidate the role of calcium metabolism in BPPV pathogenesis.

Level of Evidence: Level V

Indicate IRB or IACUC: IRB #23-206-2 at UConn Health.

Increasing Utilization of Intratympanic Injections among Medicare Providers

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Objective: To characterize national practice patterns and geographic variations in intratympanic injections among Medicare providers

Study Design: Cross-sectional analysis

Setting: Medicare Part B Public Use Files

Patients: Medicare B fee-for-service patients undergoing intratympanic injections from 2013 to 2021

Interventions: intratympanic injections (Current Procedural Terminology code 69801)

Main Outcome Measures: The Medicare Physician & Other Practitioner Public Use Files were used to identify all providers who performed in-office intratympanic injections from 2013 to 2021. Intratympanic injections were trended geographically over time. Medicare reimbursement rates were also tabulated.

Results: A total of 159,236 in-office intratympanic injections were performed. The Center for Medicare & Medicaid Services reimbursed $25,407,086; out-of-pocket patient costs were $6,591,514. The mean Medicare reimbursement rate and out-of-pocket cost per injection were $159.56 and $41.38, respectively. From 2013 to 2021, the number of intratympanic injections increased from 13,117 to 20,711 injections, representing a 57.9% increase. On linear regression, an additional 989.9 injections were performed each year (95% CI 766.4–1213.4, $p<0.001$). The number of providers performing injections also increased from 1,828 to 2,834 from 2013 to 2021 (b = 125.6 [95% CI 111.3–140.0], $p<0.001$). The population-controlled annual mean number of injections varied substantially across the U.S., ranging from 12.0 injections per 100,000 beneficiaries in Oklahoma to 255.2 injections per 100,000 beneficiaries in Alabama.

Conclusions: The number of intratympanic injections administered in the Medicare population has increased from 2013 to 2021. There is variability in practice patterns and utilization of intratympanic injections among otolaryngologists in the United States.

Professional Practice Gap & Educational Need: epidemiology and variations in practice patterns regarding intratympanic steroid injections

Learning Objective: to understand geographic variations and temporal changes in intratympanic injection practice patterns

Desired Result: to encourage self-evaluation in one's own practice patterns and encourage additional research into epidemiology and variations in otologic care

Level of Evidence – IV

Indicate IRB or IACUC: Exempt

I Want It Out! An Assessment of Patient Motivation Behind Cochlear Implant Removal

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Edward E. Dodson, MD; Oliver F. Adunka, MD, MBA; Yin Ren, MD, PhD

Objective: To assess indications behind cochlear implant (CI) removal without subsequent re-implantation

Study Design: Historical cohort study

Setting: Academic tertiary referral center

Patients: Patients who underwent CI explantation between January 2013 and December 2022

Interventions: Explantation of CI device

Main Outcome Measures: Indications for and audiometric testing prior to CI explantation

Results: Within a cohort of 743 CI patients, 16 patients (2%) underwent CI explantation without re-implantation (median age 54-years-old, interquartile range [IQR] 33-79), and 21 (3%) underwent explantation followed by re-implantation. The median time between CI insertion and removal was 28.5 months (IQR 13.2-78.4). Six explantations were due to infectious complications: 2 patients (13%) did not undergo re-implantation given illness severity, 1 (6%) underwent simultaneous contralateral implantation, 1 (6%) experienced insurance barriers preventing re-implantation, and 2 (13%) were lost to follow-up. Ten patients underwent explantation without re-implantation for non-infectious indications. Of these, 6 patients (38%) reported headache, otalgia, tinnitus, or vertigo, 3 (19%) required repeated MRIs and desired avoidance of peri-imaging procedures, and 1 patient (6%) had poor audiometric outcomes due to cochlear ossification. Compared to the aforementioned re-implantation cohort, patients who underwent explantation without re-implantation performed worse on AzBio (35%, n=7 versus 49%, n=11; p=0.43) and CNC testing (27%, n=3 versus 66%, n=4; p=0.03) after initial successful implantation, with only the latter achieving statistical significance.

Conclusions: Patients undergo explantation for a variety of reasons, with ill-defined symptoms being the motive in the majority of cases. These desires are compounded by poor postoperative audiometric performance, which likely hinders the patient's desire to undergo re-implantation and may also serve as an indication for proactive clinician involvement to prevent this outcome.

Professional Practice Gap & Educational Need: The practice gap includes identification of trends and motivation behind cochlear implant explantation rather than re-implantation.

Learning Objective: The listener should be able to identify why patients may desire removal of their cochlear implant across specific indications for explantation.

Desired Result: These data can assist the clinician in preoperative discussions and help identify situations where earlier intervention could prevent device removal.

Level of Evidence – Level IV

Indicate IRB or IACUC: The Ohio State University IRB Protocol #2020H0457

Multisensory Loss and Depression in the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS)

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Jennifer A. Deal, PhD; Alison R. Huang, PhD

Objective: Multisensory loss is a potentially modifiable risk factor for depression, but population-level evidence is lacking. This study quantified the association between multisensory loss across four senses (hearing, vision, smell, touch) and depressive symptoms in older US adults.

Study Design: Cross-sectional.

Setting: Data (N=812) were from the ARIC-NCS and the Eye Determinants of Cognition study joint cohort (2016-2017), an observational study of older adults from Washington County, MD and Jackson, MS.

Patients: 812 participants with complete data on hearing, vision, olfaction, peripheral neuropathy, depression, and demographic and health covariates were included. Sensory loss was measured using objective tests (pure tone audiometry [hearing], Early Treatment of Diabetic Retinopathy Study chart [vision], Sniffin' Sticks tests [olfaction], and monofilament tests [peripheral neuropathy]). Multisensory loss was analyzed as a count (0-4).

Interventions: None**.**

Main Outcome Measures: Depressive symptoms were measured by the 11-item Center for Epidemiologic Studies Depression (CES-D-11) scale. Scores were modeled continuously. Ratio of depressive symptoms associated with number of sensory losses was assessed using covariate adjusted negative binomial regression.

Results: Of 812 participants (aged 71-93 years, 62.7% female, 58.6% White, 43.3% with higher than a high school education) 30.3% had one sensory loss, 31.4% had two, 17.6% had three, and 5.3% had four. Each additional sensory loss was associated with a 10% (Ratio of CES-D-11 Score: 1.10; 95% CI: 1.02-1.20) increase in CES-D-11 score in the fully adjusted model.

Conclusions: Multisensory loss is associated with depression in older adults. Clinical awareness of this association is valuable for promotion of mental well-being among patients with sensory loss.

Professional Practice Gap & Educational Need: While associations between single sensory loss and depression have been characterized, the association between multisensory loss (hearing, vision, smell, touch) and depression has yet to be investigated with population-level studies.

Learning Objective: To describe the association between multiple sensory losses (hearing, vision, smell, and touch) and symptoms of depression in older adults.

Desired Result: It is essential to increase clinicians' awareness of the association between multisensory loss and depression in older adults in the US, so they can identify early signs of depression in patients with multisensory loss and refer them for care.

Level of Evidence - Level III

Indicate IRB or IACUC: Johns Hopkins School of Medicine **(**IRB00311861) & Johns Hopkins Bloomberg School of Public Health (IRB00012998)

Cochlear Implantation in Pediatric Patients with Cochlear Nerve Deficiency: A Systematic Review and Meta-Analysis

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Zachary G. Schwam, MD; Maura K. Cosetti, MD

Objective: This study aims to evaluate pre- and post-operative speech and auditory outcomes of cochlear implantation (CI) in pediatric patients with cochlear nerve deficiency (CND).

Data Sources: Search queries were developed alongside a medical librarian and performed across Medline Ovid and Ovid Embase through November 2022. All languages were covered.

Study Selection: Any study of pediatric patients with radiographically confirmed CND who underwent CI was eligible for inclusion (n=460 studies). Studies were excluded if they did not include at least two patients with CND and CI. Review articles, non-English manuscripts, and studies without pre- and postoperative outcomes were also excluded.

Data Extraction: Extracted data included number of children with CND and CI (n=14 studies, 170 patients), demographic information, study characteristics, and results of speech perception and language development testing. Risk of bias assessment was completed using the Joanna Briggs Critical Appraisal Checklist for Case Series and Cohort Studies to assess quality and validity of included studies.

Data Synthesis: All scaled outcomes measuring auditory outcomes were quantitatively meta-analyzed. Outcomes were pooled using standardized mean differences (SMDs) and weighted using the inverse variance method. A random effects model was used to account for within- and between-study variance, and results were compared with a fixed effects model.

Conclusions: Indications for CI are progressively expanding as research demonstrates benefit in populations previously thought inappropriate. Our study contributes to this growing literature and demonstrates global postoperative improvement in speech and auditory outcomes in the pediatric CND population after CI (SMD 2.04, 95% CI 1.53–2.56).

Professional Practice Gap & Educational Need: Cochlear nerve deficiency (CND), characterized by absence or reduced caliber of the cochlear nerve, is commonly implicated in moderate-to-profound pediatric sensorineural hearing loss. While cochlear implantation (CI) was previously contraindicated in patients with CND, recent studies have demonstrated the potential for auditory response to CI in a subset of CND patients, though clinical outcomes remain variable. To the authors' knowledge, this is the first systematic review to assess the role of CI in pediatric patients with CND.

Learning Objective: This study aims to contribute to growing literature by comapring pre- and post-operative speech and auditory outcomes of CI in pediatric patients with radiologically confirmed CND, which may contribute to the future management of this patient population.

Desired Result: We hypothesize that pediatric patients with CND may experience improvement in speech perception and language development following CI, though these changes may be variable in specific subsets of patients.

Level of Evidence – Level III

Indicate IRB or IACUC: Exempt

Tegmen Defects and Otitis Media: A Case Series Supporting a "Two-Hit" Mechanism of Otogenic Meningitis

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Terry P. Murphy, MD; Samuel R. Barber, MD; Moisés A. Arriaga, MD

Objective: Propose bony tegmen defects in the setting of otitis media as a cause of otogenic meningitis

Study Design: Case series

Setting: Tertiary care

Patients: Fifteen sequential cases of bacterial meningitis with otitis media in 14 adult patients without prior surgeries to the involved ear, between 2017 and 2023

Interventions: CT temporal bone, surgical repair

Main Outcome Measures: CT findings, surgical findings, clinical course

Results: All 15 cases of bacterial meningitis with otitis media had tegmen defects on CT temporal bone (average age=63, standard deviation=14). Defects were surgically confirmed with middle cranial fossa repair in 14, each performed after their meningitis was successfully treated with intravenous antibiotics. One patient declined surgery. Ten cases had three or more tegmen defects. One case had a cerebral spinal fluid (CSF) leak and four had encephalic herniation. None had cholesteatoma or idiopathic intracranial hypertension. In one case, the tegmen defect was identified prior to the episode of meningitis.

Conclusions: In these sequential cases of otogenic meningitis, each had one or more defects of the tegmen. While circumstantial and requiring additional study, this series provides compelling support for the theory that exposing purulent middle ear secretions to bare, intact dura may be a substantial cause of otogenic meningitis, even in the absence of CSF fistula or encephalic herniation. We believe the simultaneous occurrence of (1) otitis media with (2) osseous tegmen defects to be a sufficient two-hit mechanism for otogenic meningitis.

Professional Practice Gap & Educational Need: Understanding causes of otogenic meningitis

Learning Objective: Identify the association between tegmen defects and osteogenic meningitis

Desired Result: Propose bony tegmen defects in the setting of otitis media as a significant cause for otogenic meningitis

Level of Evidence - Level IV

Indicate IRB or IACUC : LSU IRB#581

Postoperative Antibiotic Prophylaxis following Cochlear Implant Surgery in the United States

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Almut G. Winterstein, RPh, PhD; Patrick J. Antonelli, MD, MS

Objective: To determine prevalence and associated determinants of postoperative antibiotic prophylaxis following cochlear implant surgery

Study Design: Retrospective cohort study

Data Source: Merative™ Marketscan® commercial claims databases and Medicare Fee-For-Service data

Patients: Cochlear implant recipients, 2012-2018, with no cochlear implant surgery in the 6 months prior.

Main Outcome Measures: Antibiotic prophylaxis within 2 days following cochlear implant surgery

Results: Of 5,432 included patients (Marketscan: 3,531; Medicare: 1,901), 2,947 (54.2%) received postoperative antibiotic prophylaxis. 46% were males with an average age of 34 years (range 1 – 64) in the Marketscan cohort and 71 years in the Medicare cohort (18+). Age was a significant determinant of prophylaxis in the Marketscan cohort, with age 1-4 years being more likely to receive antibiotic prophylaxis compared to age 18-64 years (OR 4.84, 95% CI 3.66-6.39). Older children (12-17 years) were also more likely to receive antibiotics compared to adults (Marketscan OR 1.43, 95% CI 1.02-1.99). Significant regional differences in use of antibiotic prophylaxis were seen, markedly higher in the North Central compared to West region (Marketscan OR 2.28, 95% CI 1.79-2.90 and Medicare OR 2.75, 95% CI 1.85-4.10). Comorbidities, such as diabetes and immune deficiencies, had no impact on likelihood of antibiotic prophylaxis.

Conclusions: Postoperative antibiotic prophylaxis is commonly administered in cochlear implant recipients. Postoperative antibiotic prophylaxis prescribing appears to be nominally affected by patient factors. Further research is needed to assess drivers of such therapy and their impact on the risk of infectious complications following cochlear implant surgery.

Professional Practice Gap & Educational Need: It is not clear what factors drive postoperative antibiotic prophylaxis prescribing for cochlear implant surgery.

Learning Objective: To elucidate determinants of antibiotic prophylaxis use following cochlear implant surgery

Desired Result: Clinicians will more closely adhere to best practices with postoperative antibiotic prophylaxis use following cochlear implant surgery.

Level of Evidence – III

Indicate IRB or IACUC : University of Florida IRB201900262

Current Practices and Opinions on Auditory Training in Adult Cochlear Implant Recipients

James R. Dornhoffer, MD; Christine M. Lohse, MS; Terrin N. Tamati, PhD
Aaron C. Moberly, MD; Matthew L. Carlson, MD

Objective: To examine current practices/opinions of cochlear implant (CI) providers with respect to post-implantation auditory training

Study Design: Survey to the American Cochlear Implant Alliance

Setting: Electronic survey

Patients/respondents: 79 CI providers

Interventions: Survey reviewing current practice/opinions for post-implantation auditory training for adult CI recipients

Main Outcome Measures: Review of respondent practice environment and review of current usage/opinions on auditory training, including resources used and schedule of use.

Results: Most (79%) respondents reported working at academic centers, 34% at high-volume centers (>150 CIs/year), and 38% were surgeons. Considering practices/opinions, 99% recommend auditory training for adult CI recipients. For most (52%), training resources are provided to patients in a broad list of exercises from which a patient may select. For those (30%) who recommend a specific resource, this is generally a computer-based auditory training program (e.g.,AngelSound™). Regarding timing of training, median (IQR) preferred start-time was 0(0-1) months post-activation, sessions were preferably performed for 3(2-4) hours/week, and these continued for 12(6-12) months.
Recommendations for auditory training were fairly consistent between surgeon/nonsurgeon providers and by center volume. Non-surgeons more often had specific recommendations on training resources, benefits of music, and training condition (e.g.,contralateral ear plugged).

Conclusions: Despite a lack of clinical guidelines for adult post-implantation auditory training, a cross-sectional survey of providers' current practice/opinions demonstrates that these services are widely recommended and considered valuable. Training is almost universally patient-directed and believed to be most beneficial if started soon after activation. Interestingly, specific recommendations for which training approaches to use are not common, suggesting a gap in our knowledge of which resources are most efficacious.

Professional Practice Gap & Educational Need: Cochlear implantation is a valuable modality for the rehabilitation of hearing in patients with moderate-to-profound sensorineural hearing loss. However, beyond manipulation of programming, there exist few interventions to maximize implant outcomes. Auditory training may help to improve or hasten acquisition of speech recognition skills for new adult CI recipients. However, no standardized paradigm for auditory training exists for adults, and current opinions and practices are largely unknown.

Learning Objective: To explore current practices and opinions with respect to auditory training for new adult CI recipients.

Desired Result: Practitioners and researchers will recognize important trends in auditory training. Namely, they will see that auditory training is almost universally recommended for new adult CI recipients. Training is generally patient directed, with specific recommendations generally being for some form of computer-based auditory training. Training is also generally felt to be most beneficial when started soon after CI activation. These recommendations are largely consistent with only minor differences influenced by CI center volume and CI team role.

Level of Evidence – Level V: Survey of expert opinion

Indicate IRB or IACUC: Exempt

Barriers to Ototoxicity Monitoring in Head and Neck Cancer Patients Treated with Chemotherapy

Jena Patel, MD; Amiti Jain, BS; Jacob Beiringer, BS
Irina Middleton, AuD; Jacob B. Hunter, MD

Objective: To evaluate risk factors associated with failure to obtain pre-chemotherapy audiology evaluation in head and neck cancer (HNC) patients.

Study Design: Retrospective cohort study.

Setting: Tertiary academic center.

Patients: There were 182 patients treated with chemotherapy between March 2021 and June 2022 who were referred to audiology and contacted to schedule a baseline audiogram.

Main Outcome Measures: Main outcome measure was completion of a baseline audiogram. Post-treatment otologic symptoms and hearing aid uptake were also recorded.

Results: In our cohort mean age was 64 years; there were 133 males (73%). Cisplatin was used to treat 74% (n=135) of patients. When controlling for covariates, patients who received cancer treatment in a community setting and those with stage IV cancers were associated with failure to obtain a baseline audiogram (OR = 2.33, 95% CI = 1.21-4.47, p=0.011; OR = 3.41, 95% CI = 1.74-6.71, p<0.001, respectively). There was no significant difference in receiving a baseline audiogram based on age, gender, primary language, race, social deprivation index as determined by zip code, or insurance type (p>0.05). After treatment the most common patient-reported otologic symptoms were new-onset hearing loss (n=30, 16.5%) and tinnitus (n=8, 4%). Only 14.2% of patients (n=26) underwent a post-treatment audiogram; there were no significant predictors for post-treatment follow-up. Only seven patients acquired hearing aids.

Conclusions: Stage IV tumors and community-level cancer treatment may encumber patients' ability to obtain baseline audiogram before starting chemotherapy. Post-treatment audiogram and hearing aid utilization were low, thus emphasizing a need for interventions to improve long-term audiologic follow-up to decrease hearing loss in cancer survivorship.

Professional Practice Gap & Educational Need: Highlight gaps in head and neck cancer audiologic care and a need to improve post-treatment audiologic follow-up to diagnose and treat hearing loss in cancer survivorship.

Learning Objective: 1) Identify risk factors that may prevent head and neck cancer patients from obtaining a baseline audiology evaluation prior starting ototoxic chemotherapy. 2) Understand trends in post-treatment symptoms and follow up.

Desired Result: Findings from this study may inform interventions aimed at improving ototoxicity monitoring practices and reducing chemotherapy-induced hearing loss in cancer survivorship.

Level of Evidence – IV

Indicate IRB or IACUC: IRB 22E.298 Thomas Jefferson University Hospitals

Artificial Intelligence Versus Audiologist Generated Patient Education Materials for Tinnitus

Jena Patel, MD; Daniel Campbell, MD; Jacob Hulswit, AuD
Jacob B. Hunter, MD

Objective: To quantitatively compare patient education materials made by our audiology team versus artificial intelligence (AI) for tinnitus.

Methods: An audiologist created educational handout was compared to a ChatGPT generated handout containing responses to six common questions posed about tinnitus in September 2023. Validated metrics including Flesch-Kincaid Grade Level (FKGL), Flesch Reading Ease (FRE), Patient Education Materials Assessment Tool for printed materials (PEMAT-P), and Global Quality Score (GQS) were used to score each handout. Reviewers included three otologists and two audiologists; the handouts were distributed in a blinded fashion.

Results: Across both handouts (n= 30 graded answers), the ChatGPT handout had 27/30 answers (90%) and the Audiology handout had 21/30 answers (70%) with a GQS ≥4 (good quality); there was no significant difference in GQS between the two handouts (p= 0.10). Moreover, there was no significant difference in PEMAT-P score across all 17 scored domains between the two handouts (p= 0.17). The ChatGPT handout had a significantly higher grade level (FKGL) compared to the Audiology handout (14.47 ± 2.51 vs 12.12 ± 2.12; p= 0.002). Similarly, the ChatGPT handout had a significantly lower FRE score compared to the Audiology handout (25.28 ± 16.85 [college graduate level] vs 37.78 ± 15.47 [college level]; p= 0.01).

Conclusions: ChatGPT was able to create a well-organized and accurate patient handout for tinnitus education when compared to a traditional Audiologist made handout; however, both resources exceeded the recommended 6th grade reading level. As ChatGPT evolves it may serve as a valuable tool for creating accessible patient education materials.

Professional Practice Gap & Educational Need: To help physicians further understand the potential role for artificial intelligence in patient education.

Learning Objective: 1) Identify that artificial intelligence may be able to create patient educations materials comparable to the currently used materials. 2) Understand the impact artificial intelligence may have on the development of patient education materials in the field of otology.

Desired Result: To provide a critical evaluation of a commonly used AI platform for patient education on tinnitus.

Level of Evidence - V

Indicate IRB or IACUC: Exempt

Stapedectomy with a Dehiscent and/or Anomalous Facial Nerve

William B. Thedinger, MD; Chloe Verducci, BS; Matthew Kircher, MD
Sam Marzo, MD; John P. Leonetti, MD

Objective: To determine the rate of completed stapedectomy cases in patients with a dehiscent and/or anomalous facial nerve.

Study Design: Retrospective chart review

Setting: Tertiary care academic medical center

Patients: Patients who underwent stapedectomy or revision stapedectomy at our institution from January 2007 to December 2022.

Intervention: We analyzed stapedectomy or revision stapedectomy operative reports on patients with a dehiscent and/or anomalous facial nerve along with their pre and postoperative audiograms.

Main Outcome Measures: Outcome measures included surgical details, audiologic outcomes, and facial nerve complications.

Results: Seven hundred twenty stapedectomy cases were reviewed, of which 62.5% were female, with a mean age of 47. Of these patients, 61 (8.5%) had either dehiscent or anomalous facial nerves. There were no facial nerve related complications. Forty patients had completed pre and postoperative audiograms excluding 2 patients with prosthesis related complications and 1 with postoperative profound sensorineural hearing loss. The average preoperative air-bone gap was 33±8 (13-48) dB, with an average postoperative gap of 11±8 (0-31) dB.

Conclusions: Stapedectomy with a dehiscent or anomalous facial nerve can be safely completed with successful air-bone gap closure in select cases.

Professional Practice Gap & Educational Need: Based on prior studies, 11.4% of stapedectomy cases encounter a dehiscent facial nerve while 7% experience a prolapsed or “overhanging” nerve. Few studies have examined how these anomalies impact intraoperative approach and postoperative outcomes in stapedectomy cases.

Learning Objective: To describe successful stapedectomy in most cases with a dehiscent or anomalous facial nerve.

Desired Result: To report safe and successful air-bone gap closure of patients undergoing stapedectomy with a dehiscent or prolapsed facial nerve.

Level of Evidence: Level III

Indicate IRB or IACUC: IRB #216830, Loyola University Medical Center

Endoscopic Stapedectomy: Does Oval Window Packing Matter?

Maria A. Mavrommatis, MD; Jun Yun, BS; Jennifer Ren, BA; Maura K. Cosetti, MD
Enrique Perez, MD; George B. Wanna, MD; Zachary G. Schwam, MD

Objective: To determine whether audiometric or vestibular differences exist between three different approaches to oval window packing after endoscopic stapedectomy.

Study Design: Retrospective chart review

Setting: Academic tertiary care otology-neurotology practice.

Patients: Patients who underwent endoscopic stapedectomy years 2017-2023.

Interventions: Oval window reinforcement was performed with one of three techniques: lobular fat graft, promontory blood seal, or none.

Main Outcome Measures: Our primary outcome measures were postoperative vertigo and change in air-bone gap (ABG) and pure-tone average (PTA). Patient and surgical variables such as age, sex, laterality, surgeon, primary versus revision surgery, laser versus drill stapedotomy, degree of footplate drillout, and prosthesis type were secondarily investigated.

Results: 241 patients (mean age 47.4 +/- 13.0 years) were included for analysis, with 137 receiving promontory blood seal, 54 receiving fat graft, and 50 receiving no reconstruction. There was no difference in incidence of postoperative vertigo between groups (p>0.05). Similarly, average improvements in ABG and PTA were not significantly different between groups (p>0.05). There was also no significant difference in percentage of patients achieving ABG closure to within 10dB or within 20dB (p>0.05). There were no cases of postoperative profound sensorineural hearing loss.

Conclusions: There does not appear to be audiometric or vestibular consequences of oval window reconstruction with blood patch, fat graft, or no reconstruction at all in endoscopic stapedectomy.

Professional Practice Gap & Educational Need: Since the paradigm shift in otosclerosis surgery from complete stapedectomy to stapedotomy, the utility of packing around the oval window has been questioned.

Learning Objective: The practice of oval window packing may not have audiometric or vestibular consequences in endoscopic stapedectomy.

Desired Result: An understanding that the material used in oval window reconstruction after endoscopic stapedotomy, and even the existence of reconstruction itself, may not have any effect on audiometric or vestibular outcomes.

Level of Evidence - Level IV

Indicate IRB or IACUC: STUDY-22-01733

Hybrid Canal Wall Up Mastoidectomy with Intracanal Atticotomy

Michael S. Castle, MD; Matthew M. Carter, BS; Benjamin J. Greene, MD
Paul Allen, PhD; Paul O. Dutcher, MD

Objective: To determine the long-term efficacy of a hybrid technique (canal wall up and intracanal atticotomy (CWU-IA)) for the treatment of cholesteatomas.

Study Design: Retrospective case review.

Setting: Tertiary academic hospital.

Patients: Children and adults with cholesteatoma who underwent a CWU-IA by a single surgeon.

Interventions: Tympanomastoidectomy with a hybrid canal wall up and intracanal atticotomy without "bone bridge" preservation with or without ossicular chain reconstruction.

Main Outcome Measures: Disease recurrence rates, hearing outcomes (pure tone averages in speech frequencies (1000- 4000 Hz), speech recognition scores), need for second look procedures, and conversion rate to a canal wall down procedure.

Results: Eighteen patients underwent the CWU-IA procedure. Patients were followed for an average of 73 months (1-132 months). Two patients (11%) had recurrence of disease. Fourteen out of eighteen (78%) of patients had stable dry ears after surgery. Three patients (17%) ultimately required a canal wall down mastoidectomy, two for disease recurrence and one for suspected recurrence by another surgeon. Patients averaged about 5 dB of improved hearing on pure tone averages in speech frequencies.

Conclusions: The CWU-IA procedure is an option for treatment of cholesteatomas. It provides the benefits of in office surveillance of a high-risk region of cholesteatoma recurrence, without committing the patient to a canal wall down cavity, spares most patients a second procedure, and on average provides a modest improvement in hearing in most patients.

Professional Practice Gap & Educational Need: There is significant variation in management strategies for cholesteatoma (canal wall up vs canal wall down). There likewise are variable surveillance strategies (second look vs imaging). Each strategy has both pros and cons in disease control and patient quality of life. The CWU-IA procedure attempts to maximize the pros of each strategy while minimizing its cons. To date there is limited literature on the effectiveness of this approach.

Learning Objective: To describe the CWU-IA procedure for treatment and surveillance of cholesteatoma. To compare and contrast this treatment strategy to the current common strategies of attic cholesteatomas.

Desired Result: To describe another treatment and surveillance strategy for cholesteatoma management and discuss some potential benefits and limitations of this strategy with other more well-known strategies.

Level of Evidence - V

Indicate IRB or IACUC: IRB, URMC STUDY 00008668

Facial Nerve Dysfunction Severity Determination by Facial Recognition Software and Machine Learning

Lee M. Bauter, MD; Nolan Lwin; Nick Johnson; Bingnan Hao, BS
Keith W. Buffinton, PhD; Joshua V. Stough, PhD.; Arun K. Gadre, MD

Objective: We utilized computational image processing for the quantification of facial nerve dysfunction (FND). As proof-of-concept, we hope to construct a model that detects and quantifies facial landmarks while detecting and grading the severity of FND. Ultimately, we hope that an accessible computer-driven evaluation will eliminate biases which exist in the current assessment of these patients.

Study Design: Proof-of-Concept; Non-Randomized Control Trial

Setting: Otolaryngology Clinic; Computer Science/Mechanical Engineering Laboratory

Patients: Open-source data sets; Adult patients over the age of 18 years; Normal volunteers and patients with various degrees of unilateral FND.

Interventions: A constructed model will detect facial landmarks and features automatically. This model will assess images of patients with FND. Using topographical features and machine learning abilities, clinical grading will be performed.

Main Outcome Measures: Primary endpoint: the ability of the model to perform accurate facial landmark detection. Secondary endpoint: the ability of the model to detect the presence/severity of FND when compared to trained physicians.

Results: Utilizing computer software, we have processed open-source images and images of healthy volunteers. We demonstrated that a computer model in the form of a mobile application can quantify facial landmarks reliably. We are continuing to train the model to detect FND and grade its severity utilizing patient images.

Conclusions: Numerous grading systems have been developed to quantify the severity of the FND. The objective of this proof-of-concept study/non-randomized control trial is to eliminate the subjectivity from the diagnosis and treatment by utilizing an accurate and accessible computational machine learning model.

Professional Practice Gap & Educational Need: Subjectivity of diagnosis of FND. Need for further standardization for the diagnosis of FND.

Learning Objective: Discuss the current diagnosis of FND and the potential for utilization of an objective machine learning model for future diagnosis and treatment.

Desired Result: The development of an accessible computational model that can be widely used for the diagnosis of FND.

Level of Evidence: II

Indicate IRB or IACUC: GEISINGER IRB NUMBER: 2022-0746. IRB Approved: 06/28/2023

Systemic and Intratympanic Steroid Treatment for Limited Sudden Sensorineural Hearing Loss

Ryan C. Higgins, MD; Lina M. Adwer, BS; Geoffrey C. Casazza, MD
Anne K. Maxwell, MD

Objective: To compare treatment outcomes in patients who either did or did not meet NIDCD audiometric criteria for sudden sensorineural hearing loss (SSNHL).

Study Design: Retrospective cohort study of patients with SSNHL with a 30-dB loss over 3 consecutive frequencies (Group 1 "Full Criteria") or with more limited loss not meeting this criteria (Group 2 "Limited SSNHL") and were treated with oral and/or intratympanic steroids.

Setting: Single tertiary-care institution from January 1, 2017 – May 24, 2023.

Patients: Adults (≥19 years) with unilateral, audiometrically-confirmed SSNHL treated with high-dose oral prednisone and/or intratympanic dexamethasone injection.

Interventions: High-dose oral prednisone, intratympanic dexamethasone.

Main Outcome Measures: Post-treatment pure-tone average (PTA), speech reception threshold (SRT), word recognition score (WRS).

Results: 130 patients met inclusion criteria with 78 from Group 1 and 52 from Group 2. Group 1 had an average difference in PTA, SRT, and WRS after treatment of 19.1 dB, 21.6 dB and 30.2%, respectively. Group 2 had an average difference in PTA, SRT, and WRS after treatment of 6.3 dB, 6.3 dB, and 2.8%, respectively. The percent of patients who experienced WRS improvement was significantly greater in Group 1 (79.0%) than Group 2 (28.6%; $p<0.001$). The percent of patients who experienced improvement in PTA or SRT did not differ significantly between groups ($p=0.459$ and $p=0.278$; respectively).

Conclusions: Oral and intratympanic steroids should be considered for adult patients with SSNHL, regardless of whether or not they meet full NIDCD audiometric criteria. Future prospective studies may consider including these patients, thus expanding the potential recruitment pool.

Professional Practice Gap & Educational Need: Treatment for sudden sensorineural hearing loss in patients that do not meet NIDCD audiometric criteria.

Learning Objective: To discuss treatment outcomes for patients with limited SSNHL that do not meet strict audiometric criteria for SSNHL

Desired Result: To understand if patients with more limited SSNHL respond to steroid therapy, and whether these patients should be included in future research studies for SSNHL.

Level of Evidence – Level III

Indicate IRB or IACUC: IRB PROTOCOL # 0389-23-EP

Treatment Patterns of Complex Patients Dually Diagnosed with Vestibular Migraine and Meniere's Disease: A Retrospective Single-Center Cohort Study

Jennifer Ren, BA; Susmita Chennareddy, BA; Jennifer Kelly, PT; Andrea Feghali, NP
Maura K. Cosetti, MD; Zachary G. Schwam, MD; Enrique Perez, MD

Objective: To study the diagnostic and treatment complexity of patients with dual diagnoses of vestibular migraine (VM) and Meniere's disease (MD).

Study Design: Retrospective cohort study

Setting: Academic tertiary care otology-neurotology clinic

Patients: Adult patients with VM, MD, or both seen September 2021-September 2023

Interventions: N/A

Main Outcome Measures: Demographics, treatment patterns

Results: 338 patients were eligible (235 MD-only, 81 VM-only, and 22 dual-diagnosis). 22 patients were randomly selected in each cohort for preliminary analysis. Chi-square and Student's t-tests were used. The majority of VM or dual-diagnosis patients were female (p=0.02), but no significant differences existed for race, ethnicity, or insurance status. Dual-diagnosis patients were significantly more likely to receive diagnostic vestibular testing (p=0.004), though no significant difference existed for vestibular rehabilitation referral rates. Dual-diagnosis patients were on average prescribed significantly more medications (4.6) than single-diagnosis cohorts (2.4 MD-only, 2.6 VM-only, p <0.001), though there was no difference in number of medications between single-diagnosis cohorts. Only dual-diagnosis patients were managed with ablative or surgical treatment (n=4, p=0.01).

Conclusions: The diagnosis and management of vestibulopathy can be particularly challenging when overlapping VM and MD disorders exist. In our study, patients with dual diagnoses of VM and MD received more aggressive medical and surgical treatment than patients with VM or MD alone. Consistent with gender differences in migraine prevalence, the majority of VM and dual-diagnosis patients were female. Furthermore, all patients who received ablative/surgical treatment were female.

Professional Practice Gap & Educational Need: Given the overlapping clinical presentations between vestibular disorders, recent literature suggests that many vestibular disorders, including vestibular migraine (VM) and Meniere's disease (MD), exist on a continuum. Some patients with particularly complex constellations of symptoms may receive multiple diagnoses and increasingly aggressive clinical management. Additional studies are needed to better understand the demographic, diagnostic, and treatment profiles of dual-diagnosis vestibular patients.

Learning Objective: To identify patterns of diagnostic workup and treatment in patients diagnosed with VM and MD, which may contribute to better understanding of complex vestibular disorders.

Desired Result: Complex patients with dual diagnoses of VM and MD have different demographic patterns, receive increased vestibular testing, and receive more aggressive treatment than either of their single-diagnosis counterparts.

Level of Evidence - Level IV

Indicate IRB or IACUC: STUDY-22-01733, Mount Sinai Health System

Superior Results for Mastoidectomy with Obliteration Using Bioactive Glass versus Mastoidectomy Alone in treating Chronic Suppurative Otitis Media

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Rick van de Langenberg, MD, PhD; David R. Colnot, MD, PhD
Jasper J. Quak, MD, PhD

Objective: To present the outcomes of mastoidectomy with obliteration using S53P4 bioactive glass (BAG) for chronic suppurative otitis media (CSOM) and compare this to the results of mastoidectomy alone.

Study Design: Retrospective comparative cohort study

Setting: Single-center

Patients: Patients underwent canal wall up (CWU) or canal wall down (CWD) mastoidectomy with or without mastoid obliteration in the period 2005–2022 for CSOM. Other inclusion criteria were minimal six months of follow-up, otorrhea as main preoperative symptom and involvement of mastoid air cells, defined as opacification on preoperative CT imaging.

Interventions: Mastoid obliteration using S53P4 BAG

Main Outcome Measures: Otorrhea, indicated by the postoperative Merchant grade at most recent follow-up moment, and hearing outcomes

Results: In total, 164 cases underwent mastoidectomy with mastoid obliteration and 73 cases underwent mastoidectomy alone. The median follow-up time in years was 3.0 (IQR 1.4-5.2) and 3.2 (IQR 1.8-6.1), respectively. The dry ear rate at the most recent follow-up moment, as indicated by Merchant grade 0-1, was 95% (n=155) in the obliteration group and 67% (n=49) in the non-obliterative group (Odds ratio 8.4, 95%CI 3.7-19.4, $p<0.001$). In the obliteration group, no cases suffered from Merchant grade three, compared to 11 cases (15%) in the non-obliterative group. Hearing outcomes were comparable for both groups.

Conclusions: In cases of CSOM with mastoid involvement, obliteration of the mastoid cavity using BAG is associated with superior results compared to mastoidectomy alone.

Professional Practice Gap & Educational Need: Obliteration following both CWU and CWD mastoidectomy is gaining in popularity. However, comparative studies are lacking and therefore no standard of care can be determined. Additional education on the outcomes of obliterative techniques, especially in comparison with non-obliterative techniques are warranted.

Learning Objective: The differences in outcomes between obliterative and non-obliterative techniques for CSOM, with arguments in favor and against mastoid obliteration after mastoidectomy for CSOM.

Desired Result: That ENT-surgeons will consider utilizing mastoid obliteration following mastoidectomy in cases of CSOM with mastoid involvement.

Level of Evidence – III

Indicate IRB or IACUC : Exempt by Medical Research Ethics Committees United, reference number W21.162, date 22-02-2023

Superior Canal Dehiscence and the Risk of Additional Dehiscences: A Retrospective CT Cohort Study

Ahjeetha Shankar, BS; Nimesh Nagururu, BS; Monica S. Pearl, MD
John P. Carey, MD; Bryan K. Ward, MD

Objective: Determine if superior canal dehiscence (SCD) found on flat-panel CT increases the risk for other defects in the same otic capsule.

Study Design: Retrospective cohort study

Setting: Tertiary care center

Patients: 100 ears (50 with SCD and 50 matched controls without SCD).

Interventions: Flat-panel CT imaging

Main Outcome Measures: (1) Prevalence of other dehiscences in SCD ears, (2) Dehiscences in controls and (3) Otic capsule thickness in other reported dehiscence locations (cochlea-carotid, lateral semicircular canal (SCC) and mastoid, facial nerve-lateral SCC, vestibular aqueduct, posterior SCC-jugular bulb, posterior SCC-posterior fossa).

Results: There was a mean of 0.08 additional dehiscences in the SCD group (not including the SCD) and 0.06 in the controls. Four SCD ears (8%) had an additional dehiscence, while three controls (6%) were incidentally found to have a dehiscence ($p=0.70$). The most common location of the second dehiscence in ears with SCD was between the cochlea and carotid artery (n=3 ears) and between the facial nerve and lateral SCC in controls (n=2 ears). As a group, SCD ears had wider vestibular aqueducts (0.68mm±0.20mm vs. 0.51mm±0.30mm, $p<0.01$), and thinner bone between the posterior SCC and posterior fossa (3.12mm±1.43mm vs. 4.34mm±1.67mm, $p<0.01$). The bone between the facial nerve and lateral SCC was thicker in SCD ears (0.77mm±0.23mm vs. 0.55mm±0.27mm, $p<0.01$) and no different for cochlea-carotid, and lateral SCC and mastoid ($p>0.05$).

Conclusions: SCD does not increase the likelihood of a second dehiscence in the same otic capsule. Compared to controls, SCD patients may have congenitally smaller otic capsule bones, particularly near the posterior SCC, where the vestibular aqueduct may be enlarged.

Professional Practice Gap & Educational Need: Previous literature has reported multiple dehiscences in patients as occurring at high rates. However, using a flat panel CT that we have validated against surgical findings, patients with SCD are no more likely to have a second dehiscence than controls are to have an incidental dehiscence.

Learning Objective: Ascertain the prevalence of various types of dehiscence in SCD and control patients.

Desired Result: Gain a better understanding of the prevalence of various types of dehiscence in SCD and control patients and see what interventions may be most efficacious in treating these individuals.

Level of Evidence – Level III

Indicate IRB or IACUC: Johns Hopkins University School of Medicine, IRB #: IRB00279939, Approved 4/26/2021

A Description of Tool to Tissue Forces during Robotic-Assisted Mastoidectomy

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Yuxin Chen, MSE, BS; Manish Sahu, PhD; Russell H. Taylor, PhD
Deepa J. Galaiya, MD

Introduction: We have previously validated a force-sensing otologic drill used with a cooperative control robotic arm. Force sensing instruments can be used to measure tool to tissue forces and enforce virtual force barriers during robotic surgery. The forces typically applied by the drill to bone during a mastoidectomy have not been previously described. Here we use a validated force sensing otologic drill to measure the forces during mastoidectomy at various stages of the procedure.

Methods: Seven cadaveric temporal bones were drilled by three otologists. Mastoidectomy was divided into seven phases, and drilling forces were recorded. For each temporal bone, a CT scan was obtained at four time points to assess volume loss. After each temporal bone was drilled, subjects completed a survey consisting of the NASA Task Load Index and open-ended survey questions about robotic assistance for mastoidectomy.

Results: Drilling the cortex of the temporal bone generated forces of 1.18N$\pm$0.34N (mean$\pm$standard deviation), while drilling the trabeculated portion of the cortical mastoidectomy generated tool to tissue forces of 1.07N$\pm$0.33N. Thinning bone edges along the tegmen and posterior ear canal wall with a 6mm and 4mm cutting bur respectively generated forces of 0.95N$\pm$0.21N and 0.71N$\pm$0.15N. Opening the antrum generated forces of 0.84N$\pm$0.29N. Finally, identifying the facial nerve with a 3mm diamond bur and drilling the facial recess with a 2mm diamond bur generated forces of 0.85N$\pm$0.26N and 1.00N$\pm$0.31N respectively. At all stages of the procedure, the volume of bone removed for each Newton-second of applied force was 0.01cm^3/N, indicating a constant bone milling rate. Survey results showed minimal perceived temporal demand and frustration with robotic-assisted mastoidectomy at 20/100$\pm$3.54/100 and 39/100$\pm$29.03/100 respectively.

Conclusions: We employed a validated force-sensing drill to characterize the tool-to-tissue forces in robot-assisted mastoidectomy with 0.01N precision, the first reported description of drilling forces in mastoidectomy.

Professional Practice Gap & Educational Need: Tool-to-tissue force characterization is necessary for the development of virtual force barriers and higher fidelity haptic feedback during robot-assisted surgery.

Learning Objective: Quantify the forces exerted at each stage of the mastoidectomy procedure by OHNS surgeons of various levels of training.

Desired Result: By understanding the actual forces exhibited during critical stages of a mastoidectomy, more accurate haptic feedback and force limitations can be developed and applied force can be translated to obtain desired performance in robot-assisted otologic surgeries.

Level of Evidence - Level V

Indicate IRB or IACUC: Johns Hopkins University School of Medicine, IRB # IRB00326913, Approved 10/6/2022.

Active Transcutaneous Bone-Anchored Auditory Implants: Surgical and Audiologic Outcomes

Darius Kohan, MD; Ilana Yellin, MD

Objective: To assess surgery and hearing outcomes after implantation with most recent FDA approved active transcutaneous bone-anchored hearing devices.

Study Design: Retrospective cohort study.

Setting: Tertiary academic otology-neurotology practice including ambulatory surgery center.

Patients: Adults 18 or older with hearing loss meeting criteria for active transcutaneous bone-anchored auditory implants having failed non-surgical options from April 2019 to March 2023.

Interventions: Implantation of one of two active transcutaneous bone-anchored hearing devices.

Main Outcome Measures: Percentage of maximum potential gain achieved in pure tone average (PTA4), qualitative patient satisfaction Abbreviated Profile of Hearing Aid Benefit (APHAB), dural or sigmoid sinus exposure/compression, use of lifts, implant location, surgical and postoperative complications.

Results: There were 44 patients undergoing implants during the study period performed by the same surgeon/audiologist team. 23 patients met the study criteria. 9 patients had the Cochlear Osia OSI200 (Sidney, Australia) designated "IO," 14 patients had the MED-EL BONEBRIDGE BCI 602 (Innsbruck, Austria) designated "IB." 61% of patients chose IB due to its size and MRI compatibility. There were overlapping etiologies for hearing loss, most common being: cholesteatomas (48%), chronic suppurative otitis media (26%), single sided deafness (13%), and otosclerosis (13%). 17 procedures were performed concurrent with other otologic interventions. IB: required lifts in 3 patients, bony island dural compression occurred in 4 patients, 3 placements were retro sigmoid. The only complication was with one IB patient 3 weeks post-surgery requiring explant and reimplant a few months later. Percentage of maximum potential PTA4 gain was 57% for SSD regardless of implant type, 52% with IO and 75% with IB for pure conductive hearing loss (CHL), and 100% with both implants for mixed hearing loss (MHL). Otosclerosis patients had overclosure with both devices driving better outcome. Excluding them brings the rate for MHL to 70% regardless of device. Cosmetic issues of prominent implant profile occurred in 2 IO patients. All patients had measurable audiologic benefits from implants, with overall patient satisfaction at 78% and APHAB score better for IO versus IB. One IO and 1 IB are non-users.

Conclusions: Both IO and IB provide excellent auditory benefit (including both high and low frequencies) in patients not amenable to aural rehabilitation with standard amplification. Surgical complications are very low. Devices size, MRI compatibility, and finances prefer IB. Auditory outcomes are better in patients with conductive or mixed hearing loss versus sensorineural deficits.

Professional Practice Gap & Educational Need: Challenges in constantly evolving technology on implantable active bone-conduction auditory devices relative to indications, applications, surgery, risks and audiologic benefits to be derived from different devices.

Learning Objective: 1. Understand indications for different active transcutaneous bone-anchored hearing devices. 2. Learn surgical techniques and risks associated with these devices. 3. Learn the audiologic benefit and patient satisfaction with these devices.

Desired Result: For otolaryngologist and audiologists to become familiar with the surgical and audiologic indications for active transcutaneous bone-anchored hearing devices, to become familiar with the surgery associated with them and the risks involved, and to have realistic expectations on the audiologic benefits and limitations.

Level of Evidence: Level IV

Indicate IRB or IACUC: IRB # 22-0342 Approval of Hofstra Medical School, Northwell Health

Postoperative Middle Ear Effusion is Rare following Middle Cranial Fossa Spontaneous Cerebrospinal Fluid Leak Repair

Evan Cumpston, MD; William Zhang, BS; Douglas J. Totten, MD, MBA
Charles W. Yates, MD; Rick F. Nelson, MD, PhD

Objective: Assess the rate of unilateral middle ear effusion (MEE) at 1 month after middle cranial fossa (MCF) repair in patients with spontaneous cerebrospinal fluid (sCSF) leaks.

Study Design: Retrospective cohort

Setting: Tertiary referral center

Patients: Patients with sCSF leak who underwent MCF repair

Interventions: MCF sCSF with bone cement, one-month postoperative exam, and audiogram

Main Outcome Measures: Middle ear effusion 1 month postoperatively, preoperative and postoperative audiometry.

Results: 66 patients underwent sCSF leak MCF repair with bone cement from 8/2019-3/2023. Mean post-operative follow-up was 229 (±307) days and there were no recurrent unilateral leaks. On one-month postoperative otomicroscopy, 65 (99%) had no MEE. One patient had mucoid drainage from a tube and after removal, there was no MEE at 2-month follow-up. There was significant improvement in mean PTA (12.17 [10.6] dB; $p < 0.001$; Cohen $d = 0.95$) and ABG (14.8 [9.3] dB; $p < 0.001$; Cohen $d = 0.88$) after repair. 96% of preoperative tympanograms were type B, 93% of postoperative tympanograms were type A. Average age was 56 (±11.6) years and 67% were female with an average BMI of 38.89 (±9.9) kg/m2. Only 2 (3%) had a history of previous ear disease including prior unilateral tympanoplasty and recurrent otitis media, yet neither had active chronic ear disease at the time of evaluation. 5 patients developed a contralateral sCSF leak.

Conclusions: Prior ear disease is rare in sCSF leak patients. CSF effusion is extremely rare after MCF repair with bone cement and significant audiometric improvement is expected.

Professional Practice Gap & Educational Need: The rate of concomitant Eustachian tube dysfunction and sCSF leak is unknown. This study describes the rate of MEE following MCF sCSF leak repair.

Learning Objectives: Postoperative MEE is rare following MCF repair of sCSF leaks

Desired Results: Define the rate of postoperative MEE after MCF repair of sCSF leaks.

Level of Evidence: IV

IRB: Indiana University IRB #1907071217.

A Multi-Institutional Review of the Impact of Social Determinants of Health on Vestibular Schwannoma Management

Objective: Evaluate the effect of social determinants of health (SDoH) on initial treatment recommendations for vestibular schwannoma (VS).

Study Design: Retrospective Muti-institutional Review

Setting: 8 tertiary referral centers

Patients: 4,350 patients with sporadic VS newly diagnosed between January 1, 2010, and December 31, 2020.

Interventions: Treatment recommendation including surgical management, radiation therapy, or observation

Main Outcome Measures: Differences in initial treatment recommendation as influenced by various SDoH including age, race, ethnicity, insurance status, and area deprivation index (ADI)

Results: When individual determinants were examined for overarching patterns of treatment recommendations, slight differences were seen across several SDoH. As national ADI increased (indicating increasing disadvantage), recommendation for radiation decreased. Dimensionality reduction of SDoH alongside factors such as hearing status, tumor size, tumor location, and Charlson Comorbidity Index was performed with principal component analysis to visualize data clustering. Age was found to be the major factor which influenced clustering of data into treatment groups. Machine learning modeling using random forest was also applied to the data in comparison to standard statistical modeling. Hearing status, tumor characteristics, and SDoH were considered in parallel in the analysis. Preliminary analysis showed stronger influence on treatment recommendation from age in both models and tumor size in the machine learning model. Potential contribution from other SDoH on data trends was small.

Conclusions: While several small differences in treatment recommendations for patients with VS were seen in the overall view of the data, the data clustering indicates a lack of strong influence from SDoH except for age. However, limitations in this dataset including uneven distribution of patients across SDoH groups may affect the data modeling. Further investigation is necessary to better understand the implication of these findings on patient outcomes and guide how these factors should be considered when managing patients.

Professional Practice Gap & Educational Need: The effect of SDoH on treatment recommendations for VS is not well defined.

Learning Objective: Understanding if SDoH influence physicians' treatment recommendations for VS.

Desired Result: Identification of any social determinants which affect the treatment recommendation patterns for VS.

Level of Evidence - Level III.

Indicate IRB or IACUC: Exempt

Otologic Benefits of High-Fidelity Earplug Use at Social Music Venues

Matthew E. Lin, MD; Ryan Long, MD; Oluwatobiloba Ayo-Ajibola, BS (presenter)
Eric X. Wei, MD; Janet S. Choi, MD, MPH; Joni K. Doherty, MD, PhD

Objective: Identify differences in hearing-related beliefs, exposure history, and otologic symptoms between those who use high-fidelity earplugs (HFE) and other hearing protection (OHP) modalities.

Study Design: Cross-sectional survey.

Setting: Online music communities.

Patients: Adult community participants.

Interventions: Diagnostic survey.

Main Outcome Measures: Otologic symptoms following hearing protection use at music events.

Results: Respondents (n=2,352) were primarily male (61.26%), white (71.52%), and young (mean age (S.D.)=28.68 years (6.95)). Among hearing protection users, HFEs were the most used (57.49%). HFE users were more likely than OHP counterparts to cite experiencing hearing-related symptoms after event attendance ($p<0.001$), non-impact on music quality ($p<0.001$), and accessibility ($p<0.001$) as why they used hearing protection. HFE users were less likely than OHP users to report difficulty hearing others ($p<0.001$), difficulty hearing high-pitched sounds ($p<0.001$), and dizziness/loss of balance ($p=0.002$) after events. Relative to OHP users in a multivariable logistic regression, HFE users were less likely to be female ($p=0.044$) and primarily attend country ($p=0.020$), hip-hop/R&B ($p<0.001$), and pop ($p=0.013$) events relative to electronic music events.

Conclusions: HFEs, a convenient alternative to OHPs, may offer users increased protection without affecting subjective music enjoyment.

Professional Practice Gap & Educational Need: Hearing protection use at social music venues is understudied despite these events' popularity and propensity for causing noise-induced hearing loss. HFEs, reusable options that attenuate noise exposure by 20 dBA while anecdotally preserving sound quality, are similarly understudied.

Learning Objective: After this presentation, readers should understand the otologic benefits of HFEs and factors associated with HFE use.

Desired Result: Increased awareness of HFEs may encourage healthier hearing habits among music venue attendees.

Level of Evidence: III

Indicate IRB or IACUC: University of Southern California IRB #UP-22-00936 (11/10/2022).

Charcot Marie Tooth Disease and Hearing Loss: A Systematic Review with Meta-Analysis

John F. Mills, BS; Luke D. Heiland, BS (presenter); Shaun A. Nguyen, MD
Michaela F. Close, MD; Ted A. Meyer MD, PhD

Objective: To characterize the pattern of hearing loss in Charcot Marie Tooth Disease (CMT) to help guide clinical management.

Data sources: A systematic review of CINAHL, PubMed, and Scopus databases was conducted according to PRISMA guidelines from inception to July 31, 2023.

Study selection: Two independent investigators ultimately selected 6 prospective studies (N=197) on patients with pure tone average (PTA) and auditory brainstem response (ABR) data. Case reports, case series <5 patients, and data that overlapped with another study were excluded.

Data extraction: Two independent reviewers performed data extraction, quality rating, and risk of bias assessment using the Newcastle-Ottawa Scale.

Data synthesis: Meta-analysis of mean difference using fixed/random effects models was used. Also, significant differences between objective measures were analyzed using a weighted one-way analysis of variance, with post-hoc Tukey's test for comparison.

Results: CMT4C had significantly worse hearing as measured by PTA when compared to CMT1A (Δ 28.93 dB, 95%CI 18.34 to 39.52) and CMT2A groups (Δ 28.3 dB, 95%CI: 15.98 to 40.62). For the CMT1A subtype, there were significantly prolonged ABR latency values across wave III (0.20 ms, 95%CI: 0.05 to 0.35), wave V (0.20 ms, 95%CI: 0.01 to 0.39), wave I-III (0.20 ms, 95%CI: 0.01 to 0.39), and wave I-V (0.20 ms, 95%CI: 0.01 to 0.39) when compared to controls.

Conclusions: Patients with CMT generally have normal hearing thresholds, apart from the CMT4C subtype which presents with mild hearing loss on average. The ABR interpeak latency values for some CMT subtypes are delayed when compared to controls, possibly indicating a central brainstem processing delay.

Professional Practice Gap & Educational Need: Patients with CMT have been shown to have varying patterns of hearing loss. A better characterization of this hearing loss can help guide clinical management.

Learning Objective: To better understand the pattern of hearing loss in patients with CMT. Often, patients can present with complaints of hearing with otherwise normal audiograms.

Desired Result: The use of technologies that can improve sound discrimination in noisy environments most likely offer the greatest benefit for these patients, although individual subtypes of CMT may require additional amplification or interventions.

Level of Evidence – Level II

Indicate IRB or IACUC: Exempt.

Teprotumumab and Hearing Loss in Patients with Thyroid Eye Disease: A Population Database Study

Bryce Hambach, BS; Natalie M. Perlov, BS; Zachary D. Urdang, MD, PhD
Thomas O. Willcox, MD; Dennis Fitzgerald, MD
Rebecca C. Chiffer, MD; Jacob B. Hunter, MD

Objective: To explore whether patients with thyroid eye disease are more likely to develop sensorineural hearing loss (SNHL) after teprotumumab treatment compared to patients with standard of care.

Study Design: Retrospective cohort study with propensity score matching.

Setting: TriNetX Research Network (2004-2023).

Patients: Approximately 215,145 adult patients with thyroid eye disease and no prior hearing loss or exposure to ototoxic medications.

Main Outcome Measures: Patients were divided into two cohorts based off of teprotumumab treatment. The primary outcomes of interest were diagnosis of SNHL and other conditions of the inner, middle, and external ear within 1.5 years of teprotumumab or control exposure. Cohorts were balanced using propensity-score matching (PSM) based on demographic variables and SNHL-related comorbidities, including diabetes mellitus and ischemic diseases. $P<0.05$ was set as the threshold for statistical significance.

Results: A 1:1 PSM analysis showed the teprotumumab cohort ($n=654$) had 6.69-increased odds [OR:95%CI, p] for developing all HL (6.69: 3.40-13.1, $p<0.0001$) compared to controls ($n=654$). Specifically, patients who received teprotumumab had 3.71-increased odds for developing bilateral SNHL disease (3.71: 1.82-7.53, $p<0.0001$) compared to controls.

Conclusions: Our study suggest patients with thyroid eye disease treated with teprotumumab had a significantly greater risk of developing hearing loss compared to those without teprotumumab exposure. Our study is the largest study to date looking at this association. These findings underscore the need for hearing screening and workup in these patients to manage unintended immune-related adverse events.

Professional Practice Gap & Educational Need: The prevalence of thyroid eye disease in the US adult population is 0.25%, with significant morbidity and mortality surrounding sight and aesthetic functional concerns. Biologic therapies, like teprotumumab, are used to manage the disease and may impact hearing health. Previous studies in this area lack controls and are limited by small sample sizes. This study is the largest to date; increased data on the otologic effects of these therapies may have important implications for management of patients afflicted by thyroid eye disease.

Learning Objectives: 1. Understand the association of hearing loss with teprotumumab for thyroid eye disease. 2. Guide clinicians to consider screening at-risk patients for these sequelae to manage otologic care.

Desired Result: 1. Increase awareness of unintended side effects of biologic treatment for thyroid eye disease on hearing health. 2. Inform clinical management and screening of these patients to optimize hearing health.

Level of Evidence – Level III

Indicate IRB or IACUC: Exempt

Ototoxicity in Cancer Patients Undergoing Immune Checkpoint Inhibitor Therapy: A National Database Study

Pablo Llerena, BS; Bryce Hambach, BS; Kathryn Nunes; BS
Praneet Kaki, BS; Jena Patel MD; Jacob B. Hunter MD

Objective: This study aims to investigate the impact of immune checkpoint inhibitor (ICI) therapy on the audiovestibular system in cancer patients.

Study Design: Retrospective cohort study design using the TriNetX clinical database.

Setting: TriNetX, a global research database with approximately 110 million patients.

Patients: Patients were categorized into three distinct groups: those diagnosed with lung and esophageal cancer (LEC), head and neck cancer (HNC), and melanoma. Cancer patients who received pembrolizumab post-diagnosis were compared to patients with the same diagnoses who had not received ICI treatment (cemiplimab, avelumab, atezolizumab, nivolumab, and durvalumab). The study excluded patients with prior exposure to cisplatin, aminoglycosides, or furosemide, and those with a history of hearing loss. Propensity score matching (PSM) was employed to account for 21 covariates.

Interventions: Observational

Main Outcome Measures: Odds ratios (OR) for developing sensorineural hearing loss (SNHL), vertigo, and dizziness within three months for cancer patients who received pembrolizumab

Results: Following PSM, patients with LEC who received pembrolizumab (n=6,131) exhibited an increased risk of developing vertigo and dizziness with an OR of 1.9 (95% CI: [1.3-2.7]). Similarly, those with melanoma (n=6,213) and HNC (n=2,679) receiving pembrolizumab also showed an increased risk of vertigo and dizziness: (3.1, [2.1-4.6]) and (1.4, [1.1-3.2]), respectively. However, cancer patients receiving pembrolizumab did not demonstrate an increased risk of SNHL: LEC, (0.7, [0.3-1.5]); HNC, 0.6, ([0.3-1.4]); and melanoma, 0.8, ([0.5-1.1]).

Conclusions: Employing PSM using a large global research database, pembrolizumab is linked to the development of vertigo and dizziness, but not with SNHL.

Learning Objective: Examine the impact of pembrolizumab therapy on the audiovestibular system in cancer patients.

Desired Result: Better understand the ototoxic effects of ICI in cancer patients.

Level of Evidence – III

Indicate IRB or IACUC: Exempt.

Exacerbation of Preexisting Otologic Conditions following COVID-19 Infection

Omer Baker, BS; Víctor de Cos, BS; Timothy J. Sears, BS; Olivia La Monte, BS
Omid Moshtaghi, MD; Peter Dixon, MD; Jeffrey P. Harris, MD, PhD

Objective: We aim to investigate whether pre-existing otologic conditions increase the likelihood of otologic symptom incidence and severity following COVID-19 infection.

Study Design: Retrospective review

Setting: Single tertiary care center

Patients: This study investigated patients ≥18 years of age who tested positive for COVID-19 infection between January 2020 and September 2022; of these patients, 63.2% were female, 87.5% were white, and the mean age was 58 years.

Interventions: Surveys were administered to patients ≥18 years of age who tested positive for COVID-19 infection between January 2020 and September 2022.

Main Outcome Measures: Incidence of otologic symptoms immediately following COVID-19 infection was compared between participants with a pre-existing otologic condition and control participants.

Results: Of 1,499 patients who tested positive for COVID-19, 721 (48%) reported a pre-existing otologic condition, with loss of hearing (25.5%) and history of dizziness (18.8%) being most highly represented among this sub-cohort. Individuals were more likely to report dizziness post-COVID-19 infection if they had a pre-existing history of dizziness (29.1% vs 17.8%, $p < 0.001$) or pre-existing history of vestibular neuritis (58.8% vs 19.5%, $p < 0.001$) than those who did not. Similarly, individuals with a history of vestibular migraine were more likely to report migraine symptoms post-infection than those who did not (27.9% vs. 7.2%, $p < 0.001$). Of patients with a pre-existing condition, 35.5% subjectively reported that they believed COVID-19 infection had worsened otologic symptoms of their condition.

Conclusions: These findings indicate that certain preexisting otologic conditions may be associated with a greater likelihood of exacerbation following COVID-19 infection and may help guide treatment protocols for those at greater risk.

Professional Practice Gap & Educational Need: Currently, there is a very limited clinical understanding of the relationship between COVID-19 infection and pre-existing otologic symptoms.

Learning Objective: The learning objective is to evaluate the effects of COVID-19 infection on certain preexisting otologic conditions.

Desired Result: The aim of this presentation is to inform physicians of the exacerbating symptoms that may arise for patients with preexisting otologic conditions that experienced COVID-19 infection, which can potentially improve patient counseling.

Level of Evidence – Level IV

Indicate IRB or IACUC : UCSD-Clinical & Translational Research Institute (CTRI) PID#4325

Preoperative Hearing Aid Use Associated with Device Usage after Cochlear Implantation

Natalie Schauwecker, MD; Ankita Patro MD, MS; Connie Ma, MD; Nathan R. Lindquist, MD
Michael H. Freeman, MD; David S. Haynes, MD; Elizabeth L. Perkins, MD

Objective: Device usage contributes to improved cochlear implant (CI) outcomes. This study aims to identify whether preoperative hearing aid (HA) use affects postoperative device usage in hearing preservation (HP) candidates.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 404 Adult HP CI recipients from 2012 to 2022.

Main Outcome Measures: Device usage at 1, 3, 6 and 12 months.

Results: Hearing aids were worn preoperatively in 279 (69.1%) patients. HA users were older (67 vs 64 years, p=0.012) but similar in gender distribution and duration of deafness compared to non-HA users. HA users had higher preoperative scores (CNC 19.9 vs 14.6 p=0.002; AzBio 29.2 vs 20.7, p=<0.001). On multivariate analysis including pre-operative PTA(p=0.143), CNC (p=0.103), AzBio (p=0.076), age (p=0.948), and hearing aid use, pre-operative HA use significantly predicted higher datalogging at 6 and 12 months (p=0.020). No factor was predictive of higher datalogging at 1 or 3 months.

Conclusions: Pre-operative hearing aid use predicted greater long-term device use in our cohort, which in turn, has shown to influence post-operative speech performance. Clinicians should emphasize the importance of full time CI use especially with non-HA users.

Professional Practice Gap & Educational Need: Improved methods to predict CI use and performance.

Learning Objective: Pre-operative candidacy demographics can assist in CI use and performance prediction.

Desired Result: Assistance in pre-operative and post-operative counseling for improved CI performance.

Level of Evidence -- Level IV, Historical Cohort

Indicate IRB or IACUC: Vanderbilt University Medical Center IRB# 221833

Comparison of Achievement and Time to Benchmark Cochlear Implant Performance for Traditional, Single-Sided Deafness, and Hearing Preservation Candidates

Natalie Schauwecker, MD; Ankita Patro MD, MS; Connie Ma, MD; Michael H. Freeman, MD
David S. Haynes, MD; Elizabeth L. Perkins, MD

Objective: To assess achievement of and time to benchmark performance for traditional, single-sided deafness (SSD), and hearing preservation (HP) cochlear implant (CI) candidates.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 866 CI ears implanted from 2012 to 2022 (traditional: 378, HP: 437, SSD: 51)

Main Outcome Measures: Speech recognition scores; achievement of and time to "benchmark score," defined as 80% of institution's median speech recognition score.

Results: Compared to the other groups, SSD patients were younger (51y, $p<0.001$), and traditional candidates had longer duration of deafness (6.9y, $p<0.001$). A higher proportion of the HP group (68%) achieved CNC scores compared to SSD (43%) and traditional (57%) candidates ($p<0.001$). Time to benchmark CNC performance was equivalent ($p=0.410$). Achievement of ($p=0.283$) and time to benchmark ($p=0.568$) AzBio quiet scores were not significantly different among groups. For AzBio in noise, benchmark achievement was equivalent ($p=0.467$). However, traditional candidates (5.7 months) and SSD (6.2 months) took longer to meet benchmark AzBio in noise than HP (4.8 months, $p=0.033$). Datalogging was significantly lower at 3, 6, and 12 months for the traditional and HP patients who failed to attain benchmark scores ($p<0.001$). Age and duration of deafness did not impact benchmark achievement.

Conclusions: Compared to HP patients, traditional and SSD candidates achieved benchmark speech performance less frequently and took longer to do so. Patients who did not meet benchmark scores had lower device usage. These findings can assist with counseling and establishing follow-up frequency to optimize performance.

Professional Practice Gap & Educational Need: Improved methods to predict CI performance.

Learning Objective: Pre-operative candidacy type can assist in CI performance prediction.

Desired Result: Assistance in pre-operative counseling and post-operative follow-up for expected CI performance.

Level of Evidence - Level IV, Historical Cohort

Indicate IRB or IACUC: Vanderbilt University Medical Center IRB# 221833

Self-Referral vs Physician Referral: Hearing Aid Adoption Rates and Perceptions and Attitudes of Prospective Hearing Aid Users

Natalie M. Perlov, BS; Anna Bixler, AuD; Karla Belcastro, AuD
Jacob B. Hunter, MD; Irina L. Middleton, AuD

Objective: To investigate motivating factors and perceptions of prospective hearing aid (HA) users.

Background: While about 80 percent of hearing loss cases are treatable with HA use, only one in four individuals who may benefit from them pursue them. Alongside audiologists, physicians are integral parts of the hearing healthcare team and should be aware of factors that influence their patients' perceptions and choices.

Methods: Retrospective cohort study conducted between January 2018 and December 2022 conducted across five clinical sites, four of which are considered satellite offices. Adult patients with a primary complaint of hearing loss who received a HA evaluation were sent either an email or physical copy of a 17-question survey assessing demographic characteristics and factors related to HA adoption.

Results: Of 3,164 patients surveyed, there were 321 respondents, for a response rate of 10.1%. The sample was largely female (n=182, 57%), White/Caucasian (n=274, 86%), and geriatric (n=144), with 45% of patients >75-years-old. HA adoption rates were statistically different between White/Caucasian (n=193, 70%) and Black/African American (n=9, 39%) patients (X^2=9.56, p=0.0020), but not between other race categories. There were no significant differences in the racial composition of patients who were evaluated at the five sites included in this analysis (X^2=11.85, p=0.46). Approximately 80% of patients proceeded with HA after evaluation, with cost (n=164, 27%), insurance coverage (n=99, 17%), and physician recommendation (n=76, 13%) being the most popular factors that influenced their decision. Among factors influencing patients' decisions not to adopt HA, cost (n=71, 20%) and insurance (n=43, 12%) were the most cited reasons, though 169 respondents (48%) indicated the reason was one not listed on the survey. Chi-square analysis comparing these factors between patients who did or did not adopt HA were significantly different from one another (X^2=177.8, p<0.0001). With multiple regression analysis, while age, race, and gender were not predictors of HA adoption, patients' knowledge of multiple clinical locations offering HA (95% CI, 0.23-0.98; p=0.045) and the office at which they were evaluated (0.12-0.85, p=0.019) were significant predictors of HA adoption.

Conclusions: Responses from this study align with previous research on motivating factors in HA pursuit, though there are significant differences between patients who pursued HA and those who did not. Despite response bias, these data suggest that multiple office locations offering HA services may be beneficial to increasing HA adoption rates. These findings provide physicians, audiologists, and other members of the hearing healthcare team with insights into the factors which impact HA adoption.

Professional Practice Gap & Educational Need: Hearing aid adoption rates are low in eligible patients. Physicians play an integral role in potentially having a patient purchase a hearing aid. There is an educational need for physicians to be aware of the factors influencing hearing aid utilization, as physicians are a part of the hearing healthcare team.

Learning Objective: Explore which factors impact hearing aid adoption in patients with hearing loss.

Desired Result: Provide insight into the factors which impact hearing aid adoption and help to develop a more individualized care plan for patients with hearing loss during initial evaluations for hearing aids.

Level of Evidence – IV.

Indicate IRB or IACUC: iRISID-2022-1267, Thomas Jefferson University

Phenotyping of Hearing Instability: Correlating Longitudinal Changes in Endolymph Volume and Electrocochleography

Julia Telischi, BS; Jennifer Chisholm AuD; Hui Cheng, PhD
Li-Yueh Hsu, DSc; John Butman, MD, PhD; Michael Hoa, MD

Objective: Evaluate the relationship between electrocochleography (ECochG) measurements and inner ear fluid quantifications.

Study Design: Longitudinal observational cohort study.

Setting: Tertiary referral center

Patients: Patients aged 29 – 69 shown to experience hearing fluctuation or sudden hearing loss.

Main Outcome Measures: Changes in electrocochleography potentials over time in patients experiencing hearing fluctuation compared with changes in inner ear fluid volumes extracted from MRI imaging.

Results: Patients were followed for 6-8 visits at approximately 3-month intervals. At each visit, contrast enhanced delayed FLAIR imaging was obtained alongside audiometric and vestibular testing including electrocochleography using TM electrodes. A custom developed image analysis software was used to characterize inner ear fluid volumes from MRI imaging including total volumes, endolymphatic volume, endolymph to perilymph (E/P) ratio, and endolymph to total volume (E/T) ratio for the entire labyrinth, cochlea alone, and vestibule alone. Electrocochleograms were obtained and used to calculate SP/AP area ratios. Visualization of the percent change in data across visits did not suggest that changes in SP/AP ratio follow changes in E/T ratio, E/P ratio, total volumes, endolymph volumes. Overall, hydropic ears, all of which showed some evidence of hearing instability during longitudinal observation, did not show significantly different SP/AP area ratios compared to non-hydropic ears ($p = 0.36$). Preliminary comparison of all ears of affected patients to a cohort of healthy volunteers also showed no significant difference ($p = 0.35$).

Conclusions: Preliminary analysis suggests that SP/AP area ratios do not differ in patients with MRI-proven hydrops who demonstrate evidence of hearing instability compared with healthy patients. SP/AP area ratios also do not appear to fluctuate along with endolymph to perilymph ratio fluctuation.

Professional Practice Gap & Educational Need: Change in ECochG measurements in patients with hearing instability over time is not well understood.

Learning Objective: Understand the relationship between changes in ECochG potentials and inner ear fluid volume in patients with hearing instability.

Desired Result: Characterize any relationship between SP/AP area ratios and inner ear fluid volumes, particularly with endolymph volume changes.

Level of Evidence – III

Indicate IRB or IACUC : Protocol #000141-DC

Impact of Acute Auditory Deprivation on Adaptive Head Movements during a Complex, Combined Speech-in-Noise and Localization Task

Madison V. Epperson, MD; Gerilyn Jones, AuD; Obada Abdulrazzak, BA
Nadine Ibrahim, MD; Renee M. Banakis Hartl, MD, AuD

Objective: Characterize adaptive head movements during a combined localization and speech-in-noise (SIN) task for normal hearing subjects before and after simulation of acute unilateral hearing loss with ear plugging to better understand how adaptive behaviors emerge.

Study Design: Prospective Study

Setting: Tertiary Referral Center

Patients: Normal hearing adults (n=22)

Interventions: Testing was completed in a semi-anechoic chamber with 24-speakers spaced equally in a 360-degree azimuthal configuration. Orienting stimulus followed by Harvard IEEE sentences were played from single speakers in the presence of diffuse pink noise with variable signal-to-noise ratio (SNR). Participants were asked to repeat the sentence and indicate perceived location while moving naturally to optimize listening. Head movements were recorded via an electromagnetic tracking system. Acute hearing loss was simulated with a combination of a deeply-seated foam earplug and supra-aural earmuff.

Main Outcome Measures:
1) Localization accuracy: Root-mean-square (RMS) error (degrees), linear best-fit across targets
2) Head movement: Movement delay (ms), total response time (ms), total head displacement (degrees)
3) SIN: Percent correct across SNR

Results: Statistical analyses were performed using ANOVA and Wilcoxon rank sum tests. Acute simulated unilateral hearing loss resulted in decreased localization accuracy, increased response delay and total response time, increased total head displacement, and decreased SIN percent correct compared with the unoccluded condition.

Conclusions: Acute unilateral deprivation leads to sharp decline in localization accuracy and SIN performance. This provides key initial insight into adaptive listening strategies that SSD individuals may acquire and utilize in complex listening environments. Future study comparing acute auditory deprivation to chronic SSD will further enhance our understanding of these adaptations.

Professional Practice Gap & Educational Need: SSD individuals have difficulty localizing sound and understanding SIN. They may develop adaptive listening strategies with specific head movement patterns to optimize monaural localization and speech understanding in noise. Granular understanding of these adaptive behaviors and how they develop over time may better inform aural rehabilitation in SSD.

Learning Objective: To characterize adaptive head movement listening strategies during a complex, combined localization and SIN task for those with acute unilateral hearing loss with ear plugging to better understand how adaptive head movements and behaviors emerge.

Desired Result: To provide improved understanding of development of adaptive listening behaviors with acute unilateral hearing loss, which may inform future aural rehabilitation options in the SSD population.

Level of Evidence – III

Indicate IRB or IACUC : University of Michigan HUM00190678

Risk Factors for Otitis Media in Rural Alaska Native Children

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Objective: Characterize the relationship between otitis media incidence and environmental, nutritional, and genetic risk factors in Alaska Native children

Study Design: Prospective cohort study

Setting: Thirteen communities in rural northwest Alaska

Patients: Alaska Native children ages 1-4

Interventions: Tympanometry and distortion-product otoacoustic emissions were used to evaluate ear and hearing status. Parent/guardian questionnaire assessed exposures to environmental and genetic risk factors. A six-month prospective chart review extracted ICD-10 codes for otitis media.

Main Outcome Measures: 6-month odds of otitis media infection

Results: Of 236 enrolled children, 53% were homozygous for CPT1A, 72% of children were breastfed, 23% lacked household running water, and 6% were exposed to wood smoke. The mean ratio of smokers to adults in the household was 0.4. The mean number of people in the household was 6.2. One or more otitis media episodes were diagnosed in 53% of children over six months. No significant associations were found between environmental and genetic factors and 6-month odds of otitis media.

Conclusions: No associations were found between risk factors and otitis media in rural Alaska Native children. However, results should be interpreted cautiously as the COVID-19 pandemic affected study duration, sample size, and risk of enrollment bias.

Professional Practice Gap & Educational Need: There is a need to better understand potential limitations to prospective research, such as low sample size and recruitment bias.

Learning Objective: To understand the effects of the COVID-19 pandemic on sample size, study length, and enrollment strategy.

Desired Result: Attendees should be better equipped to avoid potential pitfalls associated with unexpected changes to study methodology.

Level of Evidence - III

Indicate IRB or IACUC : Pro00105507, 5/06/2020, Duke IRB

Superior Semicircular Canal Dehiscence is Associated with Global Skull Thinning

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McKenzie Stewart; Evan Cumpston, MD; Rick F. Nelson, MD, PhD

Objective: To assess whether development of superior semicircular canal dehiscence (SSCD) may be related to isolated intracranial skull base thinning, global skull bone thinning, or an alternative process.

Study Design: Retrospective cohort study.

Setting: Tertiary referral center.

Patients: Patients with CT IAC including calvarium and zygoma either with or without SSCD as confirmed by primary author

Main Outcome Measures: Thickness of calvarium and ipsilateral extracranial zygoma in SSCD and control patients as measured using standardized 3D slicer measurements of high-resolution temporal bone computed tomography scans obtained at a tertiary referral center and height of the internal auditory canal (IAC).

Results: 41 SSCD patients (21 with bilateral SSCD) and 32 control patients were assessed for thickness of ipsilateral calvarium and extracranial zygoma. Age and BMI were similar between the cohorts ($p=0.07$ and $p=0.09$, respectively). Females comprised 25 (61%) of SSCD patients and 22 (69%) of control patients while 39 (95%) of SSCD patients and 24 (77%) of control patients were white. Calvarium thickness was significantly reduced in SSCD patients (1.94 [0.36] cm) compared to control patients (2.40 [0.51]) ($p<0.001$) as was zygoma thickness ($p<0.001$). SSCD patients also had significantly reduced calvarium-to-zygoma ratio ($p=0.01$). IAC height was significantly shorter in SSCD patients (2.9 [0.9] cm) compared to control patients (4.9 [1.4] cm) ($p<0.001$).

Conclusions: SSCD patients appear to have global thinning of cranial bones despite similar rates of obesity compared to the general population. The global nature of skull thinning suggests that SSCD may occur from a developmental process.

Professional Practice Gap: Etiology of SSCD is poorly understood. This study attempts to elucidate whether SSCD occurs as a result of an isolated skull base defect, a more systemic process, or perhaps a process yet to be explained.

Learning Objective: Patients with SSCD appear to have global skull bone thinning

Desired Result: Clinicians will gain further understanding regarding the pathophysiology of SSCD prompting additional research into understanding this complex disease process

Level of Evidence: IV

IRB: Indiana University IRB #13133 (approved 10/14/2022)

Preoperative Superaddativity Predicts Cochlear Implant Postoperative Audiologic Outcomes

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Peyton Robinson, BS; Evan Cumpston, MD; David B. Pisoni, PhD
Rick F. Nelson, MD, PhD

Objective: To assess predictive ability of multi-modal audiovisual (AV) City University of New York (CUNY) sentence test scores on postoperative AzBio sentence scores in cochlear implant (CI) patients

Study Design: Retrospective cohort study

Setting: Tertiary referral center

Patients: Patients undergoing CI with preoperative CUNY testing

Main Outcome Measures: Impact of superadditivity—(SA) defined as the combined AV CUNY score subtracted by the sum of the audio only (AO) and visual only (VO) scores—of combined audio and visual CUNY scores on postoperative AzBio testing Effect of SA was assessed using paired t-tests to compare "high performers" vs. "low performers" based on a pre-operative SA cutoff of 25 or greater for "high performers."

Results: Patients implanted from 2017-2023 with available pre-operative audio and visual CUNY testing were considered for this study. Thirty-seven patients—44 ears, as seven patients underwent implantation of both ears during the study period—met criteria and were included in this study. Most patients were white (92%) while mean implant age was 53 years. High performers had significantly higher mean (standard deviation) postoperative AzBio scores compared to low performers [63.6 (30.1)% vs. 40.5 (39.8)%, p=0.037]. There were no statistical differences in age (p=0.795), duration of deafness (p=0.586), or preoperative pure tone average (p=0.077) between the groups. Across all patients, age (p=0.88) was not predictive of postoperative AzBio score, while shorter duration of deafness (p=0.002) was associated with improved AzBio scores.

Conclusions: Patients with excellent preoperative multisensory audiovisual integration, shown using CUNY scores, and shorter duration of deafness may have improved cochlear implant outcomes.

Professional Practice Gaps: As many potential candidates pursue cochlear implantation, identifying good candidates for CI is imperative.

Learning Objectives: Patients exhibiting multisensory processing may predict improved postoperative CI performance.

Desired Results: Patients with hearing loss often utilize visual cues for communication. The effect of patient multisensory processing capacity on postoperative CI results is yet to be determined.

Level of Evidence: V

IRB: Indiana University IRB #16904 (approved 10/14/2022)

Impact of Perioperative Anticoagulation and Antiplatelet Therapy on Hearing Preservation Outcomes

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David S. Haynes, MD; Kareem O. Tawfik, MD

Objective: Report hearing preservation (HP) outcomes following cochlear implantation based on anticoagulation and antiplatelet therapy use (blood thinner, BT).

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

Patients: 338 adult patients (361 ears: no BT = 210, BT held = 86, BT continued = 65) implanted between 2012 and 2021 with preoperative residual hearing, defined as low frequency pure-tone average (LFPTA) $\leq$65 dB HL.

Main Outcome Measures: Postoperative HP, defined as LFPTA $\leq$65 dB HL, at 1, 3, 6, and 12 months.

Results: Compared to no BT, BT continued and held groups were older (60.7 vs. 72.7 vs. 73.0 years, $p<0.001$) and had diabetes (10% vs. 22% vs. 30%, $p<0.001$). Electrode type, steroid use, surgical approach, and preoperative LFPTA were equivalent among groups. Postoperative HP was significantly higher for no BT than the BT continued and held groups at 1 (31% vs. 14% vs. 13%, $p<0.001$) and 3 (36% vs. 20% vs. 19%, $p=0.012$) months, with equivalent results at 6 and 12 months. When patients were stratified by type of BT, there were no significant differences in HP outcomes. After controlling for age and diabetes on multivariable analysis, BT status was not a significant predictor of HP rates at 1 or 12 months. Younger age was the only significant predictor of 1-month (OR 0.95, 95% CI 0.93-0.97, $p<0.001$) but not 12-month HP rates.

Conclusions: BT use, regardless of whether held for surgery, was associated with inferior early HP outcomes. After controlling for age, BT status was not a significant predictor of HP, suggesting inherently poorer cochlear health in BT patients.

Professional Practice Gap & Educational Need: Minimizing blood getting into the cochlea is a key target during hearing preservation surgery. However, to our knowledge, hearing preservation outcomes in the setting of blood thinners has not been reported in the literature. As risks and benefits of holding blood thinners for our CI patients should be appropriately weighed, it is critical to identify the impact of blood thinners on postoperative hearing preservation outcomes.

Learning Objective: To understand the differences in hearing preservation based on blood thinner status for patients undergoing CI surgery.

Desired Result: Providers will have knowledge of worse hearing preservation outcomes for patients on blood thinners. As holding blood thinners does not impact rates of hearing preservation, patients should be counseled on likely poorer cochlear health and older age being drivers in decreased hearing preservation after CI surgery. Providers can also consider continuing blood thinners, especially in patients who may have significant risks if their blood thinner is held.

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

Indicate IRB or IACUC: IRB exempt (221833, Vanderbilt University, approved 10/12/22).

Inpatient Audiometry: Perspectives and Impact on Clinical Decision Making

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Objective: Evaluate the impact of inpatient audiometry on in-hospital outcomes and decision making. Assess stakeholder perspectives on the practice of inpatient audiometry and associated financial impact.

Study Design: Retrospective case review and quality improvement (stakeholder perspective and cost analysis).

Setting: Academic tertiary referral center.

Patients: Retrospective chart review of inpatients (2015-2022) who underwent inpatient audiometric evaluation.

Main Outcome Measures:
1. Changes to management plan resulting from inpatient audiometric evaluation.
2. Impact of inpatient audiometry on clinical decision making quantified by descriptive statistical analysis, including percentage of consultations resulting in change to inpatient management.
3. Test-retest reliability of inpatient vs outpatient audiograms (change in thresholds [dB] speech discrimination [%]).
4. Focus group and survey driven input from Audiology stakeholders.

Results: 701 records are being reviewed. Preliminary data yields common requests for inpatient audiograms include hearing loss, ototoxic medication monitoring, acute otitis media, ear fullness, trauma, and otorrhea. 20% of inpatient audiometric testing resulted in changes to inpatient treatment. 40% of requested evaluations were performed the same day. Focus group and survey results will elucidate the practice impact on a primarily outpatient-focused Audiology clinic. An estimate of financial cost of an inpatient relative to an outpatient audiogram will be determined.

Conclusions: Inpatient audiometry is time- and resource-intensive without significant data supporting impact and clinical utility. Results suggest that inpatient audiometry has a minor impact on clinical outcomes and that outpatient audiograms may suffice for the majority of otologic consults in combination with a thorough history and physical exam. Additional study across institutions with variable practice would be beneficial to establish broader recommendations.

Professional Practice Gap & Educational Need: Audiometry is a critical component of a detailed assessment of many otologic and neuro-otologic concerns. Clinical practice at some institutions may include obtaining an inpatient audiogram for quick assessment of hearing sensitivities in the acute setting, however the value of an inpatient evaluation relative to a delayed, outpatient audiogram has not yet been demonstrated in the literature. To our knowledge, this study will be the first to thoroughly characterize data from a large academic institution's inpatient audiometry practice. Data presented here will help guide practitioners in determining when inpatient assessment is indicated.

Learning Objective:
1. To assess the clinical significance, as well as expected versus realized improvement in outcomes, related to inpatient audiometry.
2. To quantify the test-retest reliability of inpatient audiometric evaluation compared with outpatient testing.
3. Understand stakeholder perspectives on integration of inpatient audiometric evaluation in an academic Audiology Department

Desired Result: We aim to provide context around the clinical value of an inpatient versus outpatient audiogram for providers. Ultimately, determining the clinical value of the inpatient audiogram will guide and improve clinical management when evaluating an Otologic or Neuro-Otologic concern.

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

Indicate IRB or IACUC: University of Michigan HUM00225111 – Exempt.

Correlation of Endolymphatic Volume with Disease Subtype, Symptom Duration, and Vestibular Testing in Meniere's Disease Patients

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Objective: Meniere's disease (MD) is hypothesized to arise from a heterogenous group of etiologies. Recently, our group described two MD subtypes based on distinct angular trajectories of the vestibular aqueduct measured on computed tomography (CT): degenerative (MD-dg) and hypoplastic (MD-hp). Historically, the hallmark of MD has been the histopathologic finding of endolymphatic hydrops on cadaveric temporal bone sections, but delayed gadolinium (Gd)-enhanced high-resolution magnetic resonance imaging (MRI) allows for in vivo visualization of hydrops. Here, we investigated whether endolymphatic volume measured on MRI correlates with MD subtype, symptom duration, and clinical vestibular testing.

Study Design: Retrospective cohort study

Setting: Tertiary academic medical center

Patients: Adults with unilateral/bilateral MD.

Interventions: N/A

Main Outcome Measures: Endolymphatic volume measurements on MRI calculated using OsiriX, angular trajectory of vestibular aqueduct on CT, cervical vestibular evoked myogenic potential (cVEMP).

Results: 44 adults (age: 56.4 (15.5), females: 18) were included in the analysis. Of the 18 patients (23 ears) with CT imaging, 39% (9 ears) were classified as MD-hp subtype. No significant difference was observed between the endolymphatic volumes of MD-hp and MD-dg ears. Abnormally elevated cVEMP thresholds were not associated with larger endolymphatic volumes. MD disease duration did not correlate with severity of endolymphatic hydrops.

Conclusions: Endolymphatic hydrops is an irreversible downstream effect of MD. Our study findings suggest that MD etiology and disease duration may not contribute to severity of hydrops. Additional research is required to investigate whether other factors (e.g. environmental, genetic, autoimmune) may influence endolymphatic volume.

Professional Practice Gap & Educational Need: Explore the possibility that MD arises from a diverse array of heterogeneous etiologies with a common downstream pathway resulting in endolymphatic hydrops.

Learning Objective: Etiology of Meniere's disease and symptom duration do not appear to contribute to the severity of endolymphatic hydrops.

Desired Result: Broader recognition of the ability to subtype Meniere's disease based on clinical, radiologic, and histopathologic features.

Level of Evidence – Level III

Indicate IRB or IACUC : 2019P000438, Massachusetts Eye and Ear (Exempt)

Optimizing Insertion of a Cochlear Apical Electrode Utilizing CT Measures and Techniques to Guide Surgical Placement.

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Matt Breen, MD; Joseph Lebowitz, MD; J. Thomas Roland Jr., MD

Objective: To better understand cochlear apex anatomy in relation to important anatomical landmarks and critical structures to optimize procedural success and standardize technique for an apical electrode placement.

Study Design: Retrospective imaging review and anatomical dissection.

Setting: Tertiary referral center and temporal bone lab.

Patients: Pediatric and adult cochlear implant candidates.

Interventions: NA

Main Outcome Measures: Cochlear apex measures, and distances to surrounding critical structures or identifiable surgical landmarks. Special measures were developed to assist with further surgical triangulation. Five cadaver dissections were completed to help confirm radiologic validity.

Results: Eighty-two temporal bones (50% left, 50% right) were analyzed in 44, males and 38 females, with an average age of 56.4. The mean height of the cochlea was 3.4mm (stdev 0.3), height of the apex 1.0mm (stdev 0.2mm), and width of apex 3.3mm (stdev 0.3). The mean lateral promontory width was 1.2mm (stdev 0.3), and superior promontory width 1.3mm (stdev 0.3). The minimum distance to critical structures such as the ICA and labyrinthine facial were 1.4mm and 0.6mm respectively. The craniocaudal relationship of the cochleiform process and apex demonstrated variability. A vector though the stapes crus provided a relatively reliable means of identifying the superior apical border, while a parallel line through the round window delineated the inferior border.

Conclusions: This study characterizes cochlear apex anatomy and relationships, while describing a new method to delineate the superior and inferior apical boundaries. In doing so, it provides surgeons with a more accurate blueprint for performing an apical cochleostomy than historical teachings.

Professional Practice Gap & Educational Need: A return electrode placed within an apical cochleostomy following standard cochlear implant electrode insertion can reshape electrical fields to stimulate the cochlear apex and improve low frequency precept. Atraumatic and accurate apical cochleostomy is required to achieve success, however prior anatomical apex characterization is poor in the literature.

Learning Objective: Better understand cochlear apex anatomy and learn new measures to assist in cochlear apex triangulation within the surgical theatre.

Desired Result: Increased surgeon familiarity and confidence in performing a minimal, atraumatic, cochlear apex cochleostomy for apical electrode insertion.

Level of Evidence – Level V

Indicate IRB or IACUC: IRB# s20-01964 at NYU Langone Health.

Adverse Outcomes Following Cochlear Implantation in Adults: A Multinational Database Analysis

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Richard K. Gurgel, MD, MSCI; Mana Espahbodi, MD

Objective: Rare sequelae of cochlear implantation (CI) in adults include meningitis, labyrinthitis and facial nerve disorders. The purpose of this study is to examine the complications of CI using TriNetX, a multinational database.

Study Design: Retrospective cohort study using TriNetX. When cohorts were smaller than 33,333,333, 1:1 propensity score matching (PSM) for age and sex was performed. All cohorts of 1-10 patients are reported as 10 in TriNetX, limiting estimations of risk ratios (RRs) in these cases.

Setting: TriNetX is a multinational database including 79 health care organizations, with an average of 12-14 years of data per heath care organization. 95% of patient data used in this study is from 2003-2023.

Patients: Adults with CI with a comparison group of adults with sensorineural hearing loss (SNHL) without CI.

Main Outcome Measures: RR and 95% confidence intervals (95% CIs) for incident meningitis, facial nerve disorders (including facial nerve weakness, lagophthalmos and eyelid weight placement for lagophthalmos), and labyrinthitis. Preoperative risk factors were also examined.

Results: Patients with CI (n=13,242) had an increased risk of meningitis at any time after surgery when compared to the SNHL without CI cohort (RR: 2.66, 95% CI: 1.98-3.56). Absolute risk for meningitis after CI was 1.25%. The risk of labyrinthitis any time after surgery was increased in the CI cohort (RR: 2.04, 95% CI: 1.44-2.89). The risk for facial nerve disorders any time after surgery was not increased (RR: 1.3, 95% CI: 0.59-2.88). A preoperative history of meningitis (RR: at least 7.0, 95% CI: 3.66-13.37), otitis media (RR: 3.5, 95% CI: 1.74-7.03) and otorrhea (RR: 2.4, 95% CI: 1.16-4.97) increased the risk of postoperative meningitis in those undergoing CI.

Conclusion: The risk of meningitis and labyrinthitis are significantly increased after CI compared to those with SNHL who have not undergone CI, while the risk of facial nerve disorders is not significantly elevated. Adults with a history of preoperative meningitis are at highest risk of meningitis after CI.

Professional Practice Gap & Educational Need: While cochlear implant surgery is safe and widely available, updated analyses of risks with large patient cohorts are needed.

Learning Objective: To describe the risks of cochlear implantation using a multinational database.

Desired Result: Increased understanding of risks of CI and patients who are at higher risk of adverse outcomes.

Level of Evidence: IV

Indicate IRB or IACUC: Exempt

Cautious Gait while Dual Tasking in People with Bilateral Hearing Loss

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Gerald Voelbel, PhD; Katherine Scigliano, AuD; Maura Cosetti, MD

Objective: Bilateral sensorineural hearing loss (BHL) is associated with balance problems and increased fall risk. This study aimed to understanding the underlying mechanism of this relationship. We hypothesized that people with BHL would demonstrate reduced attentional capacity during walking with a dual task (DT) paradigm due to increased attentional demands associated with loss of auditory information.
Study Design: Cross sectional study.

Setting: Motion analysis laboratory.

Patients: Normal hearing (N=28, PTA <25dB; mean age 59.14, Standard Deviation (SD)=11.96), Mild BHL (N=16, PTA 26-40dB; 74.69, SD=8.67) and Moderate or worse BHL (N=15, PTA >41dB; 70.93, SD=13.59).

Interventions: Wearing inertial measurement units, participants walked for one minute twice: single task (ST) or performing a serial-3 subtraction task (DT).

Main Outcome Measures: Gait speed, stride length, stride time

Results: Gait speed and stride time did not differ between groups on either task. The Mild BHL group had shorter stride length in ST (p=.034) and DT (p=.032) compared to Normal hearing. In DT, the Mild group had larger variability (p=.024) compared to Normal. In addition, people who exercise demonstrated longer stride length (100% of the Moderate group vs. 62.5% of the mild group reported exercising regularly).

Conclusions: Shorter stride length, suggesting a cautious gait pattern, and larger between-group differences in stride length variability while DT, suggesting limited attentional capacity, were found in people with Mild BHL but not Moderate BHL, differently than expected. The Moderate BHL group were all physically active and had a higher percentage of men potentially influencing their gait performance. Future research is needed to elucidate mechanisms underlying fall risk in individuals BHL.

Professional Practice Gap & Educational Need: Understanding why people with BHL are at an increased risk for falls will help strategize a fall prevention plan. Future research should investigate whether hearing interventions can improve walking performance and decrease fall risk in people with BHL.

Learning Objective: To explain the differences in walking dual task and attentional capacity while dual tasking between healthy and hearing loss older adults.

Desired Result: At the end of the presentation participants will understand the differences in walking dual task and attentional capacity while dual tasking between healthy and hearing loss adults.

Level of Evidence - Level IV

Indicate IRB or IACUC: The Mount Sinai Program for Protection of Human Subjects: STUDY-21-01026 and the Institutional Review Board (IRB), New York University -IRB-FY2021-5400.

Barriers to Hearing Healthcare for Rural Northern US Communities

Catherine L. Kennedy, MD; August Richter; Janet S. Choi, MD, MPH
Meredith E. Adams, MD, MS

Objective: To examine awareness of hearing loss, rehabilitation options, and barriers to hearing healthcare for rural communities in Minnesota, the third best ranked state for public hearing healthcare benefits.

Study Design: Cross-sectional study

Setting: Community based screening at Driven to Discover Research Facility (Beltrami County, Minnesota).

Patients: Adults ≥ 18 years

Interventions: In-person survey and audiometric screening performed at 25 dB across four frequencies.

Main Outcome Measures: Descriptive analysis of sociodemographics, awareness of hearing loss and hearing healthcare, and Brief Health Literacy Screening (BHLS). Hearing loss was defined as failing at least 1 frequency in 1 ear.

Results: 82 participants were included with mean age of 54.5 years (18-92), 48.8% male and 92.7% white. 79.3% were from a rural area or small city/town and health literacy was adequate based on 13.5 (4-15) mean BHLS score. 50% reported subjective hearing loss and 56.1% demonstrated audiometry-measured hearing loss. 8.5% currently wear hearing aids and 10.9% have used a hearing assistive device. Among participants with audiometry-measured hearing loss, 18.3% were unaware of their hearing loss. The rates of recent formal or screening hearing tests were low at 46.3% and 20.7%, respectively. The most common reasons given for not undergoing testing were "don't know" (20.7%), or "my healthcare provider never mentioned it" (20.7%). Participants had low awareness of Over-The-Counter hearing aids (47.5%) and of state hearing healthcare benefits (28.7%).

Conclusions: Despite hearing healthcare benefits and self-perceived accessible care in health-literate rural communities, few patients received hearing healthcare. Increasing public health initiatives in rural primary care offices may increase uptake and awareness.

Professional Practice Gap & Educational Need: This study aims to identify barriers to hearing healthcare for rural residents of the Northern US where public insurance benefits afford greater coverage than in other previously described rural US regions. Prior studies have identified that patients in rural communities are unable to obtain hearing healthcare due to lack of providers and insurance coverage. In spite of excellent insurance coverage and access to hearing healthcare, patients in Northern rural US communities do not receive adequate healthcare due to poor self-perception of hearing loss, lack of recommendation to pursue formal testing, and lack of awareness of insurance benefits.

Learning Objective:

1. To determine prevalence of hearing loss and participant awareness of hearing loss and rehabilitation options.
2. To understand barriers to access of hearing healthcare for rural Northern US communities.
3. To identify public awareness of healthcare benefits in a state with excellent public insurance hearing healthcare coverage.

Desired Result: To recognize new pathways to promote hearing healthcare in Northern US rural communities.

Level of Evidence: Level V

IRB: IRB Study # 00019167, University of Minnesota (June 22, 2023).

Risk Factors and Prevalence of Vestibular and Auditory Dysfunction in a Pediatric Sickle Cell Disease Population

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Amir Kheradmand, MD; M. Dawn Nelson, PhD; Bryan K Ward, MD
Eboni I. Lance, MD, PhD

Objective: To identify the pathophysiology and occurrence of auditory deficits and vestibular dysfunction in children with sickle cell disease (SCD).

Study Design: Retrospective chart review where demographic, hematologic, audiometric, and clinical history data were collected.

Setting: Johns Hopkins Kennedy Krieger Institute: tertiary care referral center.

Patients: One-hundred and eighty-seven children with SCD who presented to the SCD clinic between January 2000 and September 2016.

Interventions: Non-interventional study.

Main Outcome Measures: 1) Hearing loss: pure tone average (PTA) >15 dB hearing level (HL).
2) Vestibular dysfunction (VD): at least 1 episode of acute onset vertigo severe enough to present to the clinic or emergency department.

Results: The median age was 14.3 years (range 7–23); 47% were female sex, 96% were Black, and 60% were SS genotype, 29% SC, 9% SB^+, and 2% SB^0. Fifty-five (29.4%) and 36 (19.3%) patients were identified with hearing loss and VD, respectively. Forty-four patients (23.6%) received chronic transfusions, and 99 (52.9%) received hydroxyurea therapy. Older age (OR 1.01, CI 1.00–1.02, p=0.007), higher baseline hemoglobin (OR 1.36, CI 1.09–1.75, p=0.012), and hydroxyurea treatment (OR 4.71, CI 1.76–14.19, p=0.003) predicted VD. History of retinopathy (OR 3.08, CI 1–9.59, p=0.048) and tobramycin (OR 11.4, CI 1.3–100, p=0.043) were associated with hearing loss. Chronic transfusion approached significance for predicting hearing loss (OR 2.2, CI 1–4.86, p=0.051).

Conclusions: Vestibular and auditory symptoms are common in pediatric patients with SCD. Novel risk factors like hemoglobin and treatment history may improve understanding of the cause of inner ear symptoms in SCD.

Professional Practice Gap & Educational Need: Sickle Cell Disease (SCD) affects approximately 100,000 Americans and impacts multiple organ/body systems. Children with SCD have an increased risk of hearing loss, but the pathophysiology of auditory deficits and the occurrence of vestibular dysfunction in this population is largely unclear. Identifying risk factors and treatment paradigms associated with hearing loss and vestibular dysfunction can inform providers about best practices to protect this vulnerable population from preventable injury to inner ear structures and function.

Learning Objective: Readers should be able to understand the importance of questioning patients with SCD about auditory and vestibular symptoms. Furthermore, they should recognize the role of some SCD treatments in potentially exacerbating these pathologies and remember to be thoughtful in utilizing these therapies.

Desired Result: The desired result of this study is to identify any novel risk factors or hematologic associations for the development of hearing loss and vestibular dysfunction in children with SCD.

Level of Evidence - Level IV

Indicate IRB or IACUC: Johns Hopkins IRB00087766.

Sound Localization in Single Sided Deafness: Compensatory Head Movements and Localization Performance Measures

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Carolyn Kroger, PhD; Jackson Graves, PhD; Renee M. Banakis Hartl, MD, AuD

Objective: Evaluate sound localization accuracy and compensatory head movements in patients with single-sided deafness (SSD) with a cochlear implant (CI) or active transcutaneous bone conduction implant (atBCI).

Study Design: Nonrandomized, prospective study.

Setting: Academic tertiary referral center.

Patients: 14 SSD patients (6 CI, 8 atBCI) and 22 normal hearing controls.

Interventions: Subjects underwent localization testing in a dark semi-anechoic chamber with 24 speakers 15º apart. Stimuli included broadband and narrowband noise (500 Hz, 1000 Hz, 4000 Hz). Subjects indicated target source while wearing a head tracker. Accuracy was measured by comparing their perceived stimulus angle to the presented location. Statistical analyses between groups were performed using ANOVA and Wilcoxon rank sum tests.

Main Outcome Measures:
1. Localization accuracy (degrees root-mean-square [rms] error and linear best-fit across targets).
2. Head position changes (response time [ms], direction, absolute total displacement [degrees], and movement delay [ms]).

Results: Individuals with SSD demonstrate decreased localization accuracy (rms and linear best-fit), increased response time (ms), increased absolute total head displacement (degrees), and increased movement delay (ms) compared with controls, with device use resulting in relatively limited improvement across domains that was greater in CI compared with atBCI users. Head movement patterns indicate a preference for the better-hearing ear for individuals with SSD.

Conclusions: Individuals with SSD demonstrate decreased accuracy and distinct patterns of compensatory head movements when compared to controls, with relative limited improvement with device use. Further study is needed to evaluate the effect of these head movements on performance outcomes and the degree to which compensatory head movements impact binaural hearing rehabilitation.

Professional Practice Gap & Educational Need: Head movement impacts sound localization ability by altering acoustical cues for optimal performance on binaural auditory tasks. However, in individuals with SSD localization ability and the associated complex compensatory head movements remain incompletely characterized. Moreso, data on CI and atBCI modulation of sound localization in SSD is limited. Head movement and localization ability data, as well as detailed characterization of the impact of CIs and atBCIs in SSD, is critical for optimization of prosthetic device programming, efficacy, and use – ultimately laying the foundation for improved device benefit in binaural tasks for individuals with SSD.

Learning Objective: Patients with SSD demonstrate unique compensatory head movements to optimize monaural listening cues when localizing sound and have significantly decreased sound localization ability. CI use results in a limited improvement in localization with associated changes in head movements, while atBCI use results in a modest but likely not clinically significant improvement across domains relative to normal hearing individuals.

Desired Result: To provide an improved and detailed understanding of complex compensatory head movements and sound localization ability in individuals with SSD using our rigorous testing paradigm, and the ways in which localization ability is impacted by CI and atBCI use. This testing paradigm will allow us to formally characterize the reflexive behavior behind sound localization in individuals with SSD in both aided and unaided conditions, inform device programming – particularly for CIs, evaluate device benefit for patients with SSD, and add an additional variable to configure and adapt prosthetic devices for maximal functionality.

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

Indicate IRB or IACUC: Approved 1/28/21, University of Michigan HUM00190678

Realistic Approach to Managing Extensive Cholesteatoma

Roni Barzilai, MD; Keren Hod, PhD; Michal Luntz, MD

Objective: To evaluate outcomes of extensive cholesteatoma following canal wall down (CWD) mastoidectomy with reconstruction of the external ear canal (EEC), tympanoplasty, and mastoid obliteration using Bonalive®, a volume-replacing, bone-regenerating, and anti-infectious material.

Study Design: Retrospective case review.

Setting: Tertiary referral center.

Patients: 127 ears with extensive cholesteatoma followed up for 1-4 years after surgery and fully aligned with the post-operative structured clinical-imaging follow-up (FU) protocol. 52.8% of these had undergone previous ipsilateral mastoid surgery.

Interventions: CWD mastoidectomy, tympanoplasty, EEC reconstruction and mastoid obliteration with Bonalive®.

Main Outcome Measures: Achieving completely epithelialized and dry ear, developing tympanic membrane (TM)-EEC retraction, developing retraction pocket (RP) and residual cholesteatoma.

Results: Despite repeated emphasis on the importance of follow-up (FU), attendance to FU visits declined from 100% (127/127) to 65.0% (41/63) between the first and fourth yearly postoperative FUs. Mean annual prevalence of a 'disease-free' ear (completely epithelialized, dry, not retracted, and free of cholesteatoma) was 88.5%. Complete epithelialization and dryness achieved within the 1st post-op year in 96.8% (123/127). Percentage of ears remained dry throughout the entire 4-year FU period was 83%. Prevalence of TM or posterior superior EEC wall retraction development increased with time from 13.4% (17/127) at the 1st yearly visit to 34.1% (14/41) at the 4th yearly visit. Recovering of retraction did not occur, and 23.2% of the 43 ears diagnosed with TM-EEC retraction at any point during the FU developed RP cholesteatoma later on. RP cholesteatoma was diagnosed in 15 ears (11.8%). In 10 cases (66%), the cholesteatoma was preceded by retraction that had occurred 1 year or more earlier. Residual cholesteatoma was diagnosed in 9 ears (7.0%). All looked normal prior to the residual cholesteatoma diagnosis.

Conclusions: Mean annual 'Disease-free prevalence' reached 88.5% within the initial four postoperative years. However, it appears that eliminating residual and RP cholesteatoma recidivism is not attainable with surgery alone in extensive cholesteatoma, even with meticulous procedures. Despite efforts to clarify to patients/parents the importance of follow-up, attendance to follow-up visits declined over time.

Professional Practice Gap & Educational Need: There is a need for new effective solutions to eliminate tiny matrix nests and for control of middle ear under-aeration.

Learning Objective: 100% elimination of cholesteatoma, both of RP and of residual cholesteatoma is not achievable with surgery alone. This emphasizes the importance of ongoing otoscopic and MRI FU, even in cases where the ear and MRI appear normal.

Desired Result: To subtly emphasize the idea that non-surgeon professionals should be trained to perform effective postoperative micro-otoscopy, as ear surgeons should prioritize tasks that demand their unique skills like surgery and immediate post-operative follow-up.

Level of Evidence: Level III

Indicate IRB or IACUC: 0004-19-ASMC, Assuta medical center.

AMERICAN OTOLOGICAL SOCIETY RESEARCH FOUNDATION
RESEARCH GRANT AWARDS

The American Otological Society is committed to the non-promotional advancement of knowledge and science and to a free exchange of medical education in otology and neurotology. The American Otological Society, through its Research Foundation, is offering Research Grant Awards, an Award for a Clinical Trial, full-time Research Training Fellowships, exclusive medical student grants, and a Clinician-Scientist Award. The research need not be directly on an otological disease but may explore normal functions of the cochlea, labyrinth or central auditory or vestibular systems. However, the applicant must describe how the proposed research will benefit our understanding, diagnosis or treatment of otological disorders. **Research supported by all of the grant mechanisms can relate to any aspects of the ear, hearing and balance disorders. We welcome applications that address quality and safety of care as well as to improve education and training in otology.** These grant awards and fellowships are for work conducted in *United States or Canadian institutions only*. Additional details may be found on the AOS website.
https://www.americanotologicalsociety.org/aos-grant-submission-instructions

SAVE THE DATE - NOVEMBER 1, 2024

If you would like to submit a grant for consideration of funding in the next cycle, July 1, 2025 - June 30, 2026, please submit a **A LETTER OF INTENT and BIOSKETCH** including details regarding other existing support by November 1st of the year prior to funding. The letter of intent must state the desired grant mechanism for the proposal (Clinician Scientist Award (CSA), Fellowship grant, Research Grant, Clinical Investigation or Medical Student grant), the Principal Investigator and Institution(s) for the work, a working title and abstract and include Specific Aims and a proposal summary (2-page limit on abstract and aims). It should be formatted using 11-point Arial font, with page margins set to be 0.5 inches circumferentially. The Principal Investigator's name must appear on each page. The biosketch is not included in the page limit. The LOI must be submitted via email in a single Adobe PDF, save as with the mechanism and last name of PI.

Complete applications will be invited from selected applicants based on the Research Advisory Board's review of the letters of intent. Applicants will be notified whether they are invited to submit a full application the first week of December. Completed applications must be received by January 31st.

November 1: Letter of Intent due
December 5: Notification for request for a full application
January 31: Full application due
June 1: Notification of awards
Details are in the submission instructions.

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Non-invasion Imaging of the Cochlea:

The inner ear's middle compartment (Scala Media) has high potassium (K+) and low sodium (Na+) concentrations as compared to the surrounding fluid compartments (high Na+ and low K+). This ionic balance is crucial to maintaining auditory system functionality and is involved in various hearing losses, such as age-related hearing loss, noise-induced hearing loss, and drug-induced hearing loss. Presently, there is no method available to measure these ion concentrations (K+, Na+) clinically. Our study was undertaken to develop non-invasive imaging methods with clinical applications to measure Na+ and K+ concentration/flux in the inner ear for CBA/CaJ mice and guinea pigs. After our initial results (presented in the full grant proposal), we carried out more imaging experiments to build upon those results.

Methods: Young adult CBA/CaJ mice (2-3 months old) and albino guinea pigs (2-3 months old) were used for the experiments, and sodium measurements were done using two imaging techniques – Na MRI (albino guinea pigs) and Na-22 PET imaging (CBA/CaJ mice imaging). *Na MRI Imaging Technique: In vivo* MRI experiments were performed on albino guinea pigs of both sexes. Briefly, the animal was anesthetized with 1-2% isoflurane and placed on the MRI bed, with body temperature maintained at 37 ˚C. Physiological characteristics were monitored continuously. The proton (H1) channel on the surface coil was utilized for the MRI system's semiautomatic adjustment procedures, and subsequently, proton (H1) imaging confirmed that the sample and coil were correctly positioned. Proton MRI was performed using a TurboRARE-T2 pulse sequencer with standard parameters. Na MRI was performed using a FLASH pulse sequence with standard parameters. Siemens Inveon workstation software was used to analyze MRI images. Regions of Interest (ROIs) were first identified from the standard proton MRI images, and Na+ signals from the Na MRI images were matched to the ROI regions. *Na-22 PET Imaging:* Each animal was injected with approximately 250 µCi ^{22}Na radiation into tail veins using a catheter. A total of 12 projections over a 360^{O} arc were used to collect the images. During image processing, animals were under gas anesthesia (1-2% isoflurane) in an air-warmed imaging chamber (Harvard Apparatus, Cambridge, MA) to keep body temperature constant at 37 ºC, and the breathing rate and pattern was continuously monitored. For anatomical referencing of the cochlea, CT imaging was also done in combination with SPECT. ROI was drawn with the help of CT referencing. The image was reconstructed using the maximum likelihood expectation maximization (MLEM) algorithm, and finally, the 3-D image was reconstructed with scattering and attenuated corrections.

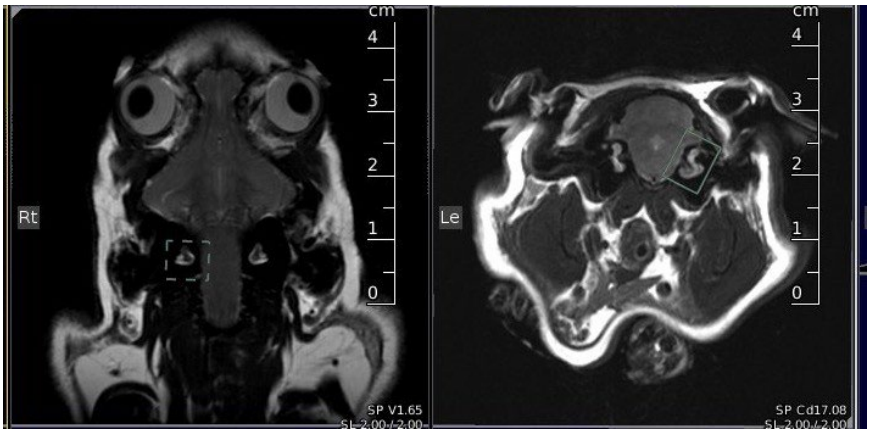


Figure 1: A representative anatomical image (Na-MRI) of guinea pigs in coronal and axial views. The square depicts the Cochlea.

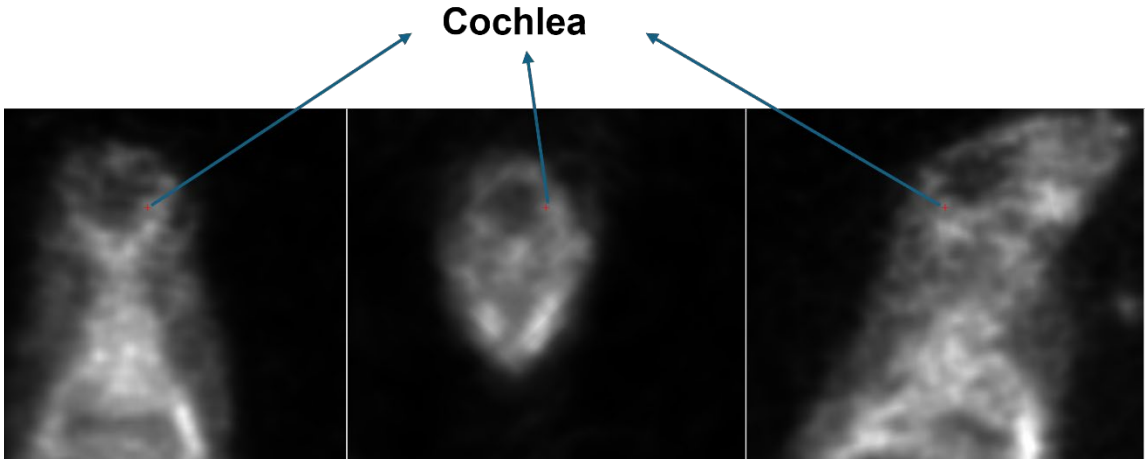


Figure 2: A representative Na-22 PET image of a mouse brain in axial, coronal, and sagittal views. An ellipse depicts the right cochlea area.

Results: Sodium signals were observed for the techniques – Na-MRI (Guinea Pigs) and Na-22 PET imaging (CBA/CaJ mice).

Figure 1 shows the Na-MRI image of guinea pig brain in coronal and axial planes. The dashed square shows the cochlea location. Similarly, **Figure 2** depicts the Na-22 PET imaging of the mouse brain in all three planes – axial, coronal, and sagittal. The red ellipse shows the cochlea location.

Conclusion: It is possible to do inner ear imaging using our proposed non-invasive imaging methodologies and further experiments are ongoing to find the relations between imaging parameters and physiological measurements (Na+, K+, and endocochlear potential).

Endocochlear Potential Measurements of the Cochlea: To establish the links between imaging results and inner ear physiological properties (endocochlear potential), physiological recordings were continued in parallel to imaging experiments, just like our preliminary experiments. The specific ion channel blocker – ouabain for NKA channels was applied location to the round window to find its effect on the endocochlear potential.

Methods: As in imaging experiments, 2-3 months old CBA/CaJ mice were used. Mice were anesthetized using ketamine and xylazine and surgery was performed to expose the bulla. A small hole was drilled, then, the glass micropipette containing 140 mM KCl was inserted through the cochleostomy opening into scala media.

Results: Using similar recording procedures as our preliminary results (presented in the grant), a step voltage above 100 mV was recorded. **Figure 3** shows one such trace recorded from a CBA/CaJ mice. The ouabain was applied to the round window at a concentration of 5 mM – Hamilton Syringe. A decrease in the endocochlear potential was observed on the application of ouabain. **Figure 4** shows the same; ouabain appears to be a relatively slow acting drug; taking approximately 10-15 minutes to reduce the endocochlear potential. We carried out experiments with the bumetanide blocker as well (blocker for NKCC1 ion channels in the cochlea), but, the application of bumetanide resulted in the animal dying within 15-20 minutes after applying bumetanide locally to the round window. It could be due to the high drug concentration. Further optimization of drug parameters is ongoing in our lab.

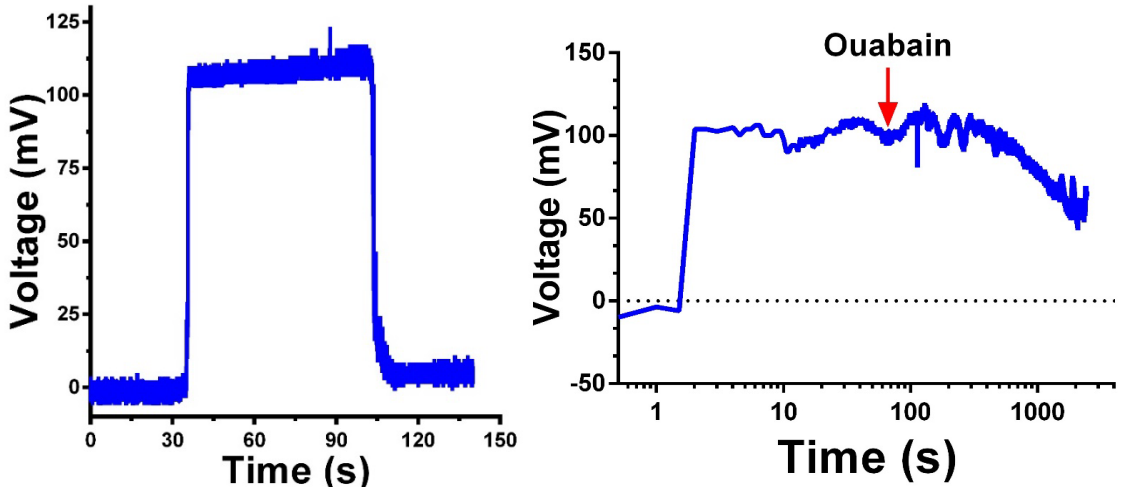


Figure 3: Left: Endocochlear potential measurements from a CBA/CaJ mice cochlea. Right: Application of Ouabain locally reduces the endocochlear Potential. The graph shows a representative trace from a CBA/CaJ mouse.

Conclusion: We continue to successfully record the endocochlear potential of CBA/CaJ mice and initial experiments show that the ouabain can reduce the endocochlear potential. These in vivo cochlear physiology results will be compared to imaging results with the application of ouabain to induce a cochlear hearing loss.

Research Outputs:

Journal Publication: Bazard, P., Mikalai, B., Zhu, X., Ding, B., **Frisina, R. D.**, Thallium-201 SPECT Imaging of Mouse Cochlea, In preparation, *Anticipated Submission within a week.*

Patent: Bazard, P., Mikalai, B., Zhu, X., Ding, B., **Frisina, R. D.**, Molecular Imaging of the Cochlea, *Final Patent Application Submitted, 1372.1440.PRC, Jan. 2024*

American Otological Society Clinician Scientist Award – Progress Report; Funding Period Start Date: 7/1/2023
PI/PD: Alexander D. Claussen MD; Mentor: Marlan R. Hansen MD
Understanding the Clinical Impact and Cellular Mechanisms of Neo-Ossification After Cochlear Implantation

Background:

Cochlear implants (CI) are an effective form of hearing rehabilitation, but multiple factors impede consistency and durability of outcomes. Post-CI tissue changes in the cochlea, and neo-ossification in particular, may be a significant limiting factor: accumulating evidence shows the ubiquity of post-CI cochlear neo-ossification and its association with insertion trauma, poor neural health and worse auditory outcomes. Correlation of in-vivo direct (i.e. radiologic) evidence of neo-ossification with simultaneous auditory and objective measurements is necessary to both understand the true clinical significance and time-course of post-CI neo-ossification and to develop methods for monitoring the efficacy of mitigative strategies (e.g. robotics and drug-eluting CIs).

The cochlea shows a predisposition to neo-ossification from multiple etiologies (e.g. infection, CI insertion). However, we lack fundamental understanding of what factors contribute to this, the unique mechanisms underlying new bone formation in the cochlea, its time course, and consequences for cochlear health and signal processing. Preliminary data from our mouse CI model demonstrated the reliable generation of robust scala tympani neo-ossification in mosaic patterns similar to that seen in human post-mortem studies, creating the opportunity to leverage the vast molecular and genetic experimental toolkit inherent in mouse models to mechanistically study cochlear neo-ossification. Understanding the mechanisms of cochlear neo-ossification is necessary to develop rationale mitigative therapies and to address barriers to implementation of future neural prosthetic technologies (e.g. thin film electrodes, optical stimulation).

The translational experiments planned through this award combine novel human inner ear imaging and CI electrophysiology (EP) techniques and a mouse model of cochlear implantation to pursue our overriding goal of understanding the mechanisms and clinical consequences of post-CI cochlear neo-ossification.

Aim 1: Characterize the time-course of post-CI neo-ossification and its effect on the electrode microenvironment, neural health and auditory outcomes.

In this aim, we proposed to recruit 40 CI recipients to undergo photon counting computed tomography (PCCT) scans at 1 month and 1 year after surgery to assess for cochlear neo-ossification after CI. Additionally, to assess neural health and the cochlear environment, these participants will undergo a schedule of complex impedance measurements (CIM) and electrically evoked 8th nerve compound actional potential (eCAP) testing, including derivation of the interphase gap (IPG) effect and electrode-neural interface index (ENI).

To date, we have now recruited 8 participants for Aim 1 and have an additional 15 participants targeted for enrollment by June of 2024. The initial 8 participants were drawn from a pre-existing randomized clinical trial at the University of Iowa examining dexamethasone eluting cochlear implants. Participants in this trial were randomized to receive either a standard Cochlear 632 array or a dexamethasone-eluting “Dex” Cochlear 632 array. Currently, the research team remains blinded to treatment condition (i.e. standard versus Dex CI), however preliminary impedance data suggests two unique groups with diverging trends in impedance change (**Figure 1**). We are cautiously optimistic this could represent a therapeutic effect of dexamethasone reducing CI-adjacent fibrosis and neo-ossification, which the planned one-year PCCT scans will examine. Thus far, 3 of the 8 enrolled participants have undergone one-year PCCT with an

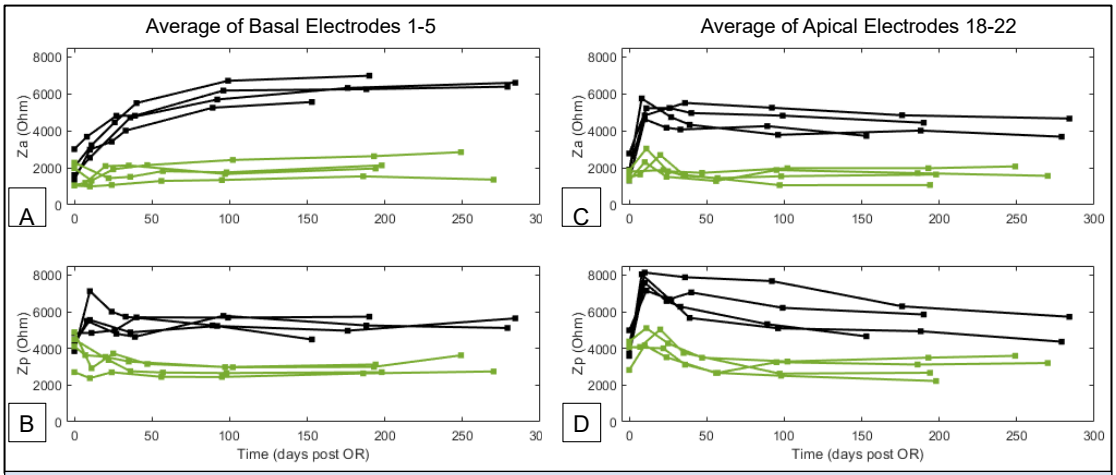


Figure 1. CIM components, including access resistance (Za) and polarization impedance (Zp) are plotted for basal (A,B) and apical (C,D) regions. Lines represent longitudinal data per individual subject and have been colorized to highlight the diverging groups with high (black line; n=4) or low (green lines; n=4) impedance trajectories

exemplary image of the segmented PCCT one-year post-CI shown in **Figure 2**. Notably these participants are from the Dex CI subcohort, which is blinded until Spring of 2024; thus, it is not yet known if participants were randomized to a Dex CI or Standard CI (a factor we hypothesize will affect the degree of neo-ossification).

Aim 2: Delineate the process of neo-ossification in a mouse model of cochlear implantation.

We aim to utilize the mouse model of cochlear implantation to assess the fundamental process of post-CI neo-ossification and classify it according to established osteogenic processes (e.g. endochondral ossification, intramembranous ossification). Further, we plan to broadly explore the role of neo-angiogenesis in cochlear neo-ossification and also identify relevant osteogenic signaling pathways and cellular populations relevant in this osteogenic pathophysiology.

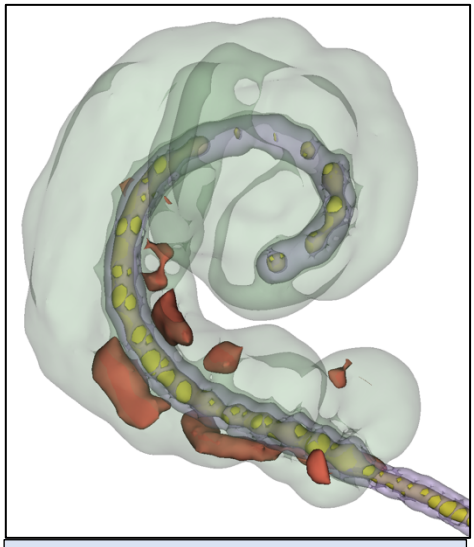


Figure 2. Photon Counting CT scan from a participant one-year after implantation. Red highlights new bone formation (1.56mm^3 – 2.06% of the total scalar volume). The implant (light purple and yellow) and open scalar volume (light green) are segmented.

We have observed a mosaic pattern of neo-ossification in the mouse cochlea when examined at 28-days post implantation. Utilizing a sequence of hard stains (Movat's Pentachrome and Hematoyxlin and Eosin) on adjacent mid-modiolar sections to distinguish fibrin, cartilage, osteoid and bone we demonstrate the presence of mineralized bone with some residual cartilage intermediates (**Figure 3**). The focused presence of cartilage around the implant tract in the mid-scala supports the role of endochondral ossification in post-CI neo-ossification, whereas our observations of bone formation without cartilage intermediates on the periphery of the implant tract indicates an intramembranous ossification process, possibly associated with sites endosteal damage. In an additional set of experiments, we administered a CSF1R specific kinase (c-FMS) inhibitor, PLX-5622, to suppress cochlear macrophages pre- and post-operatively. In macrophage suppressed mice, we see less cartilage intermediates, less neo-ossification, and more fibrin deposition at the 28-day timepoint. We hypothesize macrophages may play a role in fibrin clearance to allow neo-angiogenesis permissive for neo-ossification; with macrophage suppression, excessive fibrin deposition blocks this process.

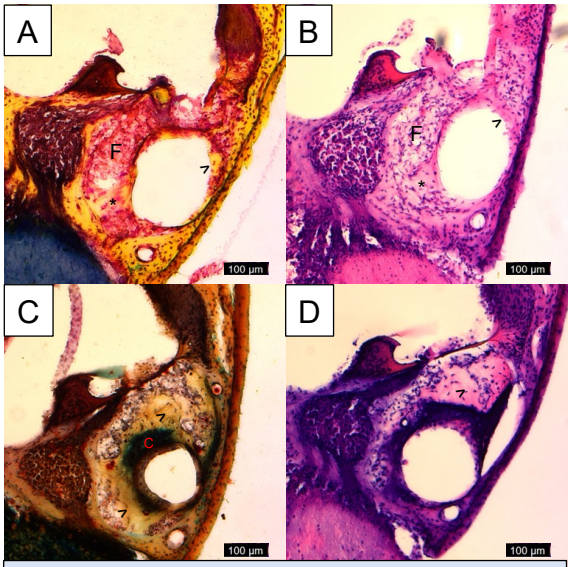


Figure 3. 28-days post-CI Mid-modiolar cochlear sections from mice with (A, B) and without (C, D) macrophage suppression via PLX-5622. Movat's Pentrachrome stain (A, C) highlights new bone formation in yellow, fibrin in red and cartilage in black / green. H&E stains (B, D) are provided for cellular detail. Greater fibrin accumulation, less endochondral ossification and less bone formation were seen with macrophage suppression. "^" Neo-ossification, ""*" Intramembranous ossification, "C" cartilage.

Future Directions:

For Aim 1, we estimate completing recruitment for 40 patients by the end of year 2. eCAP derived data will be analyzed in bulk after the first 10 patients complete the one-year experimental protocol (anticipated late summer 2024), with preliminary data to follow this. We anticipate the final results of this aim will demonstrate the time course of post-CI neo-ossification and provide an assessment of the sensitivity of CIM and eCAP derived measures in detecting post-CI neo-ossification. Additionally, inclusion of the subcohort of patients in the dexamethasone eluting CI trial and the resulting PCCT data will yield insights into the therapeutic efficacy of these experimental CIs in reducing the post-CI foreign body response.

Our preliminary data from Aim 2 suggests the presence of endochondral and intramembranous ossification occurring after CI and that macrophage activity may be necessary for this process. We are examining earlier 10-days and later 56-days post-CI time points, where we expect to see more cartilage intermediates and more mature bone, respectively. We are currently assessing neo-angiogenesis after cochlear implantation using PECAM1-GFP reporter mice to examine the association with neo-ossification. Future experiments in years 2 and 3 will focus further investigating the role of the innate immune response and neo-angiogenesis in cochlear neo-ossification and examining relevant signaling pathways and cell populations.

American Otological Society Fellowship Grant
Progress report: 07/01/2023 – 02/12/2024
PI: D. Alexander Cronkite, MD
Mentors and Co-PI: Larry Hoffman, PhD and Felix Schweizer, PhD
Title: Exploring the synaptic transcriptome of vestibular hair cells

Introduction: The sensory epithelia of the inner ear vestibular epithelia encode head movements that contribute to the stabilization of sensory gaze, whether it be visual, auditory, somatosensory, and probably even olfactory gaze. The coding of head kinematics depends on two types of mechanosensitive hair cells. Type II hair cells make synapses with afferent dendrite 'protrusions,' or boutons, at individual contact points. On the other hand, type I hair cells are fully encapsulated by an afferent calyx that receives both 'inner surface' synaptic input from the engulfed type I hair cell and 'outer surface' input from neighboring type II hair cells. Both hair cells express distinct subsets of ion channels and thus differ in their physiological properties. They are also distinguished by their synaptic neurotransmitter release properties with respect to synaptic vesicle pool dynamics and calcium sensitivity. The general aim of this proposal is to establish an unbiased transcriptome of cells in the vestibular epithelia using single-nuclei RNA sequencing (sn-RNAseq). While discovery in this proposal is open to all possible differences in gene expression resulting in coding and non-coding RNA, we will particularly focus on genes and gene-sets that are known to regulate synaptic transmission. The resulting dataset will be made available as a powerful resource to the scientific community. For this application, we will compare the transcriptomes of type I and type II hair cells from adult male and female wild-type and otoferlin-null mice. The project will directly address the following aims.

Aim 1: Establish the adult utricular transcriptome
Determine the optimal conditions to establish the transcriptome of the utricular epithelium of the adult mouse. We will use sn-RNAseq and determine the optimal strategies for specimen harvest, purification, and integrity preservation. The method that provides the largest number of intact cells or nuclei will be selected. Once we have established the optimal conditions, we will provide samples for library construction and sequencing by one of the available cores at UCLA, guided by the support that we received in the design states. The tangible outcome of this aim will be transcriptomes to be analyzed for the specific objectives in Aims 2 and 3. These transcriptomes will be made available to the scientific community through appropriate databases such as gEAR (Orvis et al., 2021).

Aim 2: Determine the major differences between type I and type II hair cells across conditions
In this Aim we will interrogate the dataset with respect to single-nuclei gene expression divergence among the conditions (male and female, wild type and otoferlin-null). As a starting point, we will use the tools available through gEAR (Orvis et al., 2021). Data available in this database, mainly from young animals, will be useful for comparison with the data obtained in Aim1 from older animals. Dimensionality reduction and Louvain cluster analysis will help to identify separate cell clusters. Hair cells will be identified as

expressing Myo7a. Expression of Spp1 will indicate type I while type II hair cells are expected to express Anxa1 and Nhlh1 (Jan et al., 2021). We will also identify hair cells in the striolar vs extrastriolar region as indicated by the expression of oncomodulin (Hoffman et al., 2018). We will compare differences in gene expression in these separate cell clusters between the conditions, using gene-ontology approaches to identify genes associated with regulation of synaptic function.

Aim 3: Test the hypothesis that type I and type II hair cells express a different set of synaptic genes

In this aim we will investigate whether networks of functionally related genes exhibit heterogeneity between type I and type II hair cells across the four conditions. We will use weighted gene co-expression network analysis (WGCNA) to determine clusters or modules of genes that are co-regulated and determine whether synaptic proteins are represented in a module.

Progress: In the last 6 months we have completed all preparatory work and optimization required to successfully harvest and process mouse vestibular epithelia for downstream sn-RNAseq and have completed a series of 5 sn-RNAseq experiments with wild-type and otoferlin-null animals. A significant portion of the first 6 months was dedicated to optimizing our methods for single-nuclei suspension generation. We utilized the 10X Genomics Chromium Nuclei Isolation kit with slight modification to the protocol after initial nuclei isolation experiments. We determined that for one mouse (2 sets of vestibular epithelia) we were able to yield ~15k nuclei in suspension that were of high enough quality for downstream processing. Based on this yield, we pooled 5-6 mice per condition in our subsequent experiments for sn-RNAseq due to ideal single-nuclei number and concentrations optimal for the 10X platform. We have worked extremely closely with the UCLA center for genomics and bioinformatics during the first 6 months of the grant duration. From the single-nuclei suspensions we have provided, we have successfully been able to create single nuclei droplet emersions with barcoding in all samples. Moreover, the quality of RNA from the single-nuclei samples and cDNA from the sample libraries have all been optimal for sequencing. We have completed all planned sn-RNAseq experiments and during the next 6 months of the grant period, will focus on the data analysis and bioinformatics portion of the specific aims. Overall, we have successfully achieved Aim 1 and the next 6 months will focus on Aims 2 and 3 with our in depth computational data analysis.

Title: Lifetime of the Tip Link in Living Hair Cells
PI: Corena Loeb
Funding Mechanism: Fellowship Grant
Mentor: David Corey
Funding Period: 7/1/23-6/30/24
Progress Report Date: 2/12/24

Background: The inner ear mechano-electric transduction (MET) complex converts the force from sound and head movement into the senses of hearing and balance. Transmitting force to, and pulling open the mechanotransducer channel is the tip link, a double-stranded protein filament containing CDH23 and PCDH15, bound to one another head- to-head. The lifetime of this CDH23-PCDH15 bond, how it behaves under force, and how mutations compromise its function are not well understood. For decades, the tip link was thought to have a lifetime of hours; however, our recent *in vitro* work suggests a lifetime on the order of seconds. Mutations in CDH23 or PCDH15 cause human deafness and vestibular dysfunction. Understanding how these mutations affect tip-link lifetime is crucial to designing therapeutic intervention, yet this interaction has never been studied in living hair cells. Here, I will investigate the lifetime of the tip-link bond in live hair cells for the first time using a combination of engineered competitor assays, kinetic modeling, and patch-clamp electrophysiology.

Specific Aim 1: Use competition assay in mouse cochlear explants to estimate lifetime.
A competition assay will allow us to directly observe dissolution of the tip link bond. I will synthesize a 'competitor' containing a stabilizing protein fused to bond interface domains EC1-2 of CDH23 that selectively binds to PCDH15 free ends. When PCDH15 unbinds from tip-link CDH23, the CDH23 fragment of the competitor will bind to PCDH15 free ends and compete with tip-link CDH23 to diminish rebinding. If the tip link unbinds while the competitor is in solution, we will see an associated decrease in FM1-43 uptake, a fluorescent dye that enters hair cells through MET channels only if the tip link is intact. Using FM1-43 in mouse cochlear explants will provide a quick way to test the efficacy of our competitor in live hair cells. By incubating hair cells with competitor for different lengths of time, I will get an estimate of tip- link lifetime.

Progress: To test whether FM1-43 experiments have the required resolution to discern rate constants, we tested FM1-43 at shorter intervals to demonstrate that FM1-43 loads linearly with time and has a resolution of several seconds **(Fig. 1A)**. This will allow us to observe the predicted off rate of about eight seconds. Further, we wanted to ensure the competitor is disrupting the tip link bond and not blocking the MET channel which could also result in decreased fluorescent intensity. I am in the process of testing individual components of the competitor to see if they block in the same manner as the entire competitor. Testing just the tail of the competitor (SpyCatcher), I found it does not block **(Fig. 1B)**. We have added more cells to each timepoint and see that at 1 minute inhibition–the shortest time tested so far–there is a decrease in FM1-43 loading, suggesting the tip link has a lifetime of less than 1 minute.

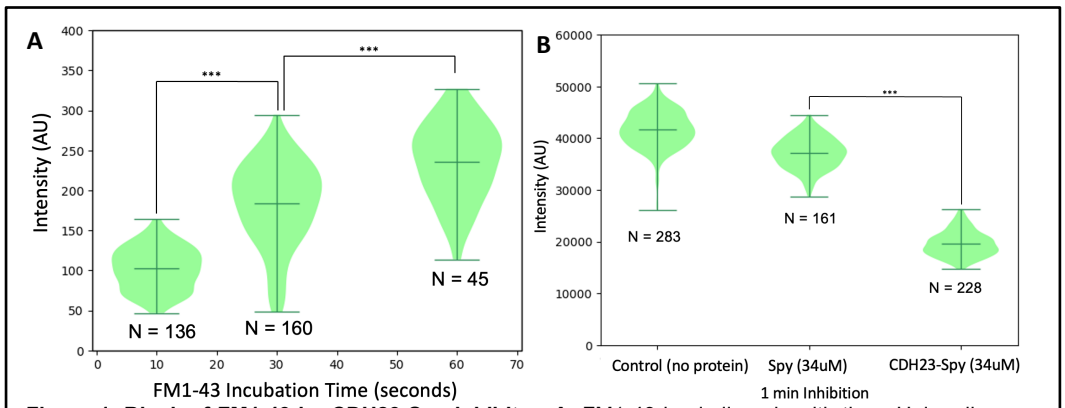


Figure 1. Block of FM1-43 by CDH23-Spy inhibitor. A. FM1-43 loads linearly with time. Hair cells were incubated with FM1-43 at 10 seconds, 30 seconds, and 1-minute intervals, and then measured for average fluorescent intensity. As incubation time increases, FM1-43 intensity also increases and is significantly different at each time (unpaired t-tests, p-values < 0.001). N = number of cells. .**B.** Data from six such experiments. Intensity is significantly less after the inhibitor (unpaired t-test, p-value < 0.001). N = number of cells. Overall, loading was inhibited by 45%

Specific Aim 2: Measure the lifetime of the tip link in live hair cells
I will characterize our knock-in mouse model, "Spy-PCDH15," expressing PCDH15 with an N-terminal SpyTag. The SpyCatcher moiety on the competitor forms a covalent bond to the SpyTag, holding the competitor sufficiently close to PCDH15 to out-compete endogenous CDH23 and prevent rebinding. By eliminating rebinding, I can directly measure off rate, offering a more accurate measurement of tip-link lifetime.

Progress: We used a dual vector AAV9-PHP.B to inject *Spy-Pcdh15* into *Pcdh15* knock-out mice (*Pcdh15*$^{fl/fl}$, *Myo15-Cre*+) as an initial test of whether the SpyTag disrupts normal PCDH15 function. We had already demonstrated that knock-in mice have restored ABR threshold and normal stereocilia bundle morphology. We developed an assay to label Spy-PCDH15 to ensure trafficking to the correct location and can see Spy-PCDH15 properly localized to hair cell stereocilia **(Fig. 2).**

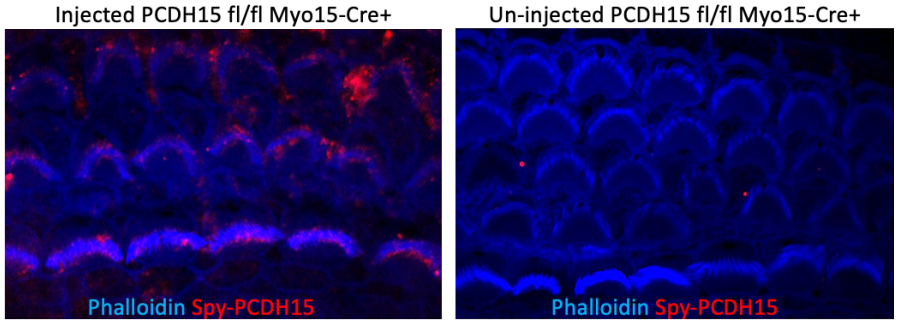


Figure 2. Pcdh15 knockout mice injected with AAV encoding Spy-Pcdh15. We observe Spy-PCDH15 labeling on stereocilia in injected mice but not uninjected controls.

While FM1-43 accumulation offers an indirect measure of MET channel open probability and tip-link lifetime, whole-cell electrophysiology provides an immediate measure of when the tip link completely unbinds. I will record from the inner hair cells of Spy-PCDH15 mouse cochlear explants while stimulating the hair bundle with a stiff probe to elicit mechanotransduction currents. With the competitor irreversibly bound to Spy-PCDH15 to prevent rebinding, I can directly observe when the tip link unbinds by a reduction in mechanotransduction current. Measuring mechanotransduction current over the course of a periodic mechanical stimulus will allow me to extrapolate the off rate of the tip link using my curve fitting model.

I have constructed an electrophysiology rig and have successfully recorded MET currents in wildtype hair cells **(Fig 3).** Over the past few months we have been breeding our founding Spy-PCDH15 knock-in mice and now finally have homozygotes. To ensure that the SpyTag does not impair trafficking of protein or normal cochlear function, I will localize the SpyTag using a SpyCatcher-based synthetic antibody (IgG-FcSpyCatcher3; BioRad). I will map localization of Spy-PCDH15 at the tips of hair cell stereocilia. To confirm normal function, I will measure auditory brainstem response in mice homozygous for the Spy-PCDH15 allele. Further, I will perform the FM1-43 competition assay in both homozygous knock-in and wildtype mouse hair cells. We can then proceed with performing the competition assay on the Spy-PCDH15 mice while recording MET currents to resolve the tip link lifetime. We are very excited to begin these experiments over the next few months and thank the American Otological Society for their generous support.

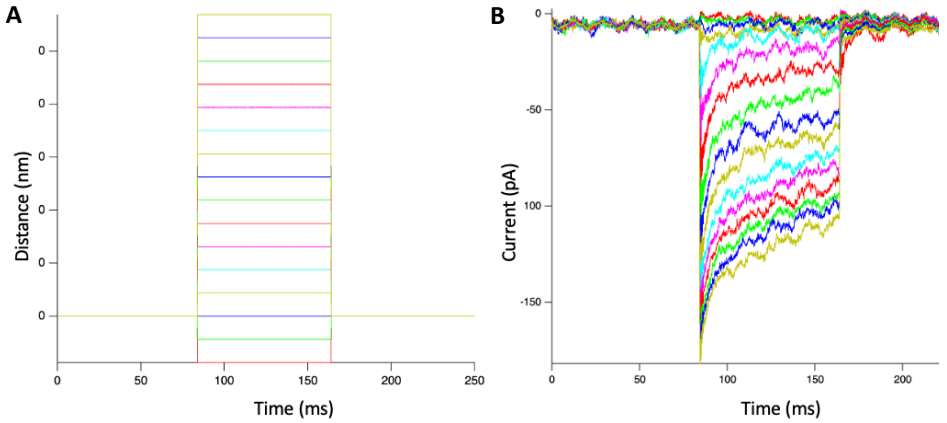


Figure 3. Mechanotransduction currents in wildtype hair cells. A. Bundle deflection using a stiff probe. **B.** Mechanotransduction currents.

Specific Aim 3: Measure the effect of human deafness mutations on tip-link lifetime.
Mutations in binding domains EC1-2 of PCDH15 and CDH23 result in human deafness, yet we do not understand the underlying pathology. Using the methods described in aim 2b, I will assess tip-link lifetime in a mouse model of human deafness caused by mutations in CDH23. Revealing the tip-link rate constants for human deafness mutations will provide insight into how tip-link mutations impair mechanotransduction and result in hearing loss.

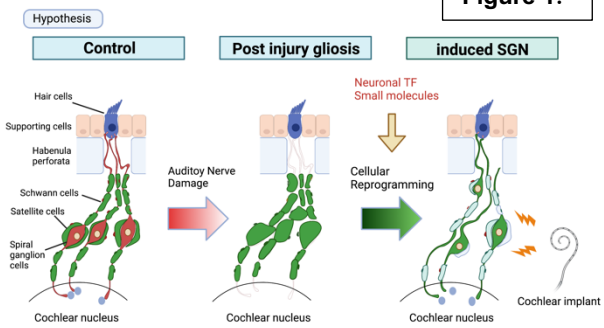
The last phase of the project, once I have reproduceable measurements of tip-link lifetime during single-cell recording, will be to repeat these experiments in mice with mutations in CDH23. I expect to do these experiments in the late spring of this year.

AOS-CSA PI: Seiji B. Shibata
American Otological Society Clinician Scientist Award –Progress Report
Fellowship Grant Funding Period: 7/1/2023 – 6/30/2024
Progress Report Date: 2/12/2024
Principal Investigator: Seiji B. Shibata MD PhD
Mentors: Justin Ichida
Project Title: *Cellular reprogramming of peripheral glial cells to generate auditory neurons*

Background:
Sensorineural hearing loss (SNHL) is a major public health issue, as by 2050, over 900 million people are predicted to have some degree of hearing loss. The auditory nerve plays a crucial role in hearing by transmitting acoustic signals generated from the inner ear to the brain. Degeneration of the auditory nerve can be induced by ototoxic drugs, noise, or aging. Because the auditory nerve lacks intrinsic regenerative capacity, damage to the nerve leads to permanent SNHL. There are no effective treatments that account for the loss of spiral ganglion neuron (SGN), as observed in auditory neuropathy (AN) or neural deafness. Thus, regenerative medicine to restore the SGN holds enormous potential.

Given the plasticity of certain somatic cells, in vivo direct reprogramming is an emerging field in regenerative medicine. One potential source in the inner ear is the peripheral glial cells, which are primarily composed of Schwann cells and satellite cells. Earlier work has shown that a subpopulation of cochlear glial cells are potent progenitors and can be coaxed into neuron-like cells by overexpression of bHLH transcription factors Ascl1, Neurog1, and NeuroD1 in vitro. However, research investigating this approach in vivo and in damaged tissue is limited. ***Hypothesis****: Direct cell reprogramming of the cochlear glial cells with neuronal transcription factors can generate induced SGN to restore hearing (*Fig. 1*).*

Figure 1.



Aim 1: Explore *in vitro* and *in vivo* direct reprogramming using cochlear glial cells.
Specific goals of Aim1:
Aim 1.1, **Determine optimal vector and promoter to transduce the cochlear glial cells in vivo.** We have screened the cochlear transduction profile of AAV serotypes 1, 6, 9, PHP.eB, DJ, and DJ/8 that harbor CMV driven GFP. P2-3 neonatal mice have been injected via the posterior semicircular canal. The whole mount and cryosection cochlear tissue were stained for neuronal marker NF200 and glial cell marker Sox10. We determined that AAV1, PHPeB, and DJ transfected the glial cells as well as many of the otic mesenchyme cells. The vectors do not affect the auditory function when injected at this age (*Poster at the ARO 2023 meeting).*To better target the glial cells, we are looking at alternative AAV serotypes such as AAV-ie and glia specific promotes.

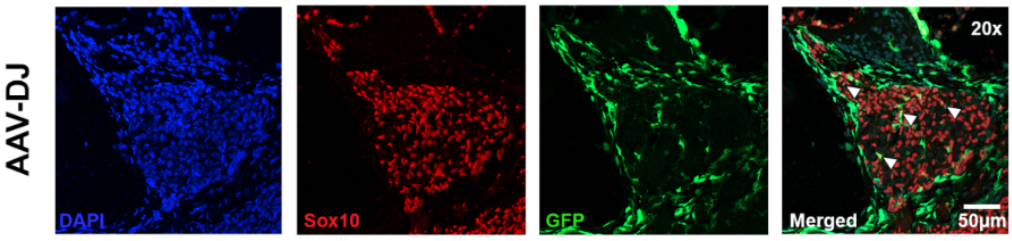


Figure 2. Neonatal cochlea following injection of AAVDJ-CMV-GFP. GFP positive glial cells (arrow head) and otic mesenchyme cells are shown in the Rosenthal's Canal.

Aim 1.2, Explore in vitro direct reprogramming of cochlear glial cells. We demonstrate that mouse embryo fibroblasts can be induced into sensory neurons with cocktail of transcription factors cloned into retroviruses. The induced neurons have morphological and molecular features consistent with sensory neurons (Fig. 3). We initially proposed using the downregulation of Ptbp1 gene to induce neurogenesis, as it demonstrated promise in the CNS. However, stringent lineage tracing of induced neurons was found to be an artifact in recent follow-up papers. We have moved away from Ptbp1 and will now focus on the neurogenic molecules miRNAs; miR-9/9 and miR-124, that are highly abundant in neuronal tissue and are essential for neural differentiation. Combination treatment of miRNAs with neuronal transcription factors has shown enhanced reprogramming efficiency in the CNS in Dr. Andrew Woo's lab (WashU) who is a collaborator in my project.

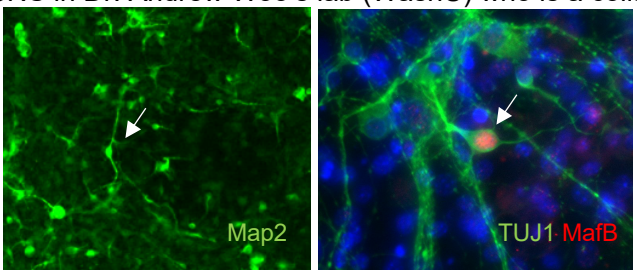


Figure 3. Induced spiral ganglion cells in vitro following cocktail of transcription factors. Induced spiral ganglion neurons (arrows) express Map2, MafB, and Tuj1.

AOS-CSA PI: Seiji B. Shibata

Aim 2: Determine the glial cell response to SGN degeneration in the AN model in neonatal mice.
We sought to develop a neonatal mouse model with primary SGN degeneration to assess reactive gliosis and regenerative competence during the early developmental stage. We hypothesized that Ouabain will selectively lesion SGNs when administered in the neonatal mice. However, we determined that while Ouabain is effective in SGN ablation in adult mice, it does not have the same effects in neonatal mice. We pivoted to SGN deletion using the viral delivery of Cre-dependent diphtheria toxin fragment A (DTA). DTA inactivates EF2 and causes inhibition of protein synthesis, and induces apoptosis. We injected AAV-Retro-EF1a/hSYN-FLEX-DTA-mCherry (AAV-DTA) in Parvalbumin-Cre (PV^{cre}) mice. The FLEX switch allows DTA expression under the control of Cre-recombinase and the AAV-Retro selectively transfects the SGN. Our data demonstrates that our mouse model allows temporal control of SGN ablation (*Poster at ARO midwinter meeting 2024*). This mouse model enables the investigation of reactive gliosis in response to selective and robust SGN degeneration in different developmental ages in mice. We also expect that this model will help unravel the regenerative competence of glial cells post-SGN damage.

We examined the primary SGN loss in the neonatal mice following the administration of AAV-DTA (Fig. 4). We injected P2 AAV-DTA in PV^{cre} mice crossed with Ai9Tdtomato mice (Fig. 4B and C). We observed rapid degeneration of SGN compared to injected wild type (C57 mice), we found 50% reduction of SGN cell density at 1 week (Fig. 4D) followed by near total ablation by one month. Increase in Caspase-3 is noted in AAV-DTA injected PV^{cre} but not wild type mice (Fig. 4E). The ABR threshold measurements confirmed profound deafness at 4 weeks with intact DPOAE. This single injection DTA-induced deafening model in neonatal mice allows us to investigate the processes of neural degeneration and regeneration during early cochlear development.

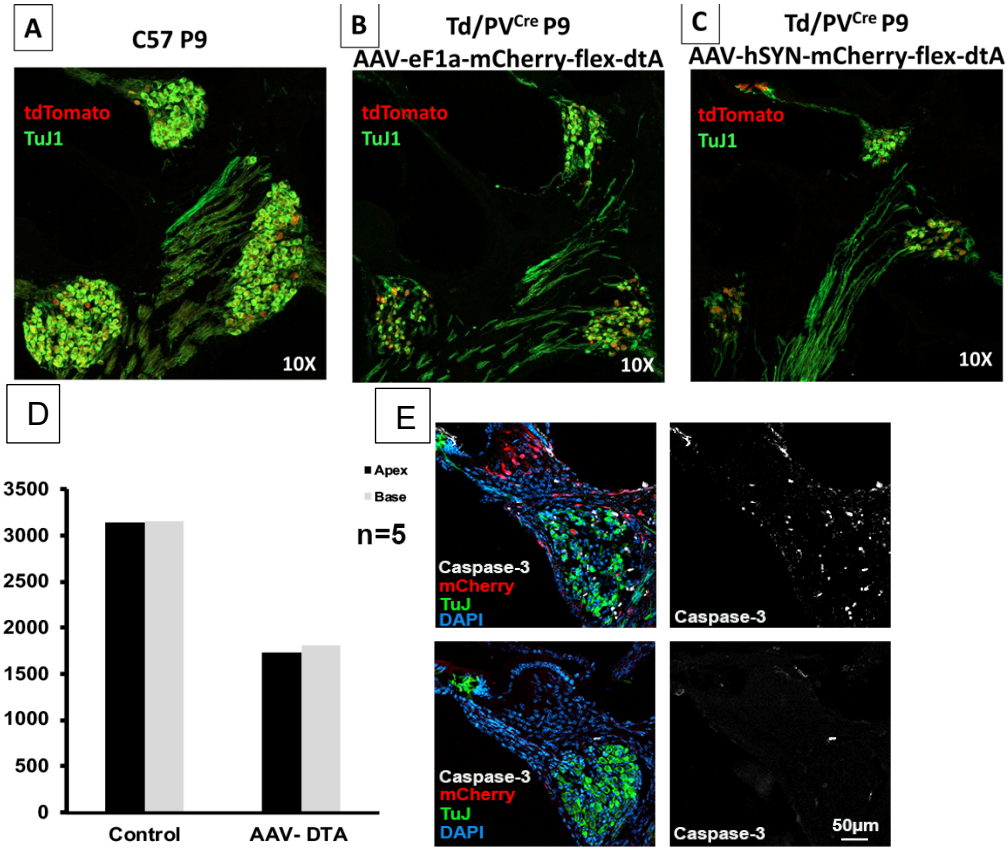


Figure 4. AAV-DTA allows rapid degeneration of SGN cells in Cre-dependent fashion. Control (A) vs AAV-DTA injected mice (B and C), there is notable loss of SGN cells by 1 week using either ubiquitous EF1a promoter or neuronal hSYN promoter to express FLEX-DTA. Quantification of the SGN density shows significant loss of SGN less at one week, this is further decreased to near notal ablation by one month (D). We demonstrate that AAV-DTA injected mice are undergoing apoptosis only in the Rosenthal's canal (E).

Continuing work on Aim 2. By establishing our model, we will now focus on the investigation of reactive gliosis in different mouse ages and variations in the transcription of glia, neuron, and apoptosis-associated genes at varying time points before and after the onset of hearing loss using bulk single-cell sequencing of glia following SGN loss. We will use PLP-GFP (marker for glia cells) mice and cross them with PV^{cre} mice to allow neonatal mice with selective SGN loss following AAV-DTA injection.

Training Progress: During the past year, I have obtained further funding support from the Triological Society Clinician Scientist Award along with my K08 from the NIDCD. We have optimized our setup in the lab with necessary equipment to perform molecular experiments in my lab. I meet regularly with Dr. Ichida to discuss progress.

American Otological Society
Fellowship Grant Funding Period: 07/01/2023 – 06/30/2024
Progress Report Date: 02/12/2024
Principal Investigator: Anna M. Wisniowiecki
Mentor: Brian E. Applegate
Project Title: Sub-Cellular 3D Vibrometry for Measuring Cochlear Mechanics in the Mouse Organ of Corti

Background

Mammalian hearing relies on sound propagation and transduction from a 3-dimensional, spatially-tuned wave to produce the broad bandwidth, frequency-place mapping and sharp frequency tuning of mammalian and human hearing. However, the mechanisms that underlie these important features are not well known and remain under debate. While the discovery of electromotility in outer hair cells (OHCs) and the motor protein, prestin, have provided clues to the mechanism of cochlear amplification[1,2], the question of how amplification occurs, including how outer and inner hair cells, and their stereocilia, are stimulated, remains[3,4]. Adjacent structures may also contribute to frequency tuning[5]. Answering these questions is key to the development of effective, restorative hearing therapies for sensorineural hearing loss (SNHL) (e.g. quantifying efficacy of gene therapies).

Due to the scale and location of the inner ear, it is particularly difficult to observe the natural function of the cochlea. Optical coherence tomography (OCT) has filled a technology gap in otology research by providing noninvasive, depth-resolved imaging with micron-scale resolution and vibrometry with pico-meter scale sensitivity in the mammalian ear[6]. While vibrometry offers a direct method to address questions in fundamental research and conduct preclinical research, established OCT-V remains limited to measuring vibration along one axis. Our lab previously developed a 3D-OCT system, using 3 beams, to resolve the vector of motion[7]. This system is complex and limits optical resolution such that single cell measurements cannot be achieved. A definitive understanding of the mechanical response of the ear requires 3D vibration measurement at sub-cellular resolution and acoustic frequencies.

To overcome the limitations of current OCT-V methods, we develop a new speckle tracking approach toward vector of motion measurement that enables the use of a single-beam OCT system and, therefore, sub-cellular resolution. Specifically, a single beam OCT system is modified using a fast scanner to encode the vibration angle in the OCT data. Combining measurements of the angle of motion in the x,z (Φx,z) and y,z (Φy,z) planes from this modified approach with vibration amplitude measurement using existing OCT-V, we can reconstruct the full vector of motion for a region of interest while reducing the imaging hardware requirements and increasing flexibility in experiment design.

Aim I. Develop an approach for the estimation of vibration angle for nano-scale vibrations to reconstruct the 3D vector of motion in the mouse inner ear using a single-beam OCT system

Approach: Cross-sectional OCT images are acquired from a single-beam OCT system while driving a tissue phantom with a pure tone. Image features are extracted to identify the vibration angle.

Progress: To make our approach applicable to imaging of the mouse ear, high vibration amplitude sensitivity (<1 nm) is necessary. We hypothesize that the vibration amplitude sensitivity of our approach scales with optical resolution. To test this theory, we acquired a new dataset with vibration amplitude at the nanometer scale using a high-resolution OCT system (lateral resolution ~2μm) and tissue phantom (Figure 1a). Pre-processing of datasets revealed high contrast patterns (Figure 1b), suggesting good correlation between derived image features and vibration angle. By increasing the number of frames used in pre-processing to enhance the SNR, we were able to resolve image features at the lowest vibration amplitude. This indicates that, since we expect low amplitudes in the mouse ear, we need to acquire >500

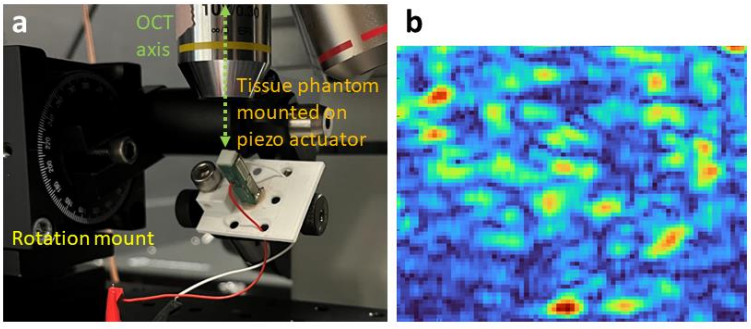


Figure 1. a) Experimental setup for nanometer scale vibration dataset. A piezoelectric phantom was driven at 100 Hz over a wide range of vibration amplitudes and angles. b) Example image of the phantom from the high-resolution OCT system.

frames for accurate predictions. In addition, we found that smaller imaging windows tend to create clearer feature maps, which is advantageous for measuring from single cells and cell regions.
We are currently in the process of comparing the accuracy of several analytical methods and a neural network-based approach to elucidate the most accurate method for measurement of the vibration angle. After the algorithm is selected and optimized, comparison of measurements using the proposed method and a 3-beam OCT-V system[7] will be used to validate the method.

Aim II. Characterize single-cell and sub-cellular 3D micro-mechanics in the organ of Corti of wildtype mice using single-beam 3D OCT-V

Approach: A high-resolution OCT system is combined with a fast scanner to create an approach capable of measuring vibrations in the best frequency range (~2-15 kHz) of the apex of the mouse cochlea. Our high-resolution OCT system allows us to identify individual cells within the Organ of Corti. Once the technique is developed, characterization of the wildtype, inner ear vector of motion will be undertaken to better define cell type-specific mechanics and their role in cochlear amplification.

Progress: In parallel with Aim I, we are working to test and implement a high frequency version of our method to capture vibrations in the mouse apex, as the algorithm performance is expected to be independent of frequency when adequate acquisition parameters are applied. As the laser sweep rate in our system is fixed, we have selected a MEMS scanner capable of a ~4 kHz frame rate to acquire 25 A-lines per B-scan. In testing, we have found that we can drive this scanner beyond its resonance frequency to achieve this result. To validate that our method can capture the best frequency range for the mouse apex and verify accurate predictions using the new scan, a high frequency dataset will be acquired with our tissue phantom using temporal interleaving[8]. By creating a mosaic of 3D-OCT measurements, we plan to present the final results in overlay plots (similar to ref.7) or vector map animations for both phantom and cochlear measurements.

Presentations

Wisniowiecki, A.M.; Ratnayake, K.; Oghalai, J.S.; Applegate, B.E. Frequency Domain Speckle Tracking for 3-D Vibrometry. Accepted as a talk at the Mechanics of Hearing Annual Meeting. 2024 June.

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4 Dewey, J. B., Altoè, A., Shera, C. A., Applegate, B. E. & Oghalai, J. S. Cochlear outer hair cell electromotility enhances organ of Corti motion on a cycle-by-cycle basis at high frequencies in vivo. *Proceedings of the National Academy of Sciences* **118**, e2025206118 (2021).
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7 Kim, W. *et al.* Vector of motion measurements in the living cochlea using a 3D OCT vibrometry system. *Biomedical optics express* **13**, 2542-2553 (2022).
8 Applegate, B. E., Shelton, R. L., Gao, S. S. & Oghalai, J. S. Imaging high-frequency periodic motion in the mouse ear with coherently interleaved optical coherence tomography. *Opt Lett* **36**, 4716-4718 (2011).

AOS Grant Progress report
Funding Period: July 1, 2023 - June 30, 2024.

American Otological Society Research Grant
Progress report: 7/1/2023 – 1/31/2024
PI: Adrien A. Eshraghi, MD
Title: Developing a Novel Treatment Modality for the Preservation of Residual Hearing Post-Cochlear Implantation

Progress Report

For the last year, we have been focused on the following aims**:**

Aim 1: Determining the optimum dosage and evaluate the efficacy of Taurodeoxycholic acid (TDCA) in hearing preservation in a preclinical rat model of cochlear implantation.

Experimental design:

- Sprague-Dawley rats (6-8 weeks old) were divided into 2 groups.
- In Group 1, cochlear implantation was performed through a cochleostomy at the basal turn of the cochlea.
- In Group 2, TDCA at various concentrations was applied on the round window membrane 30 min before cochlear implantation. Cochlear implantation was then performed similarly to group 1.
- Various concentrations of the drug were tested: 100 µM; 200 µM, and 300 µM.
- The contralateral ear served as control in each rat.
- Auditory brainstem recordings (ABRs) were performed at different frequencies (1, 4, 8, 16, 24 and 32 kHz) at baseline, Day 3, and Day 7 post-implantation to determine hearing thresholds.

Results:

- There was a significant increase in hearing thresholds of animals following implantation compared to baseline threshold values before implantation.
- Animals implanted and received TDCA through RWM showed significantly decrease in this electrode insertion trauma (EIT) elevated hearing thresholds in a dose dependent manner at all frequencies.
- Hearing thresholds were significantly lower at TDCA concentration of 300 µM at day 3 and day 7 post-implantation (**Figure 1**).

Conclusions:

- Our results suggest that TDCA provides otoprotection against EIT post-cochlear implantation at earlier days of 3 and 7.

- TDCA concentration of (300 μM) appears to be optimum dosage to provide otoprotection against cochlear implant trauma.

Aim 2: Evaluating the stability of otoprotective ability of Taurodeoxycholic acid (TDCA) over an extended period of time post-cochlear implantation.

Experimental design:

- Same as in Aim 1.
- ABRs were performed at Day 14 and Day 30 post-implantation to determine hearing thresholds.

Results:

Hearing thresholds were significantly lower at TDCA concentration of 300 μM at day 14 and day 30 post-implantation (**Figure 1**).

Conclusions:

The otoprotective ability of TDCA is stable and extends over a time period of 30-day post-cochlear implantation.

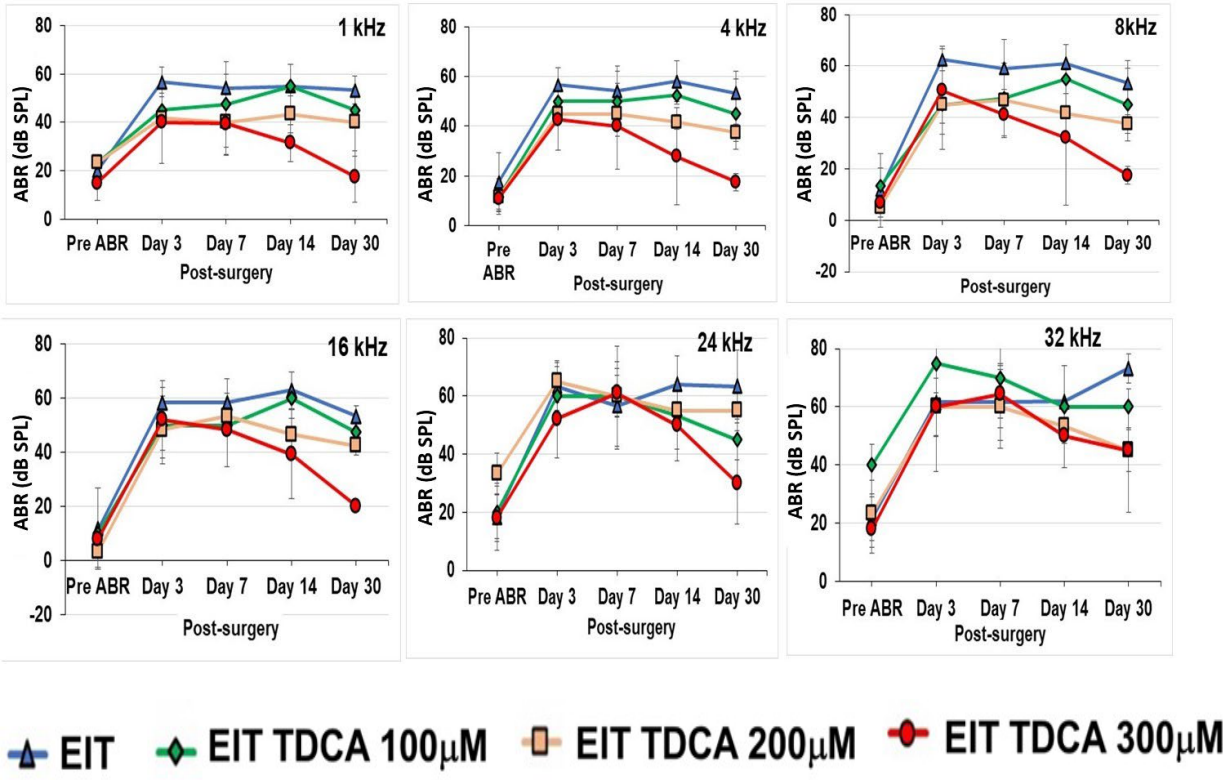

Figure 1: TDCA promotes Hearing threshold preservation in a dose dependent manner with maximum efficacy at 300 μM. Hearing preservation with TDCA was observed till 30th day post-cochlear implantation.

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1969	Sir Terence Cawthorne
1970	Senator Joseph A. Sullivan, MB
1971	Samuel Rosen, MD
1972	Howard P. House, MD
1973	Moses H. Lurie, MD
1974	George E. Shambaugh, Jr., MD
1975	Catherine A. Smith, PhD
1976	Harry Rosenwasser, MD
1977	Frank Lathrop, MD
1978	Juergen Tonndorf, MD
1979	John Bordley, MD
1980	Ben H. Senturia, MD
1981	J. Brown Farrior, MD
1982	William F. House, MD
1983	Victor Goodhill, MD
1984	Harold F. Schuknecht, MD
1985	Wesley H. Bradley, MD
1986	John J. Shea, Jr., MD
1987	Jack V. Hough, MD
1988	George D. Nager, MD
1989	Brian F. McCabe, MD
1990	Eugene L. Derlacki, MD
1991	Richard R. Gacek, MD
1992	James L. Sheehy, MD
1993	James A. Donaldson, MD
1994	Fred H. Linthicum, Jr., MD
1995	D. Thane Cody, MD
1996	F. Blair Simmons, MD
1997	Michael E. Glasscock, III, MD
1998	Michael M. Paparella, MD
1999	Mansfield F. W. Smith, MD
2000	Robert A. Jahrsdoerfer, MD
2001	Derald E. Brackmann, MD
2002	Gregory J. Matz, MD
2003	James B. Snow, Jr., MD
2004	Robert J. Ruben, MD
2005	David J. Lim, MD
2006	Herbert Silverstein, MD
2007	Richard A. Chole, MD, PhD
2008	Malcolm D. Graham, MD
2009	William H. Lippy, MD
2010	George Gates, MD
2011	Sam E. Kinney, MD
2012	Joseph B. Nadol, Jr., MD
2013	Bruce J. Gantz, MD

2014 Richard T. Miyamoto, MD

2015 Jeffrey P. Harris, MD, PhD

2016 Charles M. Luetje, MD

2017 Clough Shelton, MD

2018 Paul R. Lambert, MD

2019 John W. House, MD

2020 Steven A. Telian, MD

2021 Miriam I. Redleaf, MD

2022 Lloyd Brooks Minor, MD

2023 Debara L. Tucci, MD, MS, MBA

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(Includes the 2024 Candidates inducted at the AOS 2024 Spring Meeting)

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Sao Paulo, Brazil
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Toronto, *Ontario, Canada*
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Subiaco, Australia
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Emeritus

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Mercer Island, Washington
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Luzern, Switzerland
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Mainz, Germany
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Active/Fellow

John T. McElveen Jr., MD
Raleigh, North Carolina
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Issaquah, Washington
Senior

Stephanie A. Moody Antonio, MD
Norfolk, Virginia
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Gary F. Moore, MD
Omaha, Nebraska
Active/Fellow

William H. Moretz Jr., MD
Augusta, Georgia
Senior

Tetsuo Morizono, MD, DMS
Fukuoka City, Japan
Senior Associate

Terry P. Murphy, MD
Baton Rouge, Louisiana
Senior

Eugene N. Myers, MD
Pittsburgh, Pennsylvania
Emeritus

Joseph B. Nadol Jr., MD
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Emeritus

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Active/Fellow

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Philadelphia, Pennsylvania
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James J. Pappas, MD
Little Rock, Arkansas
Emeritus

Dennis Pappas, MD
Birmingham, AL
Emeritus

Dennis G. Pappas Jr., MD
Birmingham, Alabama
Active/Fellow

Blake C. Papsin, MD
Toronto, Ontario, Canada
Active/Fellow

Simon C. Parisier, MD
New York, New York
Senior

Albert Park, MD
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Steven M. Parnes, MD
Albany, New York
Senior

Lorne S. Parnes, MD
London, Ontario, Canada
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Cincinnati, Ohio
Senior

Rodney Perkins, MD
Woodside, California
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Harold C. Pillsbury, MD
Banner Elk, North Carolina
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Boston, Massachusetts
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Leonard R. Proctor, MD
Bel Aire, Maryland
Emeritus

Steven D. Rauch, MD
Watertown, Massachusetts
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Miriam I. Redleaf, MD
Chicago, Illinois
Active/Fellow

Jose A. Rivas, MD
Bogota, Colombia
Emeritus

Alejandro Rivas, MD
Cleveland, Ohio
Active/Fellow

Pamela C. Roehm, MD, PhD
Jenkintown, Pennsylvania
Active/Fellow

Peter S. Roland, MD
Eden, Utah
Senior

J. Thomas Roland Jr., MD
New York, New York
Active/Fellow

Max L. Ronis, MD
Philadelphia, Pennsylvania
Emeritus

Seth Rosenberg, MD
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Senior Associate

Robert J. Ruben, MD
New York, New York
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Allan M. Rubin, MD, PhD
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Celebration, Florida
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New York, New York
Active/Fellow

Clough Shelton, MD
Walla Walla, Washington
Emeritus

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Newport Beach, California
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Herbert Silverstein, MD
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St. Louis, Missouri
Emeritus

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Kansas City, Kansas
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Palo Alto, California
Active/Fellow

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Active/Fellow

Nancy M. Young, MD
Chicago, Illinois
Active/Fellow

Daniel M. Zeitler, MD
Seattle, Washington
Active/Fellow

in Memoriam

The AOS Administrative office was notified of the following members passing since the last Spring meeting.

Please take a moment of silence to remember these outstanding colleagues & friends.
(in alphabetical order)

Dr. John R. Emmett
Inducted to AOS in 1990
Passed: June 2, 2023

Dr. Cecil Hart
Inducted to AOS in 1992
Passed: August 21, 2022

Dr. James L. Parkin
Inducted to AOS in 1986
Passed: June 18, 2023

Dr. Eiji Yanagisawa
Inducted to AOS in 1996
Passed: February 1, 2024