

# PROGRAM, ABSTRACTS and MORE

One Hundred Fifty Eighth Annual Meeting

of the

American Otological Society



May 16-18, 2025 Hyatt Regency New Orleans, LA

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# AMERICAN OTOLOGICAL SOCIETY COUNCIL MEMBERS JULY 1, 2024 - JUNE 30, 2025

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Dennis S. Poe, MD, PhD Boston Children's Hospital - Boston, MA

#### **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.

#### **MISSION STATEMENT** (Revised Dec 2024)

The American Otological Society is a world-leading association in ear-related health care. We collaborate across institutional and international boundaries to advance otology, identify and support promising research, cultivate and disseminate excellence in effective and compassionate clinical practices, and elevate all those dedicated to the field of otology through education on cutting-edge discoveries and innovations.

#### **VISION STATEMENT**

The American Otological Society, a global association of preeminent physicians, surgeons, scientists and advocates for the advancement of otology, is dedicated to enabling optimal health, communication, and life experiences for all individuals impacted by hearing loss, balance disorders, and other diseases of the ear and lateral skull base.

# 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.



American Neurotology Society



# CONTINUING MEDICAL EDUCATION CREDIT



# 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.

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 and MOC points from the American Board of Otolaryngology – Head and Neck Surgery.

By attending this activity, you give us permission to share your CME data with the American College of Surgeons, the CME Accredited joint provider, and the Accreditation Council for Continuing Medical Education, (ACCME).

# Program Objectives Educational Activity Details

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

Hearing preservation after cochlear implantation Speech perception outcome after cochlear implantation Medical treatment of sensorineural hearing loss and auditory neuropathy Noise induced hearing loss prevention and treatment Diagnosis and management of otologic disease using advanced imaging technologies Management of chronic otitis media and otosclerosis

# 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 advances in gene therapy, stem cell regeneration, otoprotective medications, and advances in imaging in the diagnosis, treatment and prevention of hearing loss.

Deficiency in knowledge of evolving approaches to improve cochlear implant auditory outcomes

Deficiency of knowledge of outcomes of chronic ear disease and otosclerosis using new materials and surgical approaches.

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

# • Competence:

Increase knowledge of new and emerging treatment for hearing loss such as gene and stem cell therapies.

Increase understanding of advancing imaging technology

Increase understanding of genetic of hearing loss and it impact on diagnosis and treatment Increase understanding of studies of different management techniques for chronic otitis media and otosclerosis

• Performance:

Knowledge gained will improve physician knowledge of technologies and approaches to evaluate, medically and surgically manage otologic disease and enhance patient counseling. These improvements will improve medical and surgical treatment outcomes and patient 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 other otologic conditions to improve public health.

#### If applicable, how do you anticipate this activity impacting the health of patients and their communities?

Increased knowledge of the genetic basis of hearing loss and of noise induced hearing loss will help to identify communities that may be underserved and require more focused education and services to address these issues.

#### State the learning objectives for this activity:

- 1. Recognize how gene and stem cell therapy approaches will be used to treat hearing loss
- 2. Apply greater knowledge of imaging techniques to diagnosis and management of otologic disease
- 3. Describe and compare approaches to cochlear implantation designed to improve outcomes
- 4. Discuss noise induce hearing loss prevention and treatment
- 5. Implement alternative approaches to chronic otitis media and otosclerosis 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.







In accordance with ACCME regulations (<u>ACCME Standard 3</u>), the American College of Surgeons must ensure that anyone who is able to control the content of the activity has disclosed <u>all financial relationships with any ineligible companies in</u> <u>the 24 months prior to their involvement in the educational activity.</u> There is no minimum financial threshold; we ask that you disclose all financial relationships, regardless of the amount, with ineligible companies.

**Ineligible Company: Companies** that are ineligible to be accredited in the ACCME system (ineligible companies) are those whose primary business is producing, marketing, selling, reselling, or distributing healthcare products used by or on patients.

**Financial Relationships:** Financial relationships are relevant if the following three conditions are met for the individual who will control content of the education: 1) a financial relationship, in any amount, exists between the person in control of content and an ineligible company; 2) the financial relationship existed in the last 24 months; 3) the content of the education is related to the products of an ineligible company with whom the person has a financial relationship.

All Council Members, Planning Committee members and Speakers /Moderators/Discussants/Authors/ involved in the development and/or presentation of CME content were required to electronically complete this form. As relevant, all disclosure information for speakers will be revealed by a slide at the beginning of the presentation.

# AS IT RELATES TO THE PRESENTATION:

□ I am an owner or employee of an ineligible company. I am to be excluded from controlling content or participating as faculty in accredited education unless the planning chair determines that I meet an ACCME exception on page 2 of the Mitigation Section. For more information: <u>ACCME Standard 3</u>

□ I am a stockholder of a privately held ineligible company (not through a mutual fund or pension plan). I am to be excluded from controlling content or participating as faculty in accredited education unless the planning chair determines that I meet an ACCME exception on page 2 of the Mitigation Section. For more information: <u>ACCME Standard 3</u>

□ I do not have personal financial relationships with any ineligible companies as defined above.

L <u>do</u> have financial relationship(s) with ineligible companies as defined above.

□ I agree that I will not accept honoraria, travel expenses, in-kind contributions, or any other support from commercial companies/ineligible companies in connection with this activity.

The ACCME also requires that ACS manage any reported conflict and eliminate the potential for bias during the educational activity. Any conflicts reported 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 CME evaluation.

A complete list of disclosures is available on the <u>AOS website conference page</u>.

# THE AMERICAN OTOLOGICAL SOCIETY WOULD LIKE TO THANK THE FOLLOWING MEMBERS FOR THEIR CONTRIBUTION TO THE 2025 AOS SCIENTIFIC PROGRAM

William H. Slattery III, MD, AOS President, Chair Nancy M. Young, MD, AOS Education Director Bradley W. Kesser, MD, AOS Education Director-Elect

#### PROGRAM ADVISORY COMMITTEE

(in alphabetical order)

Gregory J. Basura, MD, PhD Kevin D. Brown, MD, PhD Matthew L. Bush, MD, PhD Kay Chang, MD Sharon L. Cushing, MD, MSc Rick Friedman, MD, PhD Soha Ghossaini, MD Ronna P. Hertzano, MD, PhD Keiko Hirose, MD Michael Hoa, MD Ana H. Kim, MD Stephanie Moody Antonio, MD Quyen Nguyen MD, PhD Ravi N. Samy, MD Yu-Lan Mary Ying, MD Daniel M. Zeitler, MD

#### **POSTER JUDGES**

(in alphabetical order)

Gregory J. Basura, MD, PhD Kevin D. Brown, MD, PhD Soha N. Ghossaini, MD Quyen Nguyen, MD, PhD

# **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 2025 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.** 

**COPYRIGHT TRANSMITTAL:** Abstracts are received with the understanding that they are not under simultaneous consideration by another publication and that they are original contributions that have not been previously published. Accepted abstracts become the permanent property of Otology & Neurotology and may not be published elsewhere without permission from Otology & Neurotology\*

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.

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 60th Annual Fall Meeting "FAB FRIDAY" October 10, 2025 Indianapolis, IN JW Marriott Indianapolis Attendees: the Marriott and the JW Marriott will be co-branded as the AAO/HNSF HQ hotels.

#### AOS 159th Annual Meeting in conjunction with COSM

April 24-26, 2026 Phoenix Convention Center/ <u>Sheraton Phoenix Hotel</u> Phoenix, Arizona

MARK YOUR CALENDAR! Due to the late date of the annual AAO meeting and ANS Fall meeting, the deadline for abstract submissions for the 159th Annual AOS Spring meeting has been extended to Wednesday, October 22, 2025. Abstract Instructions and the submission form will be available on the AOS website after September 1st.

# CONTACT US!

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# AMERICAN OTOLOGICAL SOCIETY 158<sup>th</sup> ANNUAL MEETING SCIENTIFIC PROGRAM May 17-18, 2025 New Orleans, LA

(AOS Posters will be displayed on Friday & Saturday)

# **SATURDAY, MAY 17, 2025**

**1:00 BUSINESS MEETING** and **NEW MEMBER INTRODUCTION** (All registered attendees welcome)

# **1:25 SCIENTIFIC PROGRAM** (Open to registered Members and Non-members – Badge required for admittance)

1:25 WELCOME & OPENING REMARKS BY THE PRESIDENT William H. Slattery, III, MD

# **1:27 PRESIDENTIAL CITATIONS**

Derald E. Brackmann, MD Sujana S. Chandrasekhar, MD M. Jennifer Derebery, MD John W. House, MD William M. Luxford, MD Rodney Perkins, MD Noli Fortugaleza

#### 1:37 INTRODUCTION OF GUEST OF HONOR William H Slatton, III MD

William H. Slattery, III, MD

#### **1:39 GUEST OF HONOR LECTURE**

Regenerating Auditory Nerves: Basic Science to Clinical Trials Prof Marcelo N. Rivolta Professor of Sensory Stem Cell Biology Centre for Stem Cell Biology, School of Biosciences University of Sheffield United Kingdom

# 2:24 SESSION A – COCHLEAR IMPLANTS I

Kevin D. Brown, MD, PhD & Stephanie A. Moody Antonio, MD, Moderators

# 2:25 Cochlear Reimplantations Following Device Dysfunction: A Retrospective Cohort Study

Mélyssa Fortin, MD Richard Bussières, MD Mathieu Côté, MD Daniel Philippon, MD, DMD Sandra Fortin, MPA Mathieu Trudel, MD

# 2:31 Does Early Tinnitus Improvement Influence Long-Term Quality of Life in Cochlear Implant Recipients?

Barak M. Spector, BS Katelyn A. Berg, AuD, PhD David S. Haynes, MD, MMHC Terrin N. Tamati, PhD Aaron C. Moberly, MD

# 2:37 Optimizing Cochlear Implant Activation: A Prospective Patient-Preference Study

Arman Saeedi, MD, MPH Mihai A. Bentan, BS Albina Islam, MD Nauman F. Manzoor Daniel H. Coelho, MD

#### **2:43** High-Resolution Flat-panel CT Analysis of Cochlear Implant Electrode Contact Orientation Ana Marija Sola, MD

Nicole Jiam, MD Melanie Gilbert, AuD Luke Helpard, PhD Charles J. Limb, MD

#### 2:49 Pre-Curved Versus Straight Arrays for Hearing Preservation in Cochlear Implantation: A Systematic Review and Meta-Analyses

David Elisha, BS Nicholas DiStefano, BS Rahul Mittal, PhD Andrea Monterrubio, BS Jeenu Mittal, MSc Adrien Eshraghi, MD

# 2:55 DISCUSSION WITH MODERATOR

# **3:00 BREAK WITH EXHIBITORS**

# **3:30 THE BIG EASY: LOCAL EXPERT PRESENTATION**

Introduction by Moises A. Arriaga, MD, MBA

# **Ushers Disease: Diagnosis and New Treatment Options**

Jennifer J. Lentz, PhD Associate Professor of Otorhinolaryngology & Biocommunications and Neuroscience Adjunct Associate Professor of Ophthalmology LSU Health New Orleans

# 4:00 SESSION B - CHRONIC OTITIS MEDIA

Matthew L. Bush, MD, PhD and Ana H. Kim, MD, Moderators

## 4:01 Outcomes of Tympanic Membrane Regeneration Therapy for Elderly Patients

Rie Kanai, MD Shin-ichi Kanemaru, MD, PhD Tomoya Yamaguchi, MD Ryohei Yuki, MD Razumu Shirai, MD Hiroyuki Harada, MD Toshiki Maetani, MD, PhD

# 4:07 Tympanoplasty Outcomes of Indigenous Populations

Catherine F. Roy, MD Jeffrey C. Yeung, MD, MSc Lamiae Himdi, MD Tamara Mijovic, MD, MSc

# 4:13 Comparing Pediatric and Adult Chronic Otitis Media with Cholesteatoma at the Single-Cell Level

Daniel R. Romano, MD Song-Zhe Li, MD, PhD Richard A. Chole, MD, PhD Michael Hoa, MD Sidharth V. Puram, MD, PhD Keiko Hirose, MD

# 4:19 Does Mastoid and Epitympanic Obliteration with S53P4 Bioactive Glass Reduce Cholesteatoma Recidivism in Canal-Wall-Up Surgeries? A Retrospective Clinical Study

Daniele Bernardeschi, MD, PhD Hugo Delille, MD Matteo Di Bari, MD Olivier Sterkers, MD, PhD Ghizlene Lahlou, MD, PhD Lauranne Alciato, MD

# 4:25 Meningitis and Temporal Bone Pathology - A Diagnostic Recommendation

Ava Karam, BS Frank Rizzuto, BS LTC Isaac Erbele, MD Julio Figueroa, MD Rahul Mehta, MD Moises A. Arriaga, MD, MBA

# 4:31 DISCUSSION WITH MODERATOR

# **4:36** INTRODUCTION of PANEL – William H. Slattery, III, MD

# 4:37 PANEL INNER EAR IMAGING: STATE OF THE ART

- Photon-counting CT scanners
- Intravenous versus intratympanic gadolinium injections
- Endolymph/perilymph imaging
- Advances in inner ear imaging

Yu-Lan Mary Ying, MD, Moderator Akira Ishiyama, MD John S. Oghalai, MD Hideko Heidi Nakajima, MD, PhD Bryan Ward, MD

# 5:07 CLOSING REMARKS/ADJOURNMENT William H. Slattery, III, MD

# 5:15 ANNUAL AOS MEMBER PHOTOGRAPH

# SUNDAY, MAY 18, 2025

- **7:00 BUSINESS MEETING** (*Committee Reports*) (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 William H. Slattery, III, MD
- 7:31 SESSION C COCHLEAR IMPLANTS II Sharon L. Cushing, MD, MSc & Daniel M. Zeitler, MD, Moderators
- 7:32 Retrospective Comparison of Hearing Preservation Outcomes Following Robotic-Assisted and Manual Cochlear Implantation

Ilana Yellin, MD Nathan Jacob, BS Michael Seidman, MD Ariel Brownlee, AuD

7:38 A Within-Subject Comparison of Hearing Preservation Outcomes for Bilateral Cochlear Implant Recipients

Michael W. Canfarotta, MD Ankita Patro, MD, MS Aaron C. Moberly, MD Marc L. Bennett, MD Jourdan T. Holder, AuD, PhD David S. Haynes, MD Elizabeth L. Perkins, MD

# 7:44 Speech Discrimination Outcomes in Patients with Perimodiolar vs Lateral Wall Cochlear Implant Arrays: A Systematic Review and Meta-Analysis

David Octeau, MD Lacey Cantrell, MD Molly Smeal, AuD Mary Schleider, RN, MLIS Samantha Anne, MD Edward Doyle, MD Mark Bassim, MD

# 7:50 Cochlear Implant Insertion Trauma is Associated with Spiral Ganglion Neuron "Dead Zones" in the Human

Liliya Benchetrit, MD (presenter) Christopher K. Giardina, MD, PhD (primary) Abbie K. Hall, BS Anbuselvan Dharmarajan, MD, MPH Julie G. Arenberg, PhD Alicia M. Quesnel, MD

# 7:56 Postoperative Outcomes with Bimodal Hearing and Bilateral Cochlear Implantation in the Elderly

William G. Cohen, MD Ankita Patro, MD, MS Michael W. Canfarotta, MD Natalie Schauwecker, MD Jourdan Holder, AuD, PhD David S. Haynes, MD, MMHC Elizabeth L. Perkins, MD

# 8:02 DISCUSSION WITH MODERATOR

# 8:07 SESSION D – SENSORINEURAL HEARING LOSS

Keiko Hirose, MD & Ravi N. Samy, MD, Moderators

# 8:08 GLP1 Agonist Treatment in Metabolic Syndrome Improves Hearing Outcomes - A Multi-National Database Study

Emily E. Belding, BA, MMS Zachary D. Urdang, MD, PhD Peter Eckard, BS Marlan R. Hansen, MD Douglas Bennion, MD, PhD Alexander Claussen, MD

# 8:14 Enhancing Early Detection: Evaluating Targeted Screening for Congenital Cytomegalovirus in Newborns

Peter Kfoury, MD Megna D. Reddy, BS Albert H. Park, MD 8:20 Clinical Development of AK-OTOF Gene Therapy for OTOF-Mediated Hearing Loss Marlan R. Hansen, MD Chen-Chi Wu, MD John A. Germiller, MD, PhD

# 8:26 A Novel Transcanal Catheter for Delivery of Hypothermia to the Inner Ear

Maria F. Yepes, MD Pavan S. Krishnan, MD Aparna Govindan, MD Curtis King, MS Simon I. Angeli, MD Suhrud M. Rajguru, PhD

# 8:32 DISCUSSION WITH MODERATOR

8:37 INTRODUCTION OF SAUMIL N. MERCHANT MEMORIAL LECTURE William H. Slattery, III, MD

#### 8:39 SAUMIL N. MERCHANT MEMORIAL LECTURE

Extracellular Vesicles and Treatment of Hearing Loss Hinrich Staecker, MD, PhD David and Mary Zamierowsky Endowed Professor Professor, Otolaryngology-Head and Neck Surgery University of Kansas School of Medicine Kansas City, KS

9:09 INTRODUCTION of PANEL – William H. Slattery, III, MD

# **9:10 PANEL**

THE SOUND OF SILENCE: A COMPREHSIVE DISCUSSION ON NOISE-INDUCED HEARING LOSS

- Incidence and cause of noise induced hearing loss.
- Pathophysiology of noise induced hearing loss.
- Guidelines for measuring noise, OSHA versus NIOSH
- Types of hearing protection, including gun suppressors
- Treatment of noise induced hearing loss

Matthew L. Bush, MD, PhD & Quyen Nguyen, MD, PhD, Co-Moderators Anne Morgan Selleck, MD Hamid Djalilian, MD Isaac D. Erbele, MD

# 9:40 MID-MORNING BREAK

**10:05 SESSION E - OTOSCLEROSIS, MENIERE'S DISEASE & VESTIBULAR SCHWANNOMA** *Gregory J. Basura, MD, PhD & Soha N. Ghossaini, MD, Moderators* 

#### 10:06 Risk Factors Associated with Otosclerosis: A National Database Study

Prithwijit Roychowdhury, MD Miriam Smetak, MD Matthew Shew, MD Jacques Herzog, MD Craig Buchman, MD Nedim Durakovic, MD

# 10:12 Evaluating the Necessity of Preoperative CT Imaging for Stapedectomy

Amor Niksic, BS Albert Y. Li, BA Tyler J. Gallagher, BS Hyun Sang Cho, MD Rance Fujiwara, MD, MBA Joni K. Doherty, MD, PhD Hitomi Sakano, MD, PhD

# 10:18 Endoscopic vs. Microscopic Stapedotomy for Otosclerosis: An Updated Meta-Analysis of Complications

Hamzah Jehanzeb, MBBS Dahir Ashfaq Zayan Alidina Hamdan A. Pasha, MBBS Syed A. Abbas, MBBS

# 10:24 Temporal Bone 3D Reconstruction and Analysis of Endolymph Volume in Meniere's Disease

Achilles A. Kanaris, BS Adam Y. Xiao, MD, PhD Eashan Biswas Gregory P. Lekovic, MD, PhD John L. Go, MD Stephen S. Cai, MD Ivan A. Lopez, PhD Gail P. Ishiyama, MD Akira Ishiyama, MD

# 10:30 Cochlear Signal Intensity Changes in Vestibular Schwannoma: A Balanced Fast Field-Echo (bFFE) MRI Study

Takeshi Fujita, MD, PhD Hiroko Takeda, MD Tomonori Kanda, MD, PhD Natsumi Uehara, MD, PhD Jun Yokoi, MD, PhD Akinobu Kakigi, MD, PhD Ken-ichi Nibu, MD, PhD

# **10:36 DISCUSSION WITH MODERATOR**

# 10:41 INTRODUCTION of PANEL – William H. Slattery, III, MD

# 10:42 PANEL

# PRACTICAL GENETICS FOR OTOLOGISTS: WHAT YOU NEED TO KNOW

- Review ten most common genetic causes and the pathophysiology of hearing loss
- Review process to determine if genes are associated with the hearing loss phenotype
- When should a clinician order genetic testing
- When should a genetic counselor get involved
- Review of current and potential clinical trials

Ana H. Kim, MD, Moderator Dylan K. Chan, MD, PhD Sharon L. Cushing, MD, MSc A. Eliot Shearer, MD, PhD

# 11:28 NOVEL SENSORI-NEURAL HEARING LOSS TREATEMENTS: INDUSTRY PIPELINE UPDATES

William H. Slattery, III, MD, Moderator

# 11:55 INTRODUCTION OF INCOMING PRESIDENT

Nancy M. Young, MD

# 11:58 CLOSING REMARKS

William H. Slattery, III, MD

12:00 ADJOURN

SELECTED ABSTRACTS



IN ORDER OF PRESENTATION



# 158<sup>th</sup> Annual Meeting AMERICAN OTOLOGICAL SOCIETY

May 17-18, 2025 Hyatt Regency New Orleans New Orleans, LA

#### **Cochlear Reimplantations following Device Dysfunction: A Retrospective Cohort Study**

Mélyssa Fortin, MD; Richard Bussières, MD; Mathieu Côté, MD; Daniel Philippon, MD, DMD Sandra Fortin, MPA; Mathieu Trudel, MD

**Objective:** Our cochlear implant (CI) program has over 40 years of experience in cochlear device implantation across pediatric and adult populations. As surgical indications have broadened, more patients are outliving their device's lifespan and encountering potential industry recalls. Our program's collaboration with all major CI manufacturers provides unique insights into contemporary surgical and technological challenges.

Study Design: Retrospective cohort study

Setting: Tertiary care center

Patients: All CI recipients within our program who underwent cochlear reimplantation between May 1st, 1984 - May 1st, 2024

**Intervention:** Therapeutic

**Main Outcome Measures:** The primary outcome was defined as reimplantation of a new cochlear device following the extraction of a previous CI, regardless of the reason for removal. Secondary outcomes included CI manufacturer, reasons for reimplantation, implantation-to-reimplantation interval, and associated complications.

**Results:** A total of 3,885 cochlear devices were implanted by our program (66% adults, 34% pediatric). Over the years, four industry recalls affected our patient population. We report 257 reimplantations, including 86 (33%) pediatric cases. The overall reimplantation rate was 6.6%, varying across manufacturers: 12.6% for Advanced Bionics, 3.4% for Cochlear, 8,9% for Oticon, and 1.8% for MED-EL. The majority of reimplantations (70.8%) were due to confirmed device failure, either from recalls (35.4%) or hard failures (35.4%). The average interval between implantation and reimplantation was 6.5 years, with 80% of reimplantations occurring within 10 years of the initial implantation.

**Conclusions:** Cochlear reimplantation imposes significant physical, emotional, developmental, ethical, and financial burdens on patients. The increasing need for reimplantations due to technological failures poses a modern challenge, with pediatric patients being particularly vulnerable. Surgical teams must closely monitor patients, especially those with devices from manufacturers with prior recall histories. Early identification of device issues and timely reimplantation are critical to preserving auditory function and reducing patient distress. These factors must be integrated into patient-centered care models and long-term healthcare planning.

**Professional Practice Gap & Educational Need:** This study underscores the complexities of cochlear reimplantation, encompassing both technological and human aspects. It offers valuable insights into the causes and outcomes of reimplantation within a large patient cohort. Understanding the drivers behind reimplantation, the variation in reimplantation timelines, and the unique challenges faced by pediatric patients will enable healthcare providers to better tailor their care strategies.

#### Learning Objectives:

- Describe the primary causes leading to cochlear reimplantation
- Examine the outcomes of patients who underwent cochlear reimplantation at our high-volume CI center
- Discuss the clinical, ethical, and social implications of reimplantation, particularly in the context of industry recalls

Desired Result: Optimize patient care pathways and policy planning to minimize the need for cochlear reimplantation

Level of Evidence - Level III

#### Indicate IRB or IACUC: Exempt

#### Does Early Tinnitus Improvement Influence Long-Term Quality of Life in Cochlear Implant Recipients?

Barak M. Spector, BS; Katelyn A. Berg AuD, PhD; David S. Haynes, MD Terrin N. Tamati, PhD; Aaron C. Moberly, MD

**Objective:** 1) To evaluate tinnitus outcomes in adults after cochlear implantation, 2) to examine the impact of demographic factors on tinnitus outcomes, and 3) to determine the relationship between early tinnitus outcomes and long-term quality of life (QOL).

Study design: Retrospective Review of Prospectively Obtained Data

Setting: Tertiary Care Adult Cochlear Implant (CI) Center

**Patients:** Ninety-two adult CI recipients aged 20-84 years old (mean =  $60.3 \pm 15.3$ ).

Interventions: QOL surveys

**Main Outcome Measures:** Tinnitus Handicap Inventory (THI); Speech, Spatial, and Qualities of Hearing Scale-12 (SSQ-12), and the Cochlear Implant Quality of Life-10 measure (CIQOL-10) assessed preoperatively and at one or more post-operative timepoints.

**Results:** 1) THI scores significantly improved from pre-CI to 1-month post-CI, with no additional gains within 12-months post-CI. Across timepoints, 71.7% of patients demonstrated a clinically significant improvement ( $\Delta \le 6$  points) in their tinnitus from pre-CI. 2) Comparisons of demographics between those with and without clinical improvements in their THI revealed only duration of deafness as significantly different, with shorter durations of deafness in those showing improvement. 3) Long-term (6-12 months) post-CI THI scores were negatively correlated with CIQOL-10 scores (r = -.506, p = .002) and overall SSQ-12 scores (r = -.535, p < .001). Early (1-3 months) post-CI THI scores were also negatively correlated with long-term overall SSQ-12 scores (r = -.310, p = .029).

**Conclusions:** Adult CI recipients reported tinnitus improvements at 1-month post-activation and maintained this improvement at 12 months. Patients with shorter durations of deafness reported greater tinnitus relief. Early tinnitus outcomes were associated with long-term quality of life. Clinicians should consider early evaluation of tinnitus outcomes to inform patient counseling regarding long-term CI outcomes.

**Professional Practice Gap & Educational Need:** This study aims to better understand how tinnitus changes shortly after cochlear implantation relate to patients' long-term quality of life. The findings could help clinicians provide more appropriate outcome expectations counseling.

**Learning Objective:** After this presentation, participants will be able to 1) describe the trajectory of tinnitus outcomes post-CI and 2) discuss the relationship between early tinnitus outcomes and a patient's long-term quality of life.

**Desired Result:** To improve patient counseling by providing a clearer understanding of how early tinnitus outcomes influence long-term quality of life in cochlear implant recipients.

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

Indicate IRB: 240876

#### **Optimizing Cochlear Implant Activation: A Prospective Patient-Preference Study**

Arman Saeedi, MPH; Mihai A. Bentan, BS; Albina Islam, MD Nauman F. Manzoor, MD; Daniel H. Coelho, MD

**Objective:** As many centers around the world are shifting towards earlier and earlier cochlear implant (CI) activation, there have been no studies of patient preference on such timing. The aim of this study was to determine patient timing preferences before and after standard 4-week activation, and to account for such changes.

Study Design: Prospective survey-based study.

Setting: A tertiary care academic CI center.

Patients: Adults 18 years and older receiving their first cochlear implant.

**Interventions:** Patients completed pre- and post-operative questionnaires (day of surgery, 1-week post-op, 1-week post-activation) assessing several patient-reported outcomes and their preferences regarding activation timelines. Data recorded were age, gender, BMI, preoperative CIQoL-10 Global, device brand, and processor style. Qualitative data regarding patient rationales were also recorded.

Main Outcome Measures: Percentage of patients who changed preferences between pre-op visit and 1-week post-activation visit. Several other outcomes measures were obtained.

**Results:** Thirty-nine patients (51.3% male) were included. Mean age and BMI were  $64.6 \pm 14.3$  years old and  $28.5 \pm 5.8$  kg/m<sup>2</sup>, respectively. Preoperatively, the top three preferred activation times were immediately following surgery/same day (28.2%), 3 weeks postoperatively (23.1%), and 1 week postoperatively (20.5%). The most common cited reason was the desire to hear as soon as possible (38.6%). At follow-up, the top three preferred activation times were 3 weeks postoperatively (30.8%), 2 weeks postoperatively (20.5%), and 1 week postoperatively (17.9%), with only 10.3% preferring same day activation. The odds of preferring "standard" timing (2 weeks or later) post-implantation were approximately 2.88 times (95% CI: 1.14 - 7.23, p = 0.025) higher than pre-implantation.

**Conclusions:** While patients receiving a CI do want to hear as soon as possible, many change their minds about the exact timing once they have gone through the process, likely due to an underestimation of surgical recovery. This study highlights the dynamic nature of patient preferences for cochlear implant activation, with many shifting from same-day activation preoperatively to a preference for delayed activation postoperatively. Such findings suggest possible undercounseling of patients as to immediate post-operative expectations. In addition, it highlights the notion that patient input should be considered before uniformly changing activation protocols earlier.

**Professional Practice Gap & Educational Need:** Patient preferences are important considerations when deciding CI activation timing and should be considered to align clinical practice with patient expectations. This promotes patient-centered care and can lead to improved shared decision-making.

**Learning Objective:** To understand the variability in patient preferences for cochlear implant activation timing and factors influencing these preferences.

**Desired Result:** Clinicians will appreciate the importance of patient-centered outcomes and input prior to changing CI activation timing protocols. Doing so can improve patient satisfaction, engagement, and clinical outcomes.

Level of Evidence - III

Indicate IRB or IACUC: HM20020582.

#### High-resolution Flat-panel CT Analysis of Cochlear Implant Electrode Contact Orientation

Ana Marija Sola, MD; Nicole Jiam, MD; Melanie Gilbert, AuD Luke Helpard, PhD; Charles J. Limb, MD

**Objective:** This study aims to describe a novel method for identifying cochlear implant (CI) electrode directionality from *in vivo* high-definition flat-panel computed tomographic imaging (FPCT) in post-surgical patients.

Study Design: Retrospective, observational

Setting: Tertiary care center

Patients: 6 participants with MED-EL FLEX 28 CI

**Interventions:** All patients underwent FPCT postoperatively with secondary reconstruction and transformation to a standard cochlear coordinate system.

**Main Outcome Measures:** FPCT images were aligned to a standard coordinate system where the X-Y plane corresponded to the basal turn plane and the Z-axis corresponded to the mid-modiolar axis, along which images were reformatted, and the electrode array insertion was measured. To estimate contact orientation, the two plates of the bipolar contacts and asymmetry of the monopolar contacts were identified in FPCT scans and 3D renderings. Using vectors perpendicular to the electrode contact faces, the post-operative orientations of the bipolar (0-179°) and monopolar (-179°-180°) contacts were estimated. A directionality of 0-degrees and 90-degrees corresponds to contacts oriented towards the modiolus and organ of Corti, respectively.

**Results:** Average angular insertion depth was 500.3° (444-630), in line with company-reported average of 500-550 degrees. Basal bipolar electrode contacts and the 5 most apical monopolar contacts in the MED-EL FLEX28 arrays were identified. 9/72 electrode contacts were excluded due to imaging artifact. The average contact orientation was 98° (standard deviation: 13.6) for the 7 basal electrodes and -25° (standard deviation: 13.1) for the 5 apical electrodes. In postoperative patients inserted with this flexible array, basal bipolar electrodes were reliably oriented toward the organ of Corti, while apical monopolar electrodes tended to be oriented towards the modiolus.

**Conclusions:** To our knowledge, this is the first study to use post-operative FPCT *in vivo* to identify electrode contact orientation. We have identified electrode orientation based on imaging characteristics using high-definition FPCT imaging and introduced a model for describing directionality of electrode contacts. In future studies, we will focus on correlating these rotational measurements to electrophysiologic and psychophysical outcomes, including electrode current spread, activation settings, and hearing performance.

**Professional Practice Gap & Educational Need:** Hearing outcomes with CI are influenced by electrode and patient-specific factors. Previous *in vivo* studies have examined electrode-specific factors such as location within the scala, insertion angle and depth of insertion, but not electrode orientation, which may have implications electrode performance and hearing outcomes.

Learning Objective: To describe electrode contact-level imaging characteristics and introduce a system for quantifying electrode contact rotation.

Desired Result: To provide information regarding postoperative electrode characteristics with increased resolution.

**Level of Evidence** – IV

Indicate IRB or IACUC: UCSF IRB:15-17575, Approval: 4/19/23

#### Pre-Curved Versus Straight Arrays for Hearing Preservation in Cochlear Implantation: A Systematic Review and Meta-Analyses

David Elisha, BS; Nicholas DiStefano, BS; Rahul Mittal, PhD; Andrea Monterrubio, BS Jeenu Mittal MSc; Adrien Eshraghi, MD

**Objective:** To evaluate hearing preservation (HP) outcomes across various electrode array (EA) designs specifically straight/lateral wall compared to precurved/perimodiolar arrays.

**Data Sources:** A systematic review and meta-analysis were performed following PRISMA guidelines. Databases searched included PubMed, ScienceDirect, Web of Science, Scopus, and Embase, covering studies published in English from 2019 through 2024.

**Study Selection:** Studies were included if they reported HP rates for patients undergoing cochlear implantation with LW or PM EAs. Of 455 abstracts screened, 32 studies met the inclusion criteria, comprising 3,278 patients. Twelve studies directly compared EA types, and 20 assessed general HP outcomes without comparing EA designs.

#### **Data Extraction:**

Extracted data included HP rates, low-frequency pure tone averages (LFPTA), insertion depth, surgical approach, and electrode type. Study quality were assessed, including small sample sizes, variability in surgical techniques, device selection bias, and inconsistent steroid regimens.

#### **Data Synthesis:**

Statistical analysis used the Mantel-Haenszel method for dichotomous outcomes (e.g., HP rates), with odds ratios (OR) as the effect measure. Twelve-month HP rates favored LW electrodes with an OR of 0.47 [0.26, 0.85] (Z = 2.48, p = 0.01). SlimJ electrodes outperformed Mid-Scala electrodes (48.4% vs. 30.8% HP). Predictive factors for HP included preoperative LFPTA and age at implantation, accounting for 30.8% to 41% of variance in LFPTA shifts.

#### **Conclusion:**

Straight/LW arrays, paired with atraumatic techniques, provide superior HP outcomes. Tailoring EA selection to patient-specific factors during surgery are essential for optimizing HP and improving long-term outcomes.

**Professional Practice Gap & Educational Need**: There is a lack of consensus regarding the optimal electrode array (EA) type for achieving the best hearing preservation outcomes in cochlear implant recipients. Additionally, variability in surgical techniques, electrode design, and patient selection contributes to inconsistent preservation outcomes, highlighting the need for further research and clinical guidance.

**Learning Objective**: To evaluate and compare the impact of different EA designs on hearing preservation outcomes within 12 months of cochlear implantation and explore the role of surgical techniques and insertion strategies in optimizing hearing preservation.

**Desired Result**: Attendees will gain an understanding of how electrode array design and surgical techniques affect hearing preservation, enabling them to make informed decisions regarding electrode selection and surgical approaches to improve patient outcomes in cochlear implantation.

Level of Evidence: Level III

Indicate IRB or IACUC: Exempt

#### **Outcomes of Tympanic Membrane Regeneration Therapy for Elderly Patients**

Rie Kanai, MD; Shin-ichi Kanemaru, MD, PhD; Tomoya Yamaguchi, MD Ryohei Yuki, MD; Razumu Shirai, MD; Toshiki Maetani, MD, PhD

**Objective:** To evaluate the outcome of tympanic membrane regenerative therapy (TMRT) for elderly patients age 65 years and older with tympanic membrane perforations (TMPs)

Study Design: Intervention study

Setting: Research institute hospital

**Patients:** One hundred twenty-three patients 134 ears under 65 years (mean age :37.4) as Group A, 80 patients 100 ears over 65 and under 75 years old (mean age :70.6) as Group B, 100 patients 106 ears over 75 years old (mean age :80.3) as Group C were evaluated in this study.

**Interventions:** All patients underwent TMRT: the freshening of the perforation edge, inserting a gelatin sponge with basic fibroblast growth factor, and applying fibrin glue. The treatment was repeated up to 4 times until TMP closure.

**Main Outcome Measures:** The closure rates of TMPs, hearing improvement, complications, and use of hearing aids (HAs) after the final treatment were compared between the three groups.

**Results:** The TMP closure rates were 97.8% (131/134) in Group A, 97.0% (97/100) in Group B and 97.2% (103/106) in Group C. The hearing level improved from  $34.3\pm 12.8$  dB before TMRT to  $22.8\pm 11.1$ dB after TMP closure in Group A, from  $51.7\pm 14.8$  dB to  $39.8\pm 13.4$  dB in Group B, and from  $64.3\pm 15.5$ dB to  $52.8\pm 15.2$  dB in Group C. The AB gaps improved from  $16.0\pm 9.6$  dB to  $7.6\pm 5.3$  dB in Group A, from  $17.2\pm 9.6$  dB to  $8.8\pm 6.3$  dB in Group B, and from  $17.0\pm 9.8$  dB to  $9.3\pm 7.0$  dB in Group C. No serious complications occurred in all groups. The percentage of HA user after TMRT were 0.7% (1/134) in Group A, 12.0% (12/100) in Group B, and 30.1% (32/106) in Group C.

**Conclusions:** Regardless of age, TMRT provided high TMP closure rates. After treatment, the AB gaps for all groups was within 10 dB, showing ideal hearing improvement. The results indicate that being elderly is not a disadvantage for the TM regeneration, and TMRT can be performed safely in elderly patients.

**Professional Practice Gap & Educational Need:** TMRT is a novel treatment covered by health insurance in Japan in 2019, and is currently undergoing Phase II clinical trials in the United States. TMRT is a minimally invasive treatment without cell transplantation and tissue harvesting, and it can regenerate a nearly normal-shaped TM and provide ideal hearing improvement with small AB gaps. Elderly patients often also develop presbycusis in addition to TMP. After TMP closure by TMRT, it is possible to use HAs more effectively, and this will motivate elderly patients to use HAs. In this presentation, we would like to present our treatment strategies of TMRT for elderly patients.

**Learning Objective:** Participants will be able to learn that TMRT is minimally invasive, safe, and highly successful, making it suitable for elderly patients who tend to have multiple comorbidities. They will also learn that for elderly patients, a treatment combining TMRT and HA can be provided.

**Desired Result:** We hope that TMRT or a treatment combining TMRT and HA will be widely applied to elderly patients with TMP, reducing the number of elderly people who become isolated from society due to hearing impairment. This may also lead to a reduction in the number of patients developing dementia in the future, as hearing impairment is one of the risk factors for dementia.

#### 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.

#### **Tympanoplasty Outcomes of Indigenous Populations**

Catherine F. Roy, MD; Jeffrey C. Yeung, MD, MSc; Lamiae Himdi, MD Tamara Mijovic, MD MSc

**Objective:** Chronic otitis media (COM) is highly prevalent in Indigenous populations, likely owing to risk factors (low socio-economic status, crowded housing, tobacco exposure) and limited access to specialized care. This study is one of the first contemporary accounts investigating the success rates of tympanoplasties a North American Indigenous population.

Study Design: Retrospective cohort study.

Setting: Community health center providing front-line and specialty services across seven Indigenous communities

Patients and Interventions: All patients having undergone a tympanoplasty from January 2015 to 2024.

Main Outcome Measures: The primary outcome was otoscopic confirmation of an intact tympanic membrane postoperatively, while secondary outcomes included audiometric parameters.

**Results**: A total of 194 patients (mean age  $22.4 \pm 14.7$  years) and 224 tympanoplasties were included (195 primary, 29 revision). Successful closure of the perforation was achieved in 111/172 (64.5%) of patients with otoscopic follow-up, however varied widely according to the type of graft used. Cartilage tympanoplasties had a closure rate of 86% (37/43 patients), compared to 62% (51/82) for tympanoplasties using fascia or perichondrium, and 49% (23/47) for myringoplasties using fat or a hyaluronic acid scaffold (P<0.001). The average air bone gap in 87 patients with audiometric testing available significantly decreased from 27.3 (95%CI 25.4; 29.4) to 19.0 (95%CI. 16.4;21.5) dB. The mean follow-up was  $2.3 \pm 1.9$  years.

**Conclusion**: While tympanoplasty may improve audiometric parameters and recurrent otorrhea, outcomes in Indigenous patients are modest. This emphasized the superior closure rates associated with cartilage grafts, which may help improve outcomes in this population. Further efforts should focus on addressing broader healthcare disparities to ensure better access to specialized surgical care in Indigenous communities.

**Professional Practice Gap & Educational Need**: Surgical outcomes in Indigenous populations remain largely understudied and underreported, contributing further to observed health disparities.

**Learning Objective**: This study highlights suboptimal outcomes of tympanoplasty in Indigenous patients and provides an understanding of potentially modifiable surgical factors.

**Desired Result**: Clinicians and researchers will strengthen their knowledge of chronic otitis media in Indigenous populations and its surgical management, gaining insight into potential strategies to address observed health inequities.

Level of Evidence: Level 3 (retrospective cohort study)

IRB approval: This study was approved by the Director of Professional Services of the Inuulitsivik Health Center.

#### Comparing Pediatric and Adult Chronic Otitis Media with Cholesteatoma at the Single-cell Level

Daniel R. Romano, MD; Song-Zhe Li, MD, PhD; Richard A. Chole, MD, PhD Michael Hoa, MD; Sidharth V. Puram, MD, PhD; Keiko Hirose, MD

**Hypothesis:** Pediatric and adult cholesteatoma tissue demonstrate significant differences in keratinocyte gene expression and immune cell-stromal cell signaling.

**Background:** Cholesteatoma is an otologic disease defined by keratinizing stratified squamous epithelium in the middle ear and/or mastoid. Although not a neoplasm, cholesteatomas demonstrate dysregulated differentiation, uncontrolled proliferation, and locally aggressive growth, with complications ranging from a conductive hearing loss to central nervous system infection. Surgery may be curative but published 5-year recurrence rates range from 21-38%. Cholesteatomas are especially aggressive in the pediatric population, with > 2-fold greater 5-year recurrence in children < 16 years. However, the molecular and cellular differences between pediatric and adult cholesteatomas are poorly characterized.

**Methods:** Surgical samples were collected from pediatric and adult patients undergoing planned surgery for cholesteatoma of the middle ear, and enzymatically and mechanically dissociated into a single-cell suspension. Magnetic-activated cell sorting was utilized to achieve a 1:1 ratio of CD45-positive to -negative cells, and the suspension was subjected to single-cell RNA-sequencing (scRNA-seq). Comparative analyses were performed between the adult and pediatric scRNA-seq datasets. Clinical information including audiometric results, previous ear surgeries, and STAMCO staging was obtained from the surgeon or medical records.

**Results:** scRNA-seq revealed a rich array of cell types in surgical cholesteatoma samples. Pediatric and adult scRNA-seq data are distinguished by differential gene expression, regulatory network utilization, and intercellular interactions. An interim analysis of 23,032 high quality cells has shown that adult and pediatric cholesteatoma keratinocyte clusters demonstrate differential expression of 587 genes.

**Conclusions:** These results may explain some of the observed clinical differences between pediatric and adult chronic otitis media with cholesteatoma. Future studies will investigate the relationship of the signaling pathways and regulatory networks identified to cholesteatoma pathogenesis.

**Professional Practice Gap & Educational Need:** Molecular mechanisms underlying formation of cholesteatoma remain controversial, and the increased aggressiveness of pediatric cholesteatomas is an incompletely understood phenomenon.

**Learning Objective:** Attendees will be able to describe the cellular and molecular complexity of cholesteatomas and recognize how transcriptional dysregulation may contribute to the clinical variability and pathogenesis of cholesteatoma.

**Desired Result:** We hope to improve our current understanding of the molecular mechanisms underlying the pathogenesis of cholesteatoma in the adult and pediatric populations, as well as how these may differ, which could allow for the successful identification of molecular targets for medical therapies.

Level of Evidence - III

Indicate IRB or IACUC: IRB #202302061, Washington University in St. Louis, originally approved on 02/15/23.

#### Does Mastoid and Epitympanic Obliteration with S53P4 Bioactive Glass Reduce Cholesteatoma Recidivism in Canal-Wall-Up Surgeries? A Retrospective Clinical Study

Daniele Bernardeschi, MD, PhD; Hugo Delille, MD; Matteo Di Bari, MD; Olivier Sterkers, MD, PhD Ghizlene Lahlou, MD, PhD; Lauranne Alciato, MD

**Objective:** The aim of this study was to compare two groups of patients who underwent canal-wall-up tympanomastoidectomy with or without mastoid and epitympanic obliteration, to evaluate the rate of recidivism 5 years post-surgery

Study Design: Retrospective case-control study

Setting: Tertiary otologic referral center

**Patients:** The inclusion criteria were all patients who underwent a canal-wall-up tympano-mastoidectomy, either with or without obliteration using S53P4 bioactive glass between January 2003 and December 2019. Patients who underwent canal-wall-down tympano-mastoidectomy surgery, tympanoplasty without mastoidectomy, or those with incomplete data were excluded

Interventions: Cholesteatoma removal through canal-wall-up tympano-mastoydectomy

Main Outcome Measures: the rate of recidivism (recurrence and residual rates) 5 years post-surgery calculated using Kaplan-Maier analysis.

**Results:** A total of 174 procedures had been included: 73 in the non-obliteration group and 101 in the obliteration group. At five-years, the cholesteatoma recidivism rate was 19% in the non-obliteration group and 6% in the obliteration group (p<0.01). The overall cholesteatoma-free survival rate, calculated using the log-rank test for survival analysis (95% CI), was 83.0% (70.4% - 97.8%) in the obliteration group, compared to 54.4% (38.8% - 76.4%) in the non-obliteration group (p<0.01. The residual and recurrent cholesteatoma free survival rate (95% CI) was 98.7% (96.2% - 100%) and 84.1% (71.5% - 98.9%) in the obliteration group and 88.8% (78.7% - 100.0%) and 59.3% (42.9% - 82.0%) in the non-obliteration group. Difference on recurrence was significant.

**Conclusions:** Mastoid and epitympanic obliteration using S53P4 bioactive glass significantly reduces the recidivism of cholesteatoma in patients undergoing canal-wall-up tympano-mastoidectomy. Obliteration should be always considered when mastoidectomy is necessary for cholesteatoma removal.

**Professional Practice Gap & Educational Need:** Although mastoid and epitympanic obliteration has been proposed in cholesteatoma surgery for several years, its effect on reducing the risk of recurrent and residual cholesteatoma remains debated. This study aimed to clarify if obliteration is useful in canal-wall-up surgeries.

Learning Objective: Incorporating mastoid and epitympanic obliteration in the standard-of-care management of cholesteatoma

Desired Result: Reducing cholesteatoma recidivism in canal-wall-up surgeries

Level of Evidence - III

Indicate IRB or IACUC: Exempt

#### Meningitis and Temporal Bone Pathology – A Diagnostic Recommendation

Ava Karam, BS; Frank Rizzuto, BS; Isaac Erbele, MD; Julio Figueroa, MD Rahul Mehta, MD; Moises A. Arriaga, MD, MBA

**Objective:** Evaluate the relationship between meningitis and radiologic temporal bone abnormalities by assessing the prevalence of concurrent mastoid abnormalities, tegmen defects, and lateral skull base encephaloceles in patients with meningitis.

Study Design: Cross-sectional study

Setting: Tertiary academic center

**Patients:** Patients with a history of meningitis who underwent radiographic imaging of the skull base between January 2015 and April 2024.

Interventions: Comprehensive review of radiologic imaging in patients with a history of meningitis.

Main Outcome Measures: Presence or absence mastoid abnormalities, tegmen defects, and lateral skull base encephaloceles on radiographic imaging.

**Results:** Among 2,570 patients with meningitis, 1,673 patients (68%) had cranial imaging to review. Middle ear and mastoid fluid or effusion were found in 291 individuals (17%). Additionally, tegmen dehiscence was identified in 35 patients (2%), 26 of whom also presented with concurrent mastoid abnormalities. Lastly, we identified 12 patients (1%) with lateral skull base encephaloceles.

**Conclusions:** At least 17% of patients with meningitis had imaging findings suggestive of otogenic meningitis. Based on our results, other results of high proportions of otologic causes, and recent descriptions of tegmen defects providing a pathway for otogenic meningitis, we recommend routine temporal bone CT in patients without an obvious cause for meningitis. This may identify occult mastoid pathology, tegmen defects, predisposing inner ear abnormalities, and encephaloceles. Otologic pathology is an important, common, treatable cause of meningitis which should be systemically considered.

**Professional Practice Gap & Educational Need:** There is a gap in recognizing otologic pathology as a cause of meningitis. Increasing clinician awareness and advocating for routine temporal bone CT scans in patients without obvious causes for meningitis may improve diagnostic accuracy and patient outcomes.

**Learning Objective:** Identify and recognize the significance of radiologic findings associated with otogenic meningitis and develop strategies for incorporating routine temporal bone imaging into clinical practice to improve diagnostic accuracy and patient outcomes.

Desired Result: To enhance clinician awareness of the association between otologic pathology and meningitis.

Level of Evidence – Level III

Indicate IRB or IACUC: LSUHSC 581

#### **Retrospective Comparison of Hearing Preservation Outcomes following Robotic-Assisted and Manual Cochlear Implantation**

Ilana Yellin, MD; Nathan Jacob, BS; Michael Seidman, MD; Ariel Brownlee, AuD

**Objective:** The purpose of this study is to compare low frequency hearing preservation (LFHP) in patients undergoing robotic assisted cochlear implantation (CI) to those undergoing manual CI.

Study Design: Retrospective review

Setting: Tertiary referral center

**Patients:** Adult CI patients with low frequency residual hearing defined as the low frequency pure tone average of 250Hz and 500Hz (LFPTA)  $\leq$ 80dB.

**Interventions:** Patients underwent robotic-assisted or manual CI. All patients were implanted with lateral wall electrodes while the specific manufacturer was chosen by the patient in consultation with a qualified audiologist.

**Main Outcome Measures:** The main outcomes of interest were the change in low frequency pure tone average ( $\Delta$ LFPTA) and the presence of LFHP, defined as  $\Delta$ LFPTA  $\leq$ 30, following robotic and manual CI.

**Results:** There were 76 robotic and 76 manual insertion CIs over a 28-month period. 19 robotic and 16 manual cases met the inclusion criteria for comparison of LFHP. The mean postoperative LFPTA was 86.97 dB and 86.09dB for robotic and manual insertion, respectively (p = 0.4143). The  $\Delta$ LFPTA was not significantly different between the robotic and manual insertion groups (31.05dB robotic vs 27.19dB manual, p=0.5137). LFHP as defined by  $\Delta$ LFPTA  $\leq$ 30 was similar between groups (63.2% robotic vs 56.3% manual, p=0.6777).

**Conclusions:** There is no significant difference in LFHP between robotic and manual CI. Further studies are needed to fully evaluate the efficacy of each insertion method.

**Professional Practice Gap & Educational Need:** As the indications for CI have expanded to include patients with residual hearing, LFHP has become an area of increasing interest. LFHP outcomes with use of robotic-assisted insertion devices have not yet been well established.

Learning Objective: To understand the impact of robotic-assisted CI on hearing preservation outcomes as compared to manual CI.

**Desired Result:** Attendees will have a better understanding of the relationship between the use of robotic assistance during CI and post-operative hearing preservation outcomes.

Level of Evidence – Level III

Indicate IRB or IACUC: Exempt

#### A Within-Subject Comparison of Hearing Preservation Outcomes for Bilateral Cochlear Implant Recipients

Michael W. Canfarotta, MD; Ankita Patro, MD, MS; Aaron C. Moberly, MD; Marc L. Bennett, MD Jourdan T. Holder, AuD, PhD; David S. Haynes, MD, MMHC; Elizabeth L. Perkins, MD

Objective: To compare hearing preservation outcomes between ears for bilateral cochlear implant (CI) recipients.

Study Design: Within-subject, retrospective cohort.

Setting: Tertiary referral center.

**Patients:** Adult CI recipients with preoperative residual acoustic hearing (low-frequency pure-tone average [LFPTA; 125, 250, and 500 Hz]  $\leq$  80 dB HL) in both ears.

Interventions: Bilateral cochlear implantation from 2012 to 2022.

Main Outcome Measures: Initial (1-month) and long-term (12-month) hearing preservation outcomes between ears were assessed by comparing the LFPTA shift of the first and second implanted ear.

**Results:** Among 68 bilateral CI recipients examined, the median age at first surgery and interval to second surgery was 64.0 and 1.2 years, respectively. At the 1-month postoperative interval, there was a positive correlation between LFPTA shift of the first and second implanted ear (r = 0.28, p = 0.023, n = 68), with 51 patients (75%) experiencing a similar LFPTA shift ( $\leq 20$  dB) across ears. At the 12-month interval, there was no significant correlation between LFPTA shift of the first and second implanted ear (r = -0.06, p = 0.688, n = 50), with only 46% of patients experiencing a similar LFPTA shift across ears.

**Conclusions:** A majority of CI recipients experience similar initial hearing preservation between the first and second implanted ear. However, there is a greater degree of asymmetry in LFPTA shifts across ears by 12-months postoperatively, signifying that long-term hearing preservation in the first implanted ear is poorly predictive of long-term outcomes in the second ear. These findings could suggest distinct post-implantation inflammatory responses across ears within the same individual, likely in reaction to extrinsic factors such as surgical technique and electrode array position.

**Professional Practice Gap & Educational Need:** As indications for cochlear implantation continue to expand, CI candidates are more likely to present with residual low-frequency acoustic hearing in both ears. Despite this, there is limited data to counsel patients on the likelihood of initial and long-term loss of residual hearing when considering implantation in the second ear.

**Learning Objective:** (1) To understand variability in hearing preservation outcomes between the first and second implanted ear. (2) To describe possible mechanisms to explain the correlation between hearing preservation across ears acutely but not long-term.

**Desired Result:** At the conclusion of this presentation, providers should be able to better counsel patients on initial and long-term hearing preservation outcomes for the second implanted ear.

Level of Evidence – Level IV

Indicate IRB or IACUC: IRB #240876, Vanderbilt University

#### Speech Discrimination Outcomes in Patients with Perimodiolar vs Lateral Wall Cochlear Implant Arrays: A Systematic Review and Meta-Analysis

David Octeau, MD; Lacey Cantrell, MD; Molly Smeal, AuD; Mary Schleider, RN, MLIS Samantha Anne, MD; Edward Doyle, MD; Mark Bassim, MD

**Objective:** Provide the first systematic review and meta-analysis of cochlear implant outcomes using either a perimodiolar or lateral wall electrode

**Data Sources:** Ovid Medline ALL®, Ovid Embase, and Wiley's Cochrane Central Register of Controlled Trials (searched 3/18/2024). A combination of indexing terms, keywords and brand names for cochlear implants were combined with electrode array concepts and speech or auditory outcomes. Truncation and adjacency operators were used to increase retrieval of all potentially relevant literature. No publication year or language filters were imposed on the search but letters, editorials, case reports, and conference abstract were removed.

**Study selection:** Inclusion criteria were adults >18 years of age, pre- and post- operative testing. Exclusion criteria included cochlear anatomic abnormalities, revision surgery, absence of pre- or post- operative testing, congenital malformation, prelingual never amplified individuals, meningitis, trauma and implantation with more than one array type

**Data extraction:** 2,219 studies were reviewed in accordance with the PRISMA workflow by two independent reviewers. Conflicts were resolved through discussion. Risk of bias was assessed using ROBINS-I. 18 studies were extracted for analysis. Pre- and post-operative CNC, AzBio and all other relevant testing outcomes were obtained. Standard mean differences (SMD) were calculated and meta-analysis was performed on CNC and AzBio scores to determine the weighted pooled standard mean difference using the random-effect model. Summary effect and heterogeneity were also reported.

**Data synthesis:** Nine studies of moderate to low risk of bias reported CNC results. Four studies reported statistically significant superiority of the perimodiolar array with the largest mean difference between groups of 14%. Meta-analysis revealed a pooled SMD of -0.23 [-0.45; -0.01] (p = 0.04), suggesting a statistically significant greater CNC scores in patients implanted with a perimodiolar array with a small effect size. No studies out of 6 available reported a statistically significant difference in AzBio scores. The pooled SMD -0.03[-0.36; 0.30] (p = 0.81) suggests no statistically significant difference in AzBio post-implantation scores between patients implanted with LW vs PM arrays.

**Conclusions:** Perimodiolar arrays seem to provide a slight advantage in word understanding but not in sentence recognition over LW arrays. The clinical significance of this advantage appears limited.

**Professional Practice Gap & Educational Need:** There is significant heterogeneity in the results of studies comparing the post-operative outcomes of patients implanted with a perimodiolar electrode to those implanted with a lateral wall array. This study aims to review the current literature and pool results to provide an up-to-date understanding of this topic

Learning Objective: Understanding the array features that result in improved speech recognition post-implantation

Desired Result: Improved, evidence-based electrode selection for cochlear implantation

Level of Evidence - III

Indicate IRB or IACUC: Exempt

#### Cochlear Implant Insertion Trauma is Associated with Spiral Ganglion Neuron "dead zones" in the Human

Liliya Benchetrit, MD (presenter); Christopher K. Giardina, MD, PhD (primary); Abbie K. Hall, BS Anbuselvan Dharmarajan, MD; Julie G. Arenberg, PhD; Alicia M. Quesnel, MD

**Hypothesis:** Significant Cochlear Implant (CI) insertion trauma, as evidenced by fracture of the osseous spiral lamina (OSL), is associated with localized "dead zones" and focal spiral ganglion neuron (SGN) loss.

**Background:** Hearing and structure preservation approaches to CI insertion aim to minimize trauma and preserve residual SGNs. In cases of significant insertion trauma, peripheral axons running through the bony OSL inherently become damaged if the OSL is fractured. The current investigation sought to determine if the relative location of OSL fracture was associated with focal areas of SGN loss.

**Methods:** Six adult ears from the Mass Eye and Ear Otopathology Laboratory were identified with OSL fractures. Digitized e-Slides were used to create 3D cochlear reconstructions, and a coordinate system relative to the round window allowed for angular assignment of SGNs and OSL fracture locations. Abrupt changes in SGN density, defined as a drop >50% within a single 30 degree angular step, were used as criteria for a significant and focal SGN loss.

**Results:** SGN counts ranged from 10,440 to 26,660 SGNs. Abrupt and focal drops of >50% in SGN density occurred in 5 of 6 temporal bones with OSL fracture. In two cases the only areas of localized "dead zones" were immediately adjacent the OSL fracture site, whereas in other cases drops were seen in as many as three distinct locations along the cochlear length.

**Conclusion:** In temporal bones from CI patients, the angular location of OSL fracture explains some (but not all) of the SGN drops seen in traumatic CI insertions. Distinct regions of SGN density were observed across the length of these cochleae, indicating multiple processes likely contribute to SGN dead zones.

**Professional Practice Gap & Educational Need:** A longstanding assumption is that hearing preservation techniques and atraumatic CI electrode insertions afford superior hearing outcomes, though the specific histopathologic evidence to support specific causes of trauma, such as OSL fracture, are limited. A goal is to share and educate evidence of physiologic "dead zones" with relation to OSL fractures as well as other forms of insertion-related trauma.

**Learning Objective:** Reinforce the evidence that OSL fractures cause focal SGN loss and introduce the evidence of focal SGN loss from insertion trauma other than OSL fracture.

**Desired Result:** CI surgeons continue to learn the specific mechanisms of SGN loss with respect to various mechanisms of traumatic CI insertions.

Level of Evidence – Level III (Case-Control)

IRB-2021P001593

#### Postoperative Outcomes with Bimodal Hearing and Bilateral Cochlear Implantation in the Elderly

William G. Cohen, MD; Ankita Patro, MD, MS; Michael W. Canfarotta, MD; Natalie Schauwecker, MD Jourdan Holder, AuD, PhD; David S. Haynes, MD; Elizabeth L. Perkins, MD

**Objective:** To evaluate speech recognition and quality of life in elderly patients with bimodal hearing versus sequential bilateral cochlear implantation.

Study Design: Retrospective cohort.

Setting: Tertiary referral center.

**Patients:** 265 adults who were at least 65-years-old, had preoperative AzBio scores in quiet  $\leq 60\%$  bilaterally, and received a cochlear implant (CI) between 2012-2021.

Interventions: Bimodal hearing versus sequential bilateral cochlear implantation

Main Outcome Measures: CNC; AzBio sentences in quiet and noise (+5 SNR); Speech, Spatial, and Qualities (SSQ).

**Results:** Bimodal (n=227) and bilateral CI (n=38) recipients had similar durations of deafness, preoperative SSQ score, and preoperative CNC and AzBio in quiet and noise scores in both ears (p>0.05). Bimodal users were older (76.2 vs. 73.4 years, p=0.009) and had lower preoperative PTAs in their better hearing ear (80.0 vs. 85.7 dB HL, p=0.014). At 6 months, no differences existed in device usage or SSQ scores, but bimodal users had significantly lower CNC (40.5% vs. 51.2%, p=0.008) and AzBio in quiet (48.3% vs. 61.5%, p=0.017) scores in their CI ear, compared to the initially implanted ear in bilateral CI patients. After their second implantation, bilateral CI patients had significantly higher AzBio in quiet scores than bimodal users at 6 (77.5% vs. 62.3%, p=0.010) and 12 months (80.8% vs. 70.9%, p=0.041) in everyday listening conditions. There were no significant differences in speech recognition or SSQ scores at 6 and 12 months between implantations in the bilateral CI group (p>0.05).

**Conclusions:** Among elderly patients, bilateral CI users appear to have superior speech recognition outcomes compared to those with a bimodal hearing configuration. Elderly patients perform similarly with their second implant as their first, highlighting that bilateral CIs can be beneficial in this population.

**Professional Practice Gap & Educational Need:** The benefits of bimodal hearing and bilateral cochlear implantation have been extensively reported in the pediatric population. Aggregate clinical data on how our elderly patients perform is lacking. This study compares postoperative outcomes in bimodal versus bilateral CI patients who are at least 65-years-old in order to answer this question.

Learning Objective: To understand differences in outcomes with bimodal hearing versus bilateral CI in the elderly population.

**Desired Result:** Providers will have knowledge about the impact of receiving two CIs on speech perception and quality of life outcomes among the elderly. These findings can help counsel patients and guide them in their care pathway.

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

Indicate IRB or IACUC: IRB Exempt (240876, Vanderbilt University, approved 8/23/24).

#### Working Behaviors and the Risk of Sensorineural Hearing Loss: A Large Cohort Study



Study design: Cross-sectional and prospective study.

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Setting: Biobank Study.

Patients: 90286 participants.

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Intervention: A cross-sectional analysis was conducted (2006–2010, n=90286) to assess the association between working behaviors (including shift work, night shift work and physical work) and the occurrence (yes/no), laterality (unilateral/bilateral), and severity (mild/severe) of SNHL. Additionally, a prospective analysis was conducted to explore the association betwe new-onset HL ar wor avior n=8 41). g b

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Results: Cross-sectional analysis indicated that shift work, night shift work and physical work were all associated with an increased risk of SNHL (all p<0.05). Higher frequencies of these working behaviors were also associated with increased severity of SNHL (all p < 0.05) and a higher likelihood of bilateral SNHL (all p < 0.05). In prospective studies, the trends were generally consistent with the aforementioned results. Furthermore, the relationship between night shift work and SNHL was partial and prehounced and ready duals with a morning chronotype (Pinteraction=0.003), or with  $\leq 5$  years noisy work entironments (1-interaction=0.012). Importantly, regardless of the level of genetic risk of PRS, there remained a positive association between night shift work and physical work with SNHL.

Conclusions: Both cross-sectional and prospective analysis indicated that shift work, night shift work, and physical work were associated with increased risk of occurrence, laterality and severity of SNHL, regardless of PRS for SHNL.

Learning Objective: To investigate the association between working behaviors and sensorineural hearing loss (SNHL).

Desired Result: Enhance the understanding and educate medical professionals about the impact of shift work and physical work as potential risk factors contributing to SNHL.

Level of Evidence: LEVEL IV Indicate IRB or IACUC: National Health Service National Research Ethics Service (ref. 21/NW/0157).
#### GLP1 Agonist Treatment in Metabolic Syndrome Improves Hearing Outcomes A Multi-National Database Study

*Emily Belding, BA, MMS; Zachary D. Urdang, MD, PhD; Peter Eckard, BS Marlan Hansen, MD; Douglas Bennion, MD, PhD; Alexander Claussen, MD* 

**Objective:** Test the hypothesis that GLP1 agonist treatment for patients with a formal metabolic syndrome diagnosis associates with improved hearing outcomes.

Study Design: Retrospective cohort database study.

**Setting:** TriNetX is a live HIPPA-compliant federated cloud electronic health record research network representing pooled data from 125-million patients from 95 healthcare organizations in the United States, Taiwan, Japan, Brazil, and India.

**Patients:** Subjects with metabolic syndrome with or without GLP-1 agonist treatment after diagnosis. Patients were matched using propensity score matching for medical comorbidities and ototoxic risk factors.

Interventions: GLP-1 agonist treatment.

Main Outcome Measures: Odds-ratios with 95% confidence intervals (OR, 95%CI) for SNHL, tinnitus, and cochlear implantation.

**Results:** There were 12,051 patients with metabolic syndrome treated with a GLP-1 agonist that were 1:1 propensity score matched to patients without GLP-1 agonist exposure. The average age was 56 years old, with 65% female patients. The risk for SNHL was 3.64% compared to 6.78% in controls (OR: 0.52, 0.46-0.59). The risk for tinnitus was 1.71% versus 2.60% in controls (OR 0.65, 0.54-0.78). There were not enough patients receiving cochlear implants in either group for statistical analysis.

**Conclusions:** GLP-1 agonist treatment associates with decreased odds for poor hearing outcomes in a high-risk group of patients matched with clinically similar controls. These potential benefits could be an inadvertent benefit for this popular medication and could be related to weight loss.

**Professional Practice Gap & Educational Need:** GLP-1 agonists are a popular new weight loss medication that associates with a number of health benefits. We aim to investigate GLP-1 agonist effects on the auditory system if any.

**Learning Objectives:** Understand the protective association of GLP-1 agonist treatment against hearing loss and tinnitus in high risk patients with a formal metabolic syndrome diagnosis.

Desired Result: Motivate future clinical trials on the topic of GLP-1 agonist treatment and the auditory system.

Level of Evidence – Level III

# Enhancing Early Detection: Evaluating Targeted Screening for Congenital Cytomegalovirus in Newborns

Peter Kfoury, MD; Megna D. Reddy, BS; Albert H. Park, MD

**Objective**: Update our expanded targeted screening program for congenital cytomegalovirus (cCMV) detection among newborns born in Utah.

Study Design: Retrospective Cohort Study identified prospectively.

Setting: Tertiary Referral Center.

**Patients:** Infants from Intermountain Health Care (IHC) facilities, born between September 1, 2022, and August 31, 2024, tested for CMV within 6 months of birth.

Interventions: Expanded targeted screening program for cCMV.

**Main Outcome Measures:** Prevalence of cCMV; Clinical Characteristics of cCMV-positive infants; Effectiveness of our expanded targeted screening program compared to other screening programs.

**Results:** Between September 1, 2022, and August 31, 2024, 5282 newborns (9.7%) underwent CMV testing within six months of age out of 54,283 births across 27 Intermountain Health Care (IHC) facilities. The overall positivity rate was 0.4%. Within two years, the expanded targeted screening program detected 22 confirmed cCMV cases, 18 (81.8%) were identified through urine PCR, 3 (13.6%) via dry blood spot (DBS) after 21 days, and 1 (4.5%) through saliva PCR confirmed by urine PCR. Of the infants diagnosed with cCMV, 50% were classified as small for gestational age (SGA), 45.5% exhibited hyperbilirubinemia, and 31.8% had thrombocytopenia. Six (27.2%) of the 22 cCMV-positive children failed their NBHS. If a hearing-targeted CMV testing approach was utilized, the estimated prevalence would have been 11 cases per 100,000 births. In contrast, the expanded targeted screening program estimated a prevalence of 39 symptomatic cCMV cases per 100,000 births and 41 total cCMV cases per 100,000. Of the 22 children with cCMV, 5 developed sensorineural hearing loss (SNHL). Among them, 3 had asymmetrical hearing loss, 1 experienced single-sided deafness, and 1 developed symmetrical hearing loss. The child with symmetrical hearing loss had profound bilateral hearing loss. In total, 4 out of 10 affected ears exhibited profound SNHL. To date, only one child has received bilateral cochlear implants, while three others use hearing aids.

**Conclusions:** This expanded targeted screening program identified a higher prevalence of symptomatic cCMV than universal screening estimates (30 per 100,000 births). While universal cCMV screening programs offer comprehensive detection, the cost may be prohibitive.

**Professional Practice Gap & Educational Need:** Despite advances in early cCMV testing, many institutions do not screen or test for cCMV. We present an approach for early cCMV testing that is feasible and effective in identifying those with more severe infection. These children are more likely to receive earlier access to sound and antiviral treatment to improve neurocognitive outcomes.

Learning Objective: Participants will be equipped to identify clinical indicators of cCMV infection that can be implemented into their clinical practice.

**Desired Result:** The desired result is to encourage healthcare providers' ability to test for cCMV infection. **Level of Evidence** – IV

Indicate IRB or IACUC: Institutional Review Board approval from IHC was obtained (IRB# 107443).

#### Clinical Development of AK-OTOF Gene Therapy for *OTOF*-Mediated Hearing Loss

Marlan R. Hansen, MD; Chen-Chi Wu, MD; John A. Germiller, MD, PhD

**Objective:** Assess the safety, tolerability, and bioactivity of AK-OTOF in individuals with Profound hearing loss due to *OTOF* mutations

Study Design: Phase 1/2 clinical trial

**Setting:** Multi-institutional

**Patients:** Participants in the AK-OTOF-101 Clinical Trial have Profound hearing loss as assessed by auditory brainstem response (ABR) at baseline and confirmed mutations in the otoferlin gene (*OTOF*).

**Interventions:** Transcanal intracochlear administration of AK-OTOF (AAVAnc80-hOTOF), an investigational dual adenoassociated viral vector encoding full-length human otoferlin

Main Outcome Measures: The primary outcome measure is safety, and secondary outcomes include ABR and behavioral audiometry.

**Results:** The first participant, an 11-year-old with Profound congenital hearing loss, experienced restored hearing within 30 days of AK-OTOF administration, achieving behavioral thresholds of 65 to 20 dB HL. The second participant, an 8-year-old, also experienced restored hearing within 30 days of AK-OTOF administration. The surgical administration procedure and the product candidate were well tolerated, and no serious adverse events occurred as of the date of this report. Updated safety and efficacy data from these and additional participants from Dose Cohort 1 will be presented.

**Conclusions:** Interim data suggest that AK-OTOF may be safely administered to patients with onset of restoration of hearing as early as one month following administration.

**Professional Practice Gap & Educational Need:** Gene therapy is an emerging modality currently under investigation for otologic indications. Otologists need information regarding the status of clinical trials.

**Learning Objective:** - Understand the eligibility criteria for the AK-OTOF-101 Clinical Trial Describe initial outcomes from the AK-OTOF-101 Clinical Trial

**Desired Result:** To understand the status of, and appropriate patient selection for referral to, gene therapy clinical trials for hearing loss.

Level of Evidence: Level II

**Indicate IRB or IACUC:** Children's Hospital of Philadelphia – IRB 22-019935. University of Iowa – IRB 1349813. National Taiwan University Hospital – 202208005MSD.

# A Novel Transcanal Catheter for Delivery of Hypothermia to the Inner Ear

Maria F. Yepes, MD; Pavan S. Krishnan, MD; Aparna Govindan, MD; Curtis King, MS Simon I. Angeli, MD; Suhrud M. Rajguru, PhD

**Objective:** Mild therapeutic hypothermia (MTH) has been shown to have neuroprotective effects in the cochlea, particularly against injuries such as electrode insertion trauma and noise-induced hearing loss by modulating pathways that reduce interleukin, oxygen-based free radicals, and inflammation. It has been postulated that MTH has neuroprotective effects in the vestibular system. Thus, our objective is to investigate the potential for inducing temperature decreases in the cochlea and vestibular endorgans through the application of a custom-designed cooling device placed in the ear canal.

Study Design: Cadaver study

Setting: Tertiary Laboratory

Patients: NA (Cadaver heads)

**Interventions:** We performed a mastoidectomy, facial recess approach, labyrinthectomy, and stapedotomy to access the auditory and vestibular endorgans. To record temperature, we placed thermistors through the round window into the cochlea, all three semicircular canals, near the otolith organs, and the scalp of each head. Cadaver heads were pre-warmed to 35.5-38°C to simulate human body conditions. Once stabilized, a cooling device with a saline-filled catheter and balloon tip, connected to a cooling machine, was positioned in the ear canal near the eardrum.

Main Outcome Measures: Temperature changes (recorded every 1 minute) in the inner ear organs, ear canal, and scalp

**Results:** Thermistors inserted through the round window demonstrated a mean temperature decrease of 2.5-3°C during a 30minute cooling period when the cooling device was set to 3°C. Baseline cochlear temperatures were fully restored within 15 minutes after the device was removed. Thermistors in the semicircular canals demonstrated a mean temperature decrease of 1-1.5°C during a 45-minute cooling period when the cooling device was set to 3°C. Thermistors placed on the scalp recorded no temperature fluctuations throughout the experiments. Importantly, no morphological changes were observed in the ear canals or eardrums of any specimens during the trials.

**Conclusions:** Our results demonstrate that cochlear and vestibular hypothermia can be effectively achieved using an external cooling system positioned at the ear canal. These findings provide strong evidence for adopting a more accessible and simplified clinical approach to mitigate potential inner ear damage during invasive procedures.

**Professional Practice Gap & Educational Need:** It is hypothesized that hypothermia may have a similar neuroprotective effect as it does in the auditory system due to the vestibular system's proximity to the cochlea, shared embryological origin, and comparable molecular physiology. Our objective is to address the existing gap by developing a non-invasive, localized system capable of inducing MTH in both the cochlear and vestibular systems, without obstructing the surgeon's view, while ensuring stability, reproducibility, and rigorous application.

**Learning Objective:** Attendees will understand the current state of the literature regarding therapeutic hypothermia applied to the inner ear and learn about non-invasive methods for delivery of hypothermia to the audiovestibular organs.

**Desired Result:** Attendees will understand the potential of mild therapeutic hypothermia as a therapeutic neuroprotective approach as applied to the inner ear. Our studies lay the groundwork for future implementation of hypothermia intraoperatively, and potentially in cases of inner ear diseases affecting the cochleovestibular nerve.

Level of Evidence – Level  ${\rm V}$ 

#### Risk Factors Associated with Otosclerosis: A National Database Study

Prithwijit Roychowdhury, MD; Miriam Smetak, MD; Matthew Shew, MD; Jacques Herzog, MD Craig Buchman, MD; Nedim Durakovic, MD

**Objective:** To characterize the demographics of patients with otosclerosis (OS) in the US, identify the prevalence of autoimmune & viral risk factors and understand the association of osteogenesis imperfecta (OI).

Study Design: Retrospective cohort study

Setting: National database (TriNetX) sourced from 67 HCOs in the USA

Patients: Adults diagnosed with OS (ICD-10H80).

**Interventions:** Evaluation of age, gender, race, presence of autoimmune markers (RF, ANCA, SS-A/B, ds-DNA), measles serology and clinical diagnosis of OI in patients with OS.

Main Outcome Measures: 1) Mean age, gender, race 2) Positive autoimmune markers or measles serology 3) OI diagnosis

**Results:** 31,184 subjects with OS were identified. The majority were female (62.5%, n = 19,533) and white (70.1%, n = 22,100). Age at diagnosis was similar between females and males [F:52.2  $\pm$  15.6 vs M:53.1  $\pm$  15.5 (mean  $\pm$  SD), p < 0.0001]. Subjects with OS were 34x more likely to have OI (0.257% vs 0.008%, p < 0.0001) and were about 2x as likely to be positive for at least one autoimmune laboratory marker (0.683% vs 0.304%, p < 0.0001) when compared to age-matched controls (n = 78,331,542). There was no difference in positive measles serology between OS and controls (0.087% vs 0.081%, p = 0.7077).

**Conclusions:** Age at OS diagnosis was similar between females and males. Patients with OS demonstrated significant association with OI & slight association with positive autoimmune serology but no association with positive measles serology. Findings have implications for the understanding of the etiopathogenesis of OS.

**Professional Practice Gap & Educational Need:** Prior studies have implicated genetics, viral and autoimmune factors to the development of OS. Herein we leverage a large national database of healthcare outcomes to better characterize these associations.

Learning Objective: 1) Demonstrate the impact of age & gender on cases of otosclerosis in the US 2) Describe the association between otosclerosis and osteogenesis imperfecta, measles, and positive autoimmune serology.

**Desired Result:** Attendees will appreciate the associations between osteogenesis imperfecta as well as positive autoimmune serologies on the diagnosis of otosclerosis.

Level of Evidence - IV

# **Evaluating the Necessity of Preoperative CT Imaging for Stapedectomy**

Amor Niksic, BS; Albert Y. Li, BA; Tyler J. Gallagher, BS; Hyun Sang Cho, MD Rance Fujiwara, MD, MBA; Joni K. Doherty, MD, PhD Hitomi Sakano, MD, PhD

**Objective:** Investigate the utility of preoperative computed tomography (CT) in patients undergoing middle ear surgery for presumed otosclerosis. To date, there is no uniformity in ordering preoperative imaging.

Study Design: Retrospective chart review.

Setting: Two independent tertiary referral centers.

**Patients:** 606 adult patients (689 ears) with a preoperative diagnosis of otosclerosis who underwent surgical intervention from 2007 to 2024.

Interventions: All patients underwent operative intervention for presumed otosclerosis, with or without CT.

**Main Outcome Measures:** The number needed to treat (NNT) to have prevented unnecessary surgery (i.e. non-otosclerosis etiology) was calculated among patients who had not undergone preoperative CT.

**Results:** Data were gathered from 689 ears in 606 patients, 59.6% were female, and average age was 49.9 ( $\pm$  11.9). 33.4% (230/689) had preoperative CT. Of 689, non-otosclerosis finding was discovered intraoperatively in 32 (4.6%): 16 (50.0%) lateral chain fixation, 7 (21.8%) normal ossicular chain, 6 (18.8%) ossicular chain discontinuity, 2 (6.3%) overhanging facial nerves (1 with stapes fixation), and 1 (3.1%) tympanosclerosis. 16/32 (50.0%) had a preoperative CT with findings that would not have prevented middle ear exploration. Among those without preoperative CT, the unexpected finding rate was 16/459 (3.5%), thus, the minimum NNT with preop CT is 28. Since 11 of these patients still benefited from surgery, the NNT to have prevented unnecessary middle ear surgery is 41. Based on average Medicare costs for stapes surgery (\$6491) and CT (\$163), there was no cost benefit of blanket preoperative CT to prevent unnecessary surgery.

**Conclusions:** Preoperative CTs in identifying the cause of hearing loss in presumed otosclerosis is insufficient to justify their routine use in all patients and should be reserved based on clinical judgement.

**Professional Practice Gap & Educational Need:** Variability exists in the use of preoperative CT imaging for otosclerosis, both domestically and internationally. The aim of this study was to examine the potential for improved diagnostic accuracy and cost savings with routine imaging.

Learning Objective: To evaluate the diagnostic utility of preoperative CT in preventing unnecessary surgeries in stapedotomy patients.

Desired Result: Improved diagnostic protocols and reduced unnecessary procedures in otologic practice.

Level of Evidence - Level IV

Indicate IRB or IACUC: UT Southwestern Medical Center STU-2023-1105; Keck Medicine of USC UP-23-01212

# Endoscopic vs. Microscopic Stapedotomy for Otosclerosis: An Updated Meta-Analysis of Complications

Hamzah Jehanzeb; Dahir Ashfaq; Zayan Alidina; Hamdan A. Pasha, MBBS Syed A. Abbas, MBBS

**Objective:** To evaluate and compare intraoperative and postoperative complications of endoscopic versus microscopic stapedotomy in patients with otosclerosis.

**Data Sources:** PubMed, Cochrane Library, CINAHL, and Scopus databases were searched for studies from inception to August 2024 using terms such as "endoscopic," "microscopic," "otosclerosis," and "stapes surgery," with no language restrictions.

**Study Selection:** Studies were included if they compared surgical visibility and postoperative complications between endoscopic and microscopic stapedotomy for otosclerosis. Excluded were studies involving cholesteatomas or ossicular chain reconstructions.

**Data Extraction:** Data extraction followed PRISMA guidelines. Key variables extracted included demographics, surgical visibility, postoperative complications, study design, and follow-up duration. Meta-analysis was performed using random-effects models to assess the differences.

**Data Synthesis:** In this analysis, 39 studies involving 2,309 patients (35.9% males, 64.1% females) were included. The meta-analysis revealed that endoscopic surgery significantly reduced operative time (SMD: -0.92; p=0.009) and the risk of bone removal (RR: 0.40; p=0.03), chorda tympani injury (RR: 0.55; p=0.02), chorda tympani manipulation (RR: 0.26; p<0.00001), dysgeusia (RR: 0.43; p<0.00001), and pain (RR: 0.46; p<0.0001). However, no significant differences were found in visibility (RR: 4.04; p=0.17), risk of vertigo (RR: 1.00; p=0.95), or tympanic membrane damage (RR: 0.66; p=0.28).

**Conclusions:** Endoscopic stapedotomy significantly improves operative time and reduces chorda tympani injuries, dysgeusia, pain, and bone removal compared to microscopic techniques, though surgical visibility and tympanic membrane damage remain similar.

**Professional Practice Gap & Educational Need:** Despite the advantages identified, there remains a knowledge gap among otolaryngology practitioners regarding the efficacy of endoscopic techniques in stapedotomy. This review provides critical insights that can guide preoperative counseling and decision-making for patients undergoing surgery for otosclerosis.

Learning Objective: To understand the comparative benefits and risks associated with endoscopic versus microscopic stapedotomy techniques for otosclerosis, focusing on intraoperative and postoperative outcomes.

**Desired Result:** Enhanced surgical decision-making and improved patient outcomes through increased awareness and adoption of endoscopic techniques in stapedotomy procedures for otosclerosis.

Level of Evidence - Level I (systematic review and meta-analysis including large RCTs with clear cut results)

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

# Temporal Bone 3D Reconstruction and Analysis of Endolymph Volume in Meniere's Disease

Achilles A. Kanaris, BS; Adam Y. Xiao, MD, PhD; Eashan Biswas; Gregory P. Lekovic, MD, PhD John L. Go, MD; Stephen S. Cai, MD; Ivan A. Lopez, PhD Gail P. Ishiyama, MD; Akira Ishiyama, MD

Hypothesis: Vestibular endolymph volume (VEV) differs between Meniere's disease (MD) and age-matched controls.

**Background:** Magnetic resonance imaging (MRI) is used to diagnose endolymphatic hydrops (EH) and MD. Archival human temporal bones (HTB) can be used to establish reference VEV values and the VEV to bony volume of the vestibule (VES) ratio for correlation with MRI.

**Methods:** 3D reconstruction and volume analysis were performed on HTBs from 10 patients (5 MD, 5 age-matched controls). VEV includes the volume of the utricle, saccule, and vestibular cecum of the cochlear duct (CD). VES is the volume of the bony vestibule.

**Results:** VEV was significantly higher in MD ( $22.28 \pm 2.27 \text{ mm}^3 \text{ vs } 9.66 \pm 2.29 \text{ mm}^3$ , p < 0.01). The VEV:VES ratio indicative of EH was significantly higher in MD ( $0.62 \pm 0.15 \text{ vs } 0.25 \pm 0.04$ , p < 0.01). There was no difference in VES ( $37.05 \pm 5.78 \text{ mm}^3 \text{ vs } 38.47 \pm 5.84 \text{ mm}^3$ , p = 0.84). Saccular ( $5.35 \pm 6.39 \text{ mm}^3 \text{ vs } 1.78 \pm 0.60 \text{ mm}^3 \text{ vs } p = 1$ ) and utricular volumes ( $9.81 \pm 3.87 \text{ mm}^3 \text{ vs } 7.81 \pm 2.03 \text{ mm}^3$ , p = 0.5476) were heterogenous and not different between groups. Three MD saccules were collapsed or compressed ( $0.06, 1.20, \text{ and } 1.94 \text{ mm}^3$ ) and two hydropic ( $8.32 \text{ and } 15.24 \text{ mm}^3$ ). One MD utricle was hydropic ( $15.22 \text{ mm}^3$ ). The CD was significantly larger in MD ( $27.68 \pm 12.21 \text{ mm}^3 \text{ vs } 4.25 \pm 0.87 \text{ mm}^3$ , p < 0.01).

**Conclusions:** The VEV and VEV:VES is significantly higher in MD, indicative of EH, and provides the first histopathological reference values comparable to MRI. All MD saccules exhibited either hydrops or collapse. One utricle exhibited hydrops. The CD was dilated in all MD specimens.

**Professional Practice Gap & Educational Need:** Volume measurements of both MD and age-matched controls are necessary to better define EH and improve MRI reliability for diagnosis of MD.

Learning Objective: To understand differences in VEV and VEV:VES values in MD and age-matched controls.

**Desired Result:** To quantify VEV and VEV:VES differences in MD and age-matched control to contribute to more definitive diagnostic tools for MD.

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

Indicate IRB or IACUC: UCLA IRB #22-001587

#### Cochlear Signal Intensity Changes in Vestibular Schwannoma: A Balanced Fast Field-Echo (bFFE) MRI Study

Takeshi Fujita, MD, PhD; Hiroko Takeda, MD; Tomonori Kanda, MD, PhD; Natsumi Uehara, MD, PhD Jun Yokoi, MD, PhD; Akinobu Kakigi, MD, PhD; Ken-ichi Nibu, MD, PhD

**Objective:** To evaluate the signal intensity of the cochlea in patients with vestibular schwannoma (VS) using balanced fast field-echo (bFFE) magnetic resonance imaging (MRI) sequences.

Study Design: Retrospective cohort study.

Setting: Tertiary academic center from 2008 to 2019.

Patients: A total of 165 VS patients and 30 patients with unilateral sensorineural hearing loss (SNHL).

Interventions: Patients were followed up with MRI and audiometry.

**Main Outcome Measures:** The mean signal intensity of the cochlea was assessed using regions of interest (ROIs) on bFFE MRI. The signal intensity ratio (affected/normal) was calculated and analyzed for its correlation with tumor size and hearing level. Postoperative changes in signal intensity were also evaluated.

**Results:** VS patients had significantly lower cochlear signal intensity on the affected side compared to the normal side (75.3% vs. 100%, p<0.0001). No significant difference was found in SNHL patients. A significant correlation between cochlear signal intensity ratio and hearing level was observed only in Koos grade I tumors. In contrast, tumor size was negatively correlated with the cochlear signal intensity ratio in Koos grade II–IV tumors. Postoperative evaluations demonstrated a gradual normalization of cochlear signal intensity, with levels approaching normal within 1–2 years post-surgery, regardless of hearing preservation status.

**Conclusions:** bFFE MRI sequences can effectively assess cochlear signal intensity in patients with VS. The reduced signal intensity in the affected cochlea likely indicates changes in protein concentration due to VS secretions. This method has potential for tumor evaluation, surgical planning, and postoperative monitoring in VS patients.

**Professional Practice Gap & Educational Need:** There is a gap in understanding hearing loss mechanisms in vestibular schwannoma (VS) patients, along with an underutilization of advanced MRI techniques for diagnosis and monitoring. Additionally, there is insufficient knowledge about the clinical applications of balanced fast field-echo (bFFE) MRI sequences in this context.

**Learning Objective:** Attendees will be able to explain the utility of bFFE MRI in evaluating cochlear changes in VS patients, understand the relationship between cochlear signal intensity, tumor size, and hearing function, and interpret post-surgical changes in cochlear signal intensity and their clinical significance.

**Desired Result:** Improved understanding of VS-related hearing loss pathophysiology and stimulation of research into advanced MRI techniques for assessing inner ear changes.

**Level of Evidence** – IV

Indicate IRB or IACUC: Kobe University Graduate School of Medicine Institutional Review Board (B230044)

SELECTED ABSTRACTS

# POSTER PRESENTATIONS

IN ORDER OF PRESENTATION



# 158<sup>th</sup> Annual Meeting AMERICAN OTOLOGICAL SOCIETY

May 16-17, 2025 Hyatt Regency New Orleans New Orleans, LA

(Oral presentations are Sat/Sun May 17-18)

# Evaluation of Spectral Ripple Testing as a Proxy for Speech Discrimination in Audiometric Testing

Heather D. Merkouris, MS; Arun M. Raghavan, MD; Ellise R. Minneker, BS; Gavriel D. Kohlberg MD

**Objective:** We investigated the hypothesis that spectral ripple discrimination predicts unaided word recognition scores (WRS).

Study Design: Prospective cohort study

Setting: Academic medical center

Patients: 34 English-speaking adult patients with sensorineural hearing loss

Interventions: N/A

Main Outcome Measures: Spectral ripple discrimination was measured in each ear and reported as ripples per octave (RPO).

**Results:** RPO scores were measured for 64 ears from 34 subjects. RPO scores ranged from 0.2 to 11.7. WRS ranged from 12% to 100%. Seven of eight ears with a WRS  $\leq 60$ , and 14 of 56 ears with WRS  $\geq 60$  had an RPO of  $\leq 3$ . At a cutoff of 3, RPO predicted WRS  $\leq 60$  with sensitivity of 87.5% and specificity of 75% (Chi-squared 12.4, DF = 1, p < 0.001).

**Conclusions:** Spectral ripple discrimination testing offers the potential for an efficient, language-independent CIE screening test for non-English-speaking patients. Further studies are warranted to evaluate how RPO thresholds predict aided word and sentence scores and cochlear implant candidacy for both English and non-English speaking patients.

**Professional Practice Gap & Educational Need:** Unaided WRS is a critical metric for determining if a patient should be referred for a cochlear implant evaluation (CIE). Non-English-speaking patients often do not have a WRS performed during routine audiometric testing, limiting the information available to assess the need for a CIE. Spectral ripple discrimination testing is a non-linguistic test that measures how well an individual can perceive changes in the spectral structure of sound. Evaluating whether a patient has an RPO below a particular cut-off can be performed rapidly.

Learning Objective: To evaluate if spectral ripple testing can reliably predict speech discrimination as defined by WRS.

**Desired Result:** To provide knowledge and contribute to the investigation of spectral ripple discrimination testing as a non-linguistic tool to screen patients for CIE.

Level of Evidence – Level III

Indicate IRB or IACUC: IRB is STUDY00018670. Approved 9/7/2023.

#### Contemporary Clinical Management of Otosyphilis: A Case Series for Practicing Otolaryngologist

Corinne A. Pittman, MD; Hudson Liu, BS; Erica Choe, MD; Sandeep Kowkuntla, BS Michael Hoa, MD; Selena Briggs, MD, MBA, PhD; H. Jeffrey Kim, MD

**Objective:** Amid the COVID-19 pandemic, U.S. syphilis cases increased by 80% from 2018-2022, including a 17.3% rise in 2022 alone—the highest since 1950. This study describes clinical manifestations, treatments, and hearing outcomes in patients diagnosed with otosyphilis/neurosyphilis over the past 12 years at two tertiary care hospitals in a U.S. city with a 28.6% rise in syphilis since the pandemic.

Study Design: Retrospective case series

Setting: Tertiary care center

Patients: 16 patients diagnosed with otosyphilis or neurosyphilis

Intervention: This study involved reviewing patient charts, audiograms, and serological data to assess treatment outcomes in otosyphilis/neurosyphilis management

**Main Outcome Measures:** We conducted a retrospective case series from 2011 to 2023 of patients at two tertiary care hospital otolaryngology clinics, presenting with cochleovestibular symptoms and a confirmed diagnosis of otosyphilis or neurosyphilis via treponemal testing.

**Results:** Subjects included 16 patients (13 males, 3 females) with an average age of 52 years (range, 25 to 79) and 6 (67%) positive for HIV. Symptoms appeared on average 7.5 weeks before diagnosis and included unilateral or bilateral mixed or sensorineural hearing loss, tinnitus, and vertigo. Lumbar puncture diagnosed 7/18 (40%) with otosyphilis/neurosyphilis, with over half receiving 10-14 days of Penicillin G. Two patients were treated with doxycycline as an alternative antibiotic, and others were lost to follow-up. Six patients received at least 2 weeks of corticosteroids, 4 of whom experienced an 8 to 20dB pure tone average improvement in hearing. Following treatment, 62% displayed stable or improved hearing at short and long-term follow-ups, with 31% showing symptom resolution within 3 months.

**Conclusions:** With rising syphilis rates, early detection and intervention by otolaryngologists, in collaboration with infections disease specialists, are crucial to improve treatment outcomes and address this re-emerging health challenge effectively.

**Professional Practice Gap & Educational Need:** Despite the dramatic rise in syphilis cases during the COVID-19 pandemic and the increasing incidence of otosyphilis/neurosyphilis, many otolaryngologists may lack current knowledge on evolving clinical presentations, effective treatment options, and expected hearing outcomes. This educational gap necessitates targeted learning to ensure early and effective diagnosis and treatment strategies, which are critical for improving patient outcomes in this evolving health crisis.

**Learning Objective:** The incidence of syphilis has been steadily increasing through recent years and the COVID-19 pandemic. Otosyphilis is difficult to diagnose due to its wide range of symptoms, but early detection is crucial for treatment and reversal of hearing loss.

**Desired Result:** Enhance clinical knowledge and improve patient outcomes by providing otolaryngologists with updated insights into the diagnosis, treatment, and management of otosyphilis/neurosyphilis amid increasing infection rates.

Level of Evidence - IV

Indicate IRB or IACUC: MedStar Health/Georgetown University IRB #7531, approved on 6/17/24

# RNA-Seq Analysis of Primary Vestibular Schwannoma Shows Focal Adhesion Pathway Involvement in Radiation Resistance

Aida Nourbakhsh, MD, PhD; Olena Bracho, BS; Yan Guo, PhD; Christine T. Dinh, MD

Hypothesis: Radiation-resistant VS upregulate key pathways regulated by merlin to evade cell death.

**Background:** Vestibular schwannomas (VS) are intracranial tumors caused by a deficiency in the merlin tumor suppressor protein, leading to uncontrolled cell growth through (1) impaired cell-matrix adhesion, (2) actin cytoskeleton destabilization, and (3) dysregulated receptor tyrosine kinase (RTK) signaling. Some VS are resistant to radiation; but the molecular basis for this resistance is unknown.

**Methods:** Primary VS cultures (n=10) were obtained from fresh tumors collected during VS surgery. Cultures were treated with 0 or 12 Gy of radiation and classified as "radiation-resistant" or "radiation-sensitive" based on 96-hour viability assays. RNA was extracted at 6 hours, and RNA-Seq was conducted using the Illumina TruSeq workflow. The Nextflow RNA-Seq pipeline identified differentially expressed genes and performed Gene Ontology (GO) and KEGG pathway analyses.

**Results:** Five of ten primary VS were radiation-resistant. Two VS from each radiation response group, matched by age, were selected for RNA-Seq. While samples did not cluster by radiation response, they clustered by radiation dose (0 and 12 Gy), suggesting that differential gene expression related more to radiation response than radiation dose. GO analysis showed enrichment in gene sets linked to cytoskeletal components, RTKs, and growth factor signaling in radiation-resistant VS. KEGG analysis demonstrated enriched pathways involving focal adhesion, actin cytoskeleton, and RTK signaling.

**Conclusions:** Focal adhesion pathway was found to be the most significantly enriched pathway in radiation resistant tumors. This pathway, similar to merlin signaling, regulates cellular interactions with extracellular matrix, stabilizes actin cytoskeleton, and regulates RTKs. Further investigations into the focal adhesion pathway will provide important insight on the molecular processes that can be targeted to overcome radiation resistance in VS.

Professional Practice Gap & Educational Need: The mechanisms of radiation resistance in VS are not well understood.

Learning Objective: Perform bioinformatic analysis of RNA Sequencing to determine differentially expressed genes

**Desired Result:** Knowledge of components that regulate merlin signaling pathway will lead to new therapeutics to help overcome radiation resistance in VS.

**Level of Evidence** – N/A

Indicate IRB or IACUC: University of Miami IRB #20150637.

#### Radiologic Assessment of the Round Window Anatomy in Pediatric Patients Relevant to Gene Therapy and Inner Ear Drug Delivery

Renata M. Knoll, MD; Soomin Myoung, BSE (presenter); Zachary A. Kons, MD Katherine Reinshagen, MD; Judith S. Kempfle, MD

**Objective:** This study aims to radiologically determine the transcanal anatomic angles and variations of the round window (RW) in pediatric patients.

Study Design: Retrospective radiological review.

Setting: Tertiary care center.

Patients: Pediatric patients with normal high-resolution computed tomography scan of the temporal bone.

Interventions: Diagnostic.

**Main Outcome Measures:** The transcanal angle to the RW membrane, depth, volume and opening angle of the RW niche, and the transcanal RW location relative to the umbo were assessed. The patients were divided into two groups based on age: group 1 (< 24 months) and group 2 (>24 months).

**Results:** A total of 91 ears from 50 pediatric patients (58% male) were included. The mean age was 37.9±47 months, of which 60 ears (66%) were <24 months. The overall mean transcanal angle to the RW membrane, depth, opening angle, and volume of the RW niche were 98.3±9°, 1.83±0.19 mm, 67.1±5.5°, 3.29±0.79 mm<sup>3</sup>, respectively. Depth, volume and opening angle of the RW niche were similar between groups. The transcanal angle to the RW tended to increase with age progression, and was significantly less obtuse for group 1 than group 2 (95.5±1° and 103.8±1.4°, respectively; p < .0001). The RW membrane was directed posteroinferiorly relative to the umbo tip, relatively superior compared to the adult RW location from prior literature but did not differ between pediatric subgroups.

**Conclusions:** Our findings suggest that the transcanal angle to access the RW membrane becomes more obtuse with increasing age while the RW depth and volume remain the same, which may be relevant for surgical planning and future design of novel devices for transcanal gene therapy approaches and inner ear drug delivery in pediatric patients.

**Professional Practice Gap & Educational Need:** The possibility of treating inner ear disorders through transcanal drug delivery and gene therapy has garnered increased interest. As the RW provides an ideal route for minimally invasive delivery through the external auditory canal (EAC), understanding its anatomy and variations is imperative. However, most studies on the RW anatomy either pertain to adult individuals or focus on features relevant for cochlear implantation through a facial recess approach. Furthermore, known disparities in temporal bone anatomy in children could result in different angles to access the RW, and possibly increased difficulty with transcanal delivery. Therefore, our study informs the morphological variations of the RW anatomy and how it develops with age progression, providing insight for medical therapy development to treat inner ear disorders in the pediatric population.

**Learning Objective:** To explore the radiological RW anatomic variability in relation the EAC in the pediatric population, relevant for transcanal delivery of novel medical therapies for the treatment of sensorineural hearing loss.

**Desired Result:** Clinicians will have a better understanding of the pediatric RW anatomical variability relative to the EAC, and allow for better surgical counseling, planning and choice of devices for minimally invasive transcanal delivery of novel medical therapies to restore hearing.

Level of Evidence – III.

# Regeneration of Cochlear Synapses following Intracochlear Delivery of Neurotrophin 3

Renata M. Knoll, MD; Sina Schwinn, BA; Andrea Zhang, MD; Andrew Jung, BS Brooke Wang, BS; Judith S. Kempfle, MD; David H. Jung, MD, PhD

**Hypothesis:** Intracochlear injection (ICI) offers an alternative to effectively targeting the cochlea with lower concentration requirement as compared to other methods of delivery.

**Background:** Synaptic connections between sensory hair cells (HCs) and cochlear primary afferent neurons are vulnerable to noise-induced trauma. Neurotrophin-3 (NT3) has been reported to induce synaptic regeneration when delivered to the round window (RW) niche in mice. However, the drug bioavailability may be limited by multiple factors like membrane permeability and drug distribution within the inner ear. A direct, intracochlear route may overcome these issues by providing direct access to the cochlea and allowing for more precise control over drug delivery.

**Methods:** We exposed 7-week CBA/CaJ mice to octave-band noise (8-16 kHz) for 2 hours at 98 dB SPL to induce synaptopathy. After 24 hours, mice underwent a single ICI through the RW of 100nL of either artificial perilymph (AP), 5.31 ng/uL or 10.57 ng/uL NT3 at a rate of 200 nL/min. Auditory brainstem responses (ABRs) were recorded 2 weeks after the injection. We evaluated HCs and synaptic ribbons in immunolabeled cochlear whole mount (WM) samples and compared them to those of non-noise-exposed mice (controls).

**Results:** ABR wave 1 amplitudes were in the normal range after NT3 injection, indicating synaptic regeneration. HCs populations were intact. The mean synaptic counts in both NT3 dose subgroups (5.31 ng/uL or 10.57 ng/uL) were similar to controls (p=.5824 and p=.3909, respectively), and significantly higher than in the AP only group (p=.0017 and p=.0035, respectively). Additionally, the mean synaptic counts between dose subgroups were similar (p>.9999).

**Conclusions:** Our findings suggest that low concentration ICI delivery of NT3 efficiently promotes synaptic regeneration in noise-exposed mice.

**Professional Practice Gap & Educational Need:** Trophic factors, such as NT3, have been reported to induce synaptic regeneration when delivered exogenously, and a variety of methods have been studied to directly introduce them into the cochlea. While delivery of trophic factors at the RW niche has been reported, the drug bioavailability remains a challenge through this method.

**Learning Objective:** To understand whether ICI is an effective method for enhancing drug delivery efficiency, requiring smaller doses to achieve the desired therapeutic effect.

**Desired Result:** ICI is a reliable method for delivery to reverse cochlear synapthopathy, and a promising route to study emerging therapeutic compounds for the treatment of inner ear diseases.

Level of Evidence - NA; Basic Science

Indicate IRB or IACUC: Protocol #2021N000079

#### The Longitudinal Impact of Radiotherapy on Osseointegrated Hearing Aid Outcomes and Complications

Benjamin D. Lovin, MD; Mike Hernandez, MS; Paul W. Gidley, MD; Karine Al Feghali, MD Jack Phan, MD, PhD; Catherine Wang, MD; Dianna Roberts, PhD; Marc-Elie Nader, MD

**Objective:** To evaluate the impact of radiotherapy on osseointegrated hearing aids (OIHA) outcomes and complications.

Study Design: Retrospective cohort

Setting: Tertiary referral academic practice

Patients: All percutaneous OIHA performed from 2006 to 2021

**Interventions:** Evaluation of implant and abutment-related OIHA outcomes and complications stratified by receipt of radiation and dosage. Radiation dosages were calculated at both bone and soft tissue level.

Main Outcome Measures: Abutment, implant, and major complications assessed using the modified Holgers and IPS grading scales.

**Results:** Total of 190 OIHA were included of which 124 (65%) were placed in irradiated temporal bones. Radiation cohort was older (p=0.002) and more often prior/current smokers (p=0.003). Total of 84 (44%) OIHA experienced at least one complication at mean follow-up of 43.3 months. Radiation cohort had greater rates of having any complication (p=0.032), major complication (p=0.014), implant complication (p=0.007), and abutment complication (p=0.032). When comparing scales, IPS score distribution was significantly different between groups (p=0.011); a similar trend, yet not significant, was found with Holgers classification (p=0.075). Logistic regression identified radiation (p=0.029) and abutment size (p=0.048) as significantly associated with any complication. Notably, every 1mm increase in abutment size decreased the risk of any complication by 11%. There was a trend towards more implant and abutment complications with higher radiation doses (p=0.208 and 0.186, respectively). Cumulative incidence plots demonstrate a greater discrepancy in complication rates between groups as time increases.

**Conclusions:** Radiation significantly increases the risk of both abutment and implant-related OIHA complications, particularly in the long-term. The IPS grading scale may be more sensitive to detecting differences in complication rates. Increasing the abutment size and decreasing radiation dosages may decrease the risk of complication.

**Professional Practice Gap & Educational Need:** There is a paucity of literature on long-term evaluation of OIHA complications, particularly after radiation. This data may prove helpful in patient counseling before percutaneous OIHA or when considering alternatives, such as non-operative bone conduction technology or transcutaneous devices. There has also not been prior comparison of OIHA complication grading scales.

**Learning Objective:** The rate of OIHA complications is significant in long-term follow up and appears potentiated by radiation. IPS grading scale may be more helpful in identifying these complications. Using a longer abutment or decreasing radiation dosage may reduce risk of complications.

Desired Result: Thoughtful implantation and follow up of patients with OIHA and a history of temporal bone irradiation.

Level of Evidence – III

Indicate IRB or IACUC: MD Anderson Cancer Center, PA19-0106

#### Intraoperative Continuous Electrocochleography in Cochlear Implant Surgery Using Slim Perimodiolar Electrodes

Allen Khudaverdyan, BA; Justin Cottrell, MD; Emily Kay-Rivest, MD; David Friedmann, MD Daniel Jethanamest, MD; Sean McMenomey, MD; J. Thomas Roland Jr., MD

**Objective:** To explore the use of electrocochleography (ECochG) during cochlear implant (CI) surgery utilizing a slim perimodiolar electrode.

Study Design: Retrospective chart review

Setting: Single institution academic hospital

Patients: Patients who underwent cochlear implantation (CI) and intraoperative ECochG.

Interventions: Continuous ECochG recording at 250Hz stimulation frequency using Cochlear Research Platform 1.2.1

Main Outcome Measures: Final insertion cochlear microphonic (CM) and 3-month post-operative CNC word score. Hearing preservation rates were also evaluated for patients with pre-operative residual hearing.

**Results:** Fourteen patients (6 male, 8 female, mean age 55.8) had mean pre and 3-month postoperative CNC word scores of 14.4% (SD = 23%) and 57.7% (SD = 23%), respectively (p=0.0004\*). The mean change in CNC word scores at 3 months was 43.46% (SD = 25). Thirteen patients had idiopathic hearing loss, with four undergoing unilateral implantation for single-sided deafness. The mean peak and final insertion CM were 24.25  $\mu$ V and 16.8  $\mu$ V respectively. Area under the curve (AUC) of the root mean square of CM was 1225 Volt-sec. The AUC of F0 Fast Fourier transform of CM curve was 1167 Volt-sec. Hearing preservation and 3-month postoperative CNC word scores are reported in conjunction with final CM measurements.

**Conclusions:** ECochG utilizing perimodiolar electrodes has been reported upon less than straight electrodes. Our results reinforce the feasibility of ECochG in the setting of perimodiolar insertion, although how this data might inform a real time change in surgical technique remains uncertain.

Professional Practice Gap & Educational Need: Understanding the clinical utility of ECochG utilizing perimodiolar electrodes.

**Learning Objective:** Evaluate the use of electrocochleography tracing features to predict hearing preservation and CNC outcomes following perimodiolar electrode insertion.

**Desired Result:** To add to the growing literature of perimodiolar electrode ECochG use to reinforce feasibility and clinical utility.

Level of Evidence –  $\rm V$ 

IRB: s24-00530, NYU Langone Health

#### **Musical Perception and Enjoyment in Cochlear Implant Users**

Richa S. Nathan, BS; Christopher R. Cai, BA; Julie Hanson, AuD; Nathan C. Tu, MD

**Objective:** To examine the effects of cochlear implantation on musical perception and enjoyment at least 9 months postoperatively, focusing on user experiences.

Study Design: Descriptive survey study

Setting: Outpatient Audiology Clinic at a tertiary Medical Center

**Patients:** Adult cochlear implant (CI) users (ages 18 and older) at least 9 months postoperatively. Exclusion criteria include significant cognitive impairment, psychiatric disorders, less than 9 months of CI use, and non-English speakers.

Interventions: Qualtrics survey administration via survey link or QR code

Main Outcome Measures: Qualitative survey data

**Results:** Current survey responses (n=23) reflect a population of 43% male and 57% female participants, with 39% having bilateral CIs, 39% in the right ear only, and 22% in the left ear only. Time since implantation ranges from 9 months to 40 years. Most participants (57%) listen to music daily, but 61% report no formal musical training while 10% have professional musical backgrounds. Notably, 58% reported diminished musical enjoyment compared to pre-implantation, while 38% noted an improvement. 78% reported equal or improved enjoyment compared to initial experiences post-implantation, though still below pre-implantation levels. Participants found lyrics to be the most challenging aspect of musical perception, followed by timbre, pitch, harmony, melody, and rhythm. Pop/rock was the most pleasant, with classical music deemed the most unpleasant. 48% described their music perception as "somewhat unnatural" compared to what would be expected with normal hearing and 53% found streaming music equally or more enjoyable than pre-implantation. Participants expressed a desire for clearer lyrics, better high-pitch clarity, improved note recognition, and accurate pitch perception.

**Conclusions:** CIs significantly impact musical perception and enjoyment of users, with many reporting challenges in specific musical elements such as lyrics and pitch. While most participants experienced some improvement in their enjoyment of music compared to their initial post-implantation experience, it often did not reach pre-implantation levels. The findings highlight the need for enhanced auditory training and technological advancements to support music listening for cochlear implant users.

**Professional Practice Gap & Educational Need:** Despite the widespread use of CIs, there is limited understanding of how they affect musical perception and enjoyment. Audiologists and otolaryngologists must be aware of the specific challenges faced by users to better inform and guide their patients post-operatively.

Learning Objective: To understand the effects of CIs on musical perception and enjoyment, and to identify areas where patients may require additional support to improve their music listening experience and quality of life.

**Desired Result:** To foster greater awareness among healthcare professionals about the unique challenges faced by CI users and to promote the development of targeted interventions and technological advancements to enhance musical enjoyment and perception.

Level of Evidence - V

# Repair of Partial Ossicular Discontinuity Restores High Frequency Middle Ear Function: A Basic Science and Clinical Correlation

Keelin A. Fallon, BA; Jeffrey T. Cheng, PhD; Aaron K. Remenschneider MD, MPH

**Hypothesis**: We expect repair of partial ossicular discontinuity in cadaveric temporal bones (TB) with bone cement to restore stapes velocity to baseline levels. Clinically, we expect to see improvement in high frequency conductive hearing loss (HFCHL) after surgical repair of partial ossicular discontinuity.

**Background**: In cadaveric TB, partial ossicular discontinuity results in a decrease in stapes velocity, primarily at HFs (>4 kHz). Clinically, this manifests as a HFCHL. The impact of joint reestablishment on HF hearing has not been widely studied.

**Methods**: Five, fresh, previously frozen human TBs from donors with no known history of ear disease were used to study the mechanical effects of partial ossicular discontinuity before and after repair, using dual laser Doppler vibrometry to measure stapes and umbo velocities. Results were correlated with audiometric outcomes of two patients who underwent endoscopic repair of surgically confirmed partial ossicular joint disarticulation with bone cement.

**Results**: Experimentally, partial joint disarticulation produced a decrease in stapes velocity by an order of magnitude beginning between 2-3kHz and primarily recorded between 4-20kHz. Repair with bone cement restored stapes velocity to baseline levels across frequencies. Clinically, both patients presented with a 4kHz air bone gap (ABG)  $\geq$ 25dB, and evidence of a hypercompliant middle ear on tympanometry. Postoperatively the 4kHz ABG closed by  $\geq$ 25dB, completely closing the ABG for one patient. Air conduction thresholds improved between 6-8kHz, and tympanometry normalized.

**Conclusions**: Partial ossicular discontinuity repair with bone cement can restore HF ossicular function and audiometric outcomes, suggesting some HF hearing losses are surgically correctable.

**Professional Practice Gaps and Educational Needs**: Our understanding of the impact of partial ossicular discontinuity repair on high frequency ossicular function and audiometric outcomes remains poor. There is a need to understand how joint reestablishment influences the mechanics of the middle ear and how this relates to clinical outcomes.

**Learning Objectives**: To study the mechanical effects of partial ossicular discontinuity and repair in cadaveric temporal bones, and correlate outcomes with clinical cases of surgically repaired partial ossicular discontinuity.

**Desired Result**: Repair of partial ossicular discontinuity experimentally and clinically with a hard drying substance will result in restoration of middle ear function and therefore audiometric outcomes, which may warrant further evaluation of high frequency conductive hearing loss in patients as it may be surgically correctable.

# Level of Evidence: V

IRB: UMass Chan Medical School #H00020062

# Acute Complicated Mastoiditis Risk Factors and Presentation in National Emergency Departments

Lisa Zhang, MD; Robert J. Macielak, MD; Oliver F. Adunka, MD; Yin Ren, MD, PhD

**Objective:** To determine patient and hospital risk factors for acute complicated mastoiditis

Study Design/Setting: Retrospective review of the National Emergency Department Sample (NEDS) database from 2020-2021

**Patients:** A total of 1,351 (86%) patients presented with a primary diagnosis of acute mastoiditis without complications (H70.00x) and 226 (14%) patients with acute complicated mastoiditis (H70.01x, H70.8x, H70.09x, H70.2x). Patient demographics and hospital characteristics were included.

Main Outcome Measures: Patient disposition and hospital characteristics for those diagnosed with acute mastoiditis with and without complications.

**Results:** Patients diagnosed with acute complicated mastoiditis were younger (31.0 [SD 26] vs 40.3 [SD 23.6] years, p<0.0001), with twice as many pediatric patients (40% vs 20%, p<0.001). These patients were significantly more likely to be admitted (70% vs 56%, p<0.0001) and had longer lengths of stay (7 vs 3.7 days, p<0.001). One patient diagnosed with complicated mastoiditis died during their inpatient stay (1% vs 0%, p=0.04). There were no differences in rates of discharge home following inpatient admission between the cohorts (p>0.05). Multivariable logistic regression with all patient demographics demonstrated age to still be significantly predictive of mastoiditis with complications (OR 0.98 [0.976-0.988]). Trauma and teaching hospitals had significantly higher rates of acute complicated mastoiditis (20% vs 9%, p<0.001; 15% vs 9%, p=0.04, respectively). Complicated mastoiditis patients had higher inpatient (\$59,362 vs \$25,968, p<0.001) and total hospitalization costs (\$98,329 vs \$43,666, p<0.001). The most common associated diagnoses with complicated mastoiditis included suspected coronavirus-19 (COVID-19) infection (20%), hypertension (18%), nicotine dependence (16%), and type 2 diabetes mellitus (12%).

**Conclusions:** Younger age is the most predictive patient factor for acute complicated mastoiditis. Higher rates of diagnosis at trauma and teaching hospitals may be due to a higher index of suspicion and access to resources.

Professional Practice Gap & Educational Need: To identify patient and hospital risk factors associated with acute complicated mastoiditis in emergency departments on the national level.

Learning Objective: Learners should be able to identify the most predictive risk factor for complications associated with acute mastoiditis.

**Desired Result:** We hope to improve awareness for increased risk of complications associated with acute mastoiditis in the younger population, especially in pediatric patients.

Level of Evidence - NA

#### Standardized Cognition Scores Predict Performance on an Auditory Working Memory Task

Nathan G. Sattah, BA; Sherri L. Smith, AuD, PhD; Erin Hernon, AuD Hannah Martin, MD; Kristal M. Riska, AuD, PhD

**Objective:** Investigate the relation between cognitive function and performance on an auditory working memory task in older adults with hearing loss.

Study Design: Prospective cohort study.

Setting: Single-institutional, academic center.

Patients: Patients aged 60 or older diagnosed with sensorineural hearing loss (ICD-10 codes H90.3, H90.5, H91.1).

**Interventions:** National Institute of Health Toolbox Cognition Battery (NIHTCB), abbreviated Word Auditory Recognition and Recall Measure (aWARRM).

Main Outcome Measures: NIHTCB age-adjusted standard scores, aWARRM recall score.

**Results:** 66 participants were included (43 (65.2%) females, mean age of  $71.2 \pm 5.9$  years, mean pure tone average of  $27.9 \pm 6.4$  dB HL). The mean NIHTCB age-adjusted standard score was  $106.4 \pm 13.1$  and the mean aWARRM recall score as  $63.6\% \pm 13.6\%$ .

Higher aWARRM recall scores were significantly correlated with higher picture vocabulary (r = 0.30, p < 0.05), oral reading recognition (r = 0.28, p < 0.05), list sorting working memory (r = 0.42, p < 0.01), picture sequence memory (r = 0.29, p < 0.05), and total composite scores (r = 0.43, p < 0.01). Linear regression adjusting for sex, race, and hearing level demonstrated that higher performance on list sorting working memory (F = 2.502, p < 0.05) and higher total composite scores (F = 3.122, p = 0.01) were independently associated with higher aWARRM recall scores.

**Conclusions:** Auditory working memory is positively correlated with standardized measures of receptive and expressive language, as well as episodic and working memory. Performance on a visual-and-auditory list sorting working memory task and on the NIHTCB overall predicted performance on an auditory-only working memory task in older adults with hearing loss. These results may provide additional construct validity to the use of the aWARRM as a measure of auditory working memory.

**Professional Practice Gap & Educational Need:** The aWARRM is a useful tool for evaluating auditory working memory in older adults with hearing loss, but research is needed to compare performance on this task with other measures of cognition in order to assess its potential for clinical use.

Learning Objective: Understand the association and impact of cognition on an auditory working memory task, specifically in adults with hearing loss.

**Desired Result:** Demonstrate that scores on a validated cognition battery are correlated with and predictive of scores on an auditory working memory task.

Level of Evidence – Level III.

Indicate IRB or IACUC: Approved. Duke Health IRB, Pro00113750.

#### Seasonal Variation in Autoimmune Inner Ear Disease: A Preliminary Study

Sriprachodaya Gaddam, BS; Adam Gardi, BS; Philip Maxwell, MD; Robert T. Sataloff, MD, DMA

**Objective:** To determine whether there is seasonal variation in the audiogram data of patients with autoimmune inner ear disease (AIED).

Study design: Retrospective chart review.

Setting: Academic.

Patients: 141 adult patients with a diagnosis of AIED from January 2010 to June 2023 were included.

Intervention: Audiometry.

**Main outcome measures:** For patients' better- and worse- hearing ears, as defined by audiogram metrics, pure tone average (PTA), high-frequency PTA (HFPTA), low-frequency PTA (LFPTA), and average word discrimination score (WDS) were calculated for each season.

**Results:** For better-hearing ears, PTA was worse in the summer compared to the winter (p = 0.04), HFPTA in the spring and summer was worse than in the winter (p = 0.047 and p = 0.03, respectively) and LFPTA in spring (p = 0.04) and summer (0.04) was worse than in the winter. For worse-hearing ears, only LFPTA was worse in the spring (p = 0.01), summer (p = 0.0003), and autumn (p = 0.005) than the winter. WDS showed no significant differences across seasons. However, more patients were found to have "flares," sudden decreases in hearing or increases in subjective symptoms, as indicated by patient complaints and prednisone prescriptions, in the winter compared with other seasons. Control patients showed no seasonal variation. Paired t-tests, repeated measures ANOVA, and Bonferroni post-hoc tests were used.

**Conclusion:** AIED audiogram changes and flares may be influenced by complex interactions between environmental factors. The implications of seasonal factors as a consideration in the symptoms and treatment of AIED warrant further study.

**Professional Practice Gap & Educational Need**: The pathogenesis of AIED is currently unclear. However, its characterization as an autoimmune disease suggests that environmental factors could influence clinical status as previous studies have shown seasonality in other autoimmune conditions (multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis). Hearing fluctuations in AIED may be influenced by seasonality. Evidence of a seasonal association may lead to better understanding of AIED flares and subsequent advancements in evaluation and treatment.

Learning Objective: To determine whether there is seasonal variation in the onset, progression, severity, and treatment response of AIED.

Desired Result: Enhance our understanding of the seasonality of AIED.

**Level of Evidence** – Level IV

**Indicate IRB or IACUC:** Exempt, Protocol Number 2303009771, Drexel University College of Medicine (Exemption Granted 3/22/2023)

# Patient-Reported Outcomes after Cochlear Implantation in U.S. Military Veterans

Douglas J. Totten, MD, MBA; Hunter L. Elms, MD; Abdul Saltagi, MD; Karen Libich, AuD David B. Pisoni, PhD; Evan C. Cumpston, MD; Rick F. Nelson, MD, PhD

Objective: To assess patient-reported hearing outcomes in United States Military Veterans after cochlear implantation

Study Design: Retrospective review

Setting: Tertiary VA Medical Center

Patients: U.S. Military Veterans receiving cochlear implantation from May 2019 through March 2024

Interventions: Cochlear implantation, audiologic rehabilitation

**Main Outcome Measures:** Measures included pre-operative and six month post-operative 12 item Speech, Spatial, and Qualities of Hearing Scale (SSQ12) responses, 12 month post-operative International Outcome Inventory for Hearing Aids modified for Cochlear Implantation (IOI-CI) responses, and 12 month CI usage. Change in scores were assessed with Student's T-test. CI usage was also assessed. SSQ12 and IOI-CI responses were also compared to AzBio sentence and CNC word scores.

**Results:** 75 U.S. Military Veterans (89 ears) were implanted from May 2019 through March 2024. All patients were male, average age at implantation was 74 (standard deviation 9) years, and 73 (97%) patients were white. Average pre-operative SSQ12 score was 3.5 (2.0) while SSQ12 average was 6.1 (1.9) six months postoperatively. Mean IOI-CI score 12 months postoperatively was 29 (4) out of a maximum of 35. Patients used CIs at an average of 12 (4) hours daily 12 months after implantation. There was little correlation between 6 month SSQ12 and AzBio sentence scores (R-squared=0.10) or CNC word scores ( $R^2$ =0.06) or between 12 month IOI-CI scores and AzBio sentence scores ( $R^2$ =0.004) or CNC word scores ( $R^2$ =0.006).

**Conclusions:** U.S. Military Veterans report subjective CI benefit in addition to previously-documented improvement in objective scores. SSQ12 scores increase as expected six months after cochlear implantation. Both SSQ12 and IOI-CI scores indicate good subjective outcomes in these patients. Subjective outcomes do not necessarily correlate with objective audiometric testing in this population.

**Professional Practice Gap & Educational Need:** U.S. Military Veterans historically have had limited access to cochlear implantation. Furthermore, few studies have examined CI outcomes in this population. Even fewer have examined subjective patient outcomes. This study shows that U.S. Military Veterans derive substantial subjective benefit from CI and that this benefit is not necessarily correlated with objective outcomes.

Learning Objective: U.S. Military Veterans report subjective benefit after cochlear implantation

Desired Result: U.S. Military Veterans have improvement in subjective hearing outcomes after cochlear implantation

Level of Evidence – Level IV

Indicate IRB or IACUC: Richard L. Roudebush VA Medical Center IRB # 13588 (Approved 11/30/2021)

#### Temporal Trends, Regionalization, and Total Cost Analysis of Meniere's Disease Management in the United States

Ayush G. Iyer, BS; Rance J. T. Fujiwara, MD, MBA; Walter Kutz, MD

**Objective:** This study aims to describe patient demographics and to analyze how regionalization of care to academic centers, total admissions costs, and procedural trends in the inpatient management of Meniere's disease (MD) changed from 2002-2021.

Study Design: Cross-sectional analysis

Setting: National Inpatient Sample, 2002-2021

Patients: 30,838 inpatient admissions with a primary diagnosis of Meniere's disease

**Interventions:** Rates of admission and total inflation-adjusted admission cost trends stratified by academic vs. nonacademic regionalization, rates of patients undergoing endolymphatic sac decompression (ESD) vs. other inner ear procedure (labyrinthectomies, vestibular nerve sections, etc.)

**Main Outcome Measures:** Patient- and hospital-level characteristics of inpatient MD admissions were first described and subsequently used as covariates to perform a multivariate regression analysis, gauging their association with total adjusted admission cost and length of stay. Adjusted total admissions costs and rates of procedures additionally plotted temporally.

**Results:** The majority of patients were white (61.6% [SE = 1.4%]), female (66.9% [SE = 0.7%]), above the age of 65 (55.0% [SE = 1.0%]), and had an Elixhauser comorbidity index of 0-1 (49.3% [SE = 0.7%]). There was a significant decrease in the weighted number of admissions for Meniere's disease from 2503 (SE = 378.3) in 2002 to 640 (SE = 64.9) in 2021. Starting in 2012, there was a noticeable decline in admission to non-academic centers, with 72.8% (SE 4.6%) of admissions to academic centers in 2021. Adjusted admissions cost appeared to increase independent of the teaching status of the hospital (*b* = 35.35 USD [30.91, 39.58], *p* < 0.001 for academic and *b* = 67.84 USD [64.17, 71.51], *p* < 0.001 for nonacademic). While the proportions of patients receiving an ESD stayed relatively the same throughout the study period, there was a decrease in all other inner ear procedures from 17.38% (SE = 10.1%) in 2002 to 6.25% (SE = 2.3%) in 2021. It was found that patients between 40 and 65 (*b* = 6610.75 USD [487.00, 12734.51], *p* = 0.03), admission to hospitals in the southern United States (*b* = 2360.17 USD [692.71, 4027.64], *p* = 0.01, and other inner ear procedures (*b* = 5491.10 USD [714.22, 10267.99], *p* = 0.02) were significantly associated with higher admission costs. Patients who received ESDs were predicted to have shorter admissions (*b* = -0.782 days [-1.197, -0.367], *p* < 0.001).

**Conclusions:** There was a significant decrease in total Meniere's disease admissions. In conjunction, there was an overall increase in regionalization to academic hospitals. When these trends are taken in the context of an observed increase in inflation-adjusted admissions cost over time, it is vital that future endeavors be focused on analyzing resource allocation and overall cost-drivers in the management of Meniere's disease.

**Professional Practice Gap & Educational Need:** There is a paucity of epidemiological data in regard to MD management patterns over a prolonged period of time. This study aims to shed light on how national practice patterns have changed over time to better inform MD management guidelines.

Learning Objective: Determine regionalization, total admissions cost, and procedural trends in the inpatient management of MD

**Desired Result:** Attendees should understand that MD care is becoming increasingly specialized and that this may be associated with the general shift away from more destructive surgical management methods and rising admissions costs.

Level of Evidence: Level V

# Utility of Intrathecal Fluorescein in Transmastoid Repair of Temporal Encephaloceles

Keshav V. Shah, BS; Kevin Wong, MD; Randall Harley, MD; Tiffany Hwa, MD Michael J. Ruckenstein, MD; Douglas C. Bigelow, MD

**Objective:** To evaluate preoperative fluorescein utility for transmastoid repair of lateral skull base encephaloceles and identify predictors for fluorescein identification intraoperatively.

Study Design: Retrospective case-control study of patients before and after implementing routine intrathecal fluorescein administration for transmastoid encephalocele repairs.

Setting: Single academic medical center

**Patients:** Consecutive patients with temporal lobe encephaloceles repaired via transmastoid approach from October 2012 to October 2024.

**Interventions:** Electronic medical records of qualifying patients were searched for relevant demographics, diagnostic workup, disease characteristics (defect number, size, and location), and intraoperative and postoperative outcomes. Analysis incorporated the independent t-test, Mann-Whitney U test, and Fischer's exact test.

Main Outcome Measures: Intraoperative fluorescein identification; fluorescein complications; encephalocele recurrence rates.

**Results:** 38 patients met inclusion criteria. Mean age was 59.8 years old (SD 11.9 years), and 23 (60.5%) patients were female. Mean BMI was 35.8 kg/m<sup>2</sup> (SD 8.7 kg/m<sup>2</sup>). Fluorescein was administered in 12 cases (31.6%) and intraoperatively detected in 6 (50%). Tegmen defects were identified in all cases. The most common fluorescein dose was 10 mg. No intraoperative or immediate postoperative complications were associated with fluorescein administration. There was no significant difference in recurrence rates between patients who received and did not receive intrathecal fluorescein (0% vs 11.5%, p=0.54). There were no significant differences in gender, BMI, or defect location, size, or number on the likelihood of fluorescein identification intraoperatively.

**Conclusions:** Routine preoperative intrathecal fluorescein administration does not appear to improve recurrence rates for transmastoid repair of lateral encephaloceles, but given its relatively safe risk profile, it can supplement the identification of the leak source in many cases. Higher-powered studies are warranted to explore its utility in specific circumstances, such as multiple defects or revision surgeries.

**Professional Practice Gap & Educational Need:** Given the potentially serious complications and quality of life concerns related to unrepaired encephaloceles, continued empiric review of the safety and efficacy of adjunctive surgical techniques, such as fluorescein administration, is critical to improving patient safety, surgical outcomes, and quality of care.

**Learning Objective:** 1) Assess the safety and efficacy of fluorescein administration during transmastoid repair of temporal lobe encephaloceles and 2) recognize patients who may benefit from intraoperative fluorescein administration.

**Desired Result:** Refinement of the transmastoid approach to temporal lobe encephalocele repair with regards to the potential incorporation of fluorescein based on patient and disease characteristics.

Level of Evidence: IV – Retrospective case-control study

Indicate IRB or IACUC: University of Pennsylvania Institutional Review Board (#856621)

# Increased Risk of Cerebrovascular Accident After Sudden Sensorineural Hearing Loss

Mihai Bentan, BS; Daniel Long, MD; Lawrance Lee, MD; Brendon K. Warner, MD Arman Saeedi, MPH; Nauman F. Manzoor, MD

**Objective:** To analyze increased risk of subsequent cerebrovascular accident (CVA) after sudden sensorineural hearing loss (SNHL) event.

Study Design: Cohort analysis using aggregate data from TriNetX Research Network.

Setting: TriNetX Research Network

**Patients:** Patients diagnosed with either ICD-10 code H91.2 (sudden idiopathic hearing loss) or ICD-10 code H83.0 (labyrinthitis) with subsequent development of ICD-10 codes: I60-I63 (CVA) compared to development of CVA in cohorts without diagnosis of hearing loss and cohorts with diagnosis of non-sudden SNHL (ICD-10 codes H90.3, H90.4, H90.5).

**Main Outcome Measures:** Absolute risk (AR) and relative risk (RR) of experiencing a CVA (defined by ICD-10 codes I60-I63).

**Results:** After propensity score matching, a total of 183,178 patients were analyzed to compare the impact of sudden SNHL on the risk of CVA compared to a cohort with no hearing loss. The sudden SNHL cohort demonstrated a significantly higher risk of CVA (3.65%) compared to the control (2.63%, AR: 1.02, 95% Confidence Interval [CI] 0.86-1.18, p<0.05) with RR of 1.39 (95% CI 1.32-1.46, p<0.05). Similarly, after propensity score matching, a total of 264,974 patients were analyzed to compare the impact of sudden SNHL on the risk of CVA against patients with non-sudden SNHL. The sudden SNHL cohort demonstrated a significantly higher risk of CVA (4.87%) compared to the non-sudden SNHL cohort (2.80%, AR: 2.06, 95% CI 1.92-2.21, p<0.05) with RR of 1.74 (95% CI 1.67-1.81, p<0.05).

**Conclusion:** Sudden SNHL confers a higher risk of subsequent CVA compared to patients with non-sudden SNHL as well as patients without diagnosis of hearing loss. Further prospective studies are needed to delineate this finding as a risk factor for CVA.

**Professional Practice Gap & Educational Need:** Professionals need to identify a higher likelihood of subsequent CVA in patients with SSNHL. This has implications for risk stratification and referrals for optimal preventative strategies.

Learning Objective: Understand higher risk of subsequent CVA after a SSNHL event.

Desired Result: Highlight need for identification and further investigation of SSNHL as a risk factor for CVA

Level of Evidence: Level III

# Comparing Cochlear Implant Quality of Life Outcomes in Patients Who Qualify in Quiet vs Noise

Amy L. Ho, BA; Donald Tan, MD; Rance J.T. Fujiwara, MD, MBA J. Walter Kutz, MD; Jacob B. Hunter, MD

**Objective:** To assess differences in improvements in Cochlear Implant Quality of Life-35 Profile scores for patients who qualify in quiet versus in noise only.

Study Design: Retrospective cohort study

Setting: Tertiary academic institution

Patients: 91 cochlear implant patients with peri-operative CIQOL-35 surveys

Interventions: Cochlear implantation

**Main Outcome Measures:** Pre-operative and post-operative CIQOL surveys were administered to patients at the time of their initial CI evaluation, as well as subsequent follow-up appointments. Patients with preoperative AzBio <60% only in multitalker babble comprised the noise-qualifying group and were compared to those with AzBio in Quiet <60%.

**Results:** Of 91 patients undergoing cochlear implantation, 57 patients completed pre- and post-operative surveys. 74 qualified in quiet, while 17 qualified in noise only. The mean age of the quiet- and noise-qualifying groups was 64.8 years (SD 15.8) and 69.0 years (SD 10.1), respectively. No statistically significant differences in mean CIQOL-10 global scores or the six CIQOL domains were appreciated between the quiet- and noise-qualifying groups, either preoperatively or postoperatively. Baseline preoperative CIQOL-10 global scores in the quiet- and noise-qualifying groups were 38.2 (SD 10.3) and 39.0 (SD 6.4). Post-operative mean CIQOL-10 global scores was lower in patients who only qualified in noise, 43.6 (SD 5.6) versus 47.3 (SD 10.6) but did not meet statistical significance (p=0.19). Amongst patients with pre- and post-operative data (n=57), there was a significant increase in correlated samples CIQOL with a mean difference of 8.5 (p <.0001). There were no statistically significant predictors of change in CIQOL after CI on multivariate analysis. Relative to the noise-qualifying group (n=7), patients in the quiet-qualifying group (n=50) experienced greater increases in emotional (b=9.3 [95% CI -8.4 to 27.1]), environmental (b=8.8 [95% CI -12.8 to 30.4]), and social (b=12.7 [95% CI -5.7 to 31.2]) domains, though these differences were not statistically significant. Patients in the noise-qualifying group experienced a greater though nonsignificant increase in listening effort (b=10.9 [95% CI -6.2 to 28.0], p=0.2).

**Conclusions:** Decision to proceed with CI was associated with increased CI specific quality of life, and the benefit was not different in patients who qualified in quiet versus those who only qualified in noise.

**Professional Practice Gap & Educational Need:** This study assessed whether patients qualifying in quiet vs. noise-only conditions for cochlear implantation had differences in their improvements in patient-reported qualify of life measures.

Learning Objective: To investigate the patient reported quality of life outcomes for cochlear implant candidates who do not qualify in the quiet setting.

Desired Result: To improve patient counseling on expected outcomes with CI.

Level of Evidence - IV

# **Evaluating Optimal Bone-Anchored Hearing Aid Placement Using 3D-Modeling Software**

Jason K. Adams, MD; Maura K. Cosetti, MD; George Wanna, MD, MHCM Zachary G. Schwam, MD; Enrique Perez, MD

**Objective:** There has been limited evaluation of the utility of 3D-modeling software in determining optimal bone-anchored hearing aid (BAHA) implant placement, especially in BAHA implants that employ a floating-mass transducer. This study sought to assess surgeon preferred BAHA implant location using 3D-modeling software in patients that have previously undergone BAHA implant surgery.

Study Design: Retrospective cohort study

Setting: Tertiary, specialty clinic

**Patients:** Adults or children with prior transcutaneous bone-anchored hearing aid (BAHA) implantation with floating mass transducer and pre-operative computed tomography scan

Interventions: Three-dimensional modeling with placement of BAHA

Main Outcome Measures: Preferred and possible BAHA locations

**Results:** 29 patients (mean age 44, range 8-74, n=17 female, n=12 left side, n=11 prior ipsilateral mastoid surgery) underwent BAHA implant with 19 (65.5%) in the mastoid, 10 (34.4%) in the retrosigmoid space, and none overlying the middle cranial fossa. Using 3D-modeling software, three independent reviewers' preferred location matched to surgical placement in 72.6% of cases. When asked to identify possible appropriate locations these reviewers matched to surgical placement in 95.2% of cases. Inter-rater reliability (IRR) amongst reviewers for preferred location was minimal (Kappa ( $\kappa$ ) = 0.286, p<0.0001) whereas possible placement location was substantial ( $\kappa$ =0.795, p<0.0001). Notably, 37% of actual cases used lifts, 31% had sigmoid exposure, and 34% had dural exposure. In reviewer preferred placement, rates of lift use, sigmoid exposure, and dural exposure were 8%, 5%, and 6% respectively.

**Conclusions:** IRR for possible BAHA location agreement was substantial with a percent correct rate of 95.2%. 3D-modeling software is useful in identifying preferred BAHA implant locations that minimize use of lifts, or exposure of the sigmoid or dura. Further research is needed to prospectively study whether 3D-modeling software can be used preoperatively to accurately determine optimal implant location.

**Professional Practice Gap & Educational Need:** The role of 3D-modeling software prior to BAHA has not been well established within the field of otology.

Learning Objective: Learners will recognize the utility of evaluating BAHA implant location using 3D-modeling software.

**Desired Result:** Improve understanding of the role of 3D-modeling software in evaluation of patients undergoing BAHA implant surgery.

Level of Evidence – Level IV

Indicate IRB or IACUC: Icahn School of Medicine at Mount Sinai IRB, 23-01194

#### Real-World Analysis of Meniere Disease: Treatment Patterns, Surgical Trends, and Associated Comorbidities Using TriNetX Data

# Huseyin Isildak, MD

Objective: This study addresses four key questions about Meniere disease (MD) utilizing TriNetX data:

- 1. What are the most used medications for patients with MD?
- 2. Which otologic surgeries are most frequently performed?
- 3. Are there demographic differences between surgical and non-surgical patients?
- 4. What are the common comorbidities associated with MD?

Study Design: Retrospective analysis using TriNetX, a global network of healthcare organizations.

Setting: Academic and non-academic.

Patients: Patients with MD (ICD-10 CM, H81.0-9).

Interventions: N/A

Main Outcome Measures: This retrospective analysis of Meniere patients highlights key medical treatments, surgeries, demographic differences, and associated comorbidities.

**Results:** A total of 117,059 patients were identified (F: 60.91%, M: 34.97%). The most common medications used for Meniere disease included steroids (64%), benzodiazepines (55%), diuretics (52%), and antacids (49%). Surgical interventions comprised cochlear implantation (1,314 pts, 1%), endolymphatic sac operation (1,219 pts, 1%), labyrinthectomy (407 pts, 0.3%), and vestibular nerve section (138 pts, 0.1%). Demographically, 34.62% of non-surgical patients were male compared to 44.29% of surgical patients, and 8.29% of non-surgical patients were Asian, while only 1.55% of surgical patients were Asian. Common comorbidities included musculoskeletal disorders (69%), metabolic disorders (56%), hypertension (50%), anxiety/depression (48%), GER (35%), sleep disorders (28%), thyroid disorders (25%), vasomotor/allergic rhinitis (22%), DM (20%), migraine (19%), asthma (15%), and melanoma (6%). **Conclusions:** Corticosteroids, benzodiazepines, and diuretics were the most prescribed in patients with MD. Nearly half of the patients also used antacids or gastric medications. Cochlear implantation and endolymphatic sac surgery were the most frequent surgical interventions. Surgical patients had a higher percentage of males and a lower percentage of Asians compared to non-surgical patients. Comorbidities noted as musculoskeletal, metabolic, mental health, and hypertensive.

Additionally, GER, sleep disorders, and thyroid disorders were prevalent.

**Professional Practice Gap & Educational Need:** Even though there are recent practice guidelines for Meniere's disease, there is no standardized treatment for the condition. Additionally, there is a need to recognize the associated comorbidities in Meniere patients. Some of these comorbidities, or the medications used for them, may shed light on better understanding the disease through a cause-and-effect relationship.

**Learning Objective:** To identify the most common medical treatments and surgical procedures for Meniere disease, and to explore demographic differences between surgical and non-surgical patients. This study also aims to examine the comorbidities frequently associated with Meniere disease.

**Desired Result:** By recognizing the demographic patterns in surgical and non-surgical patients and understanding the common comorbidities associated with Meniere's disease, we may gain valuable insights into the disease through a cause-and-effect relationship.

Level of Evidence - Level IV

#### Predictive Factors for Facial Nerve Palsy in Malignant Otitis Externa Using TriNetX Data

#### Huseyin Isildak, MD

**Objective:** This study aims to determine whether gender, ethnicity, biochemical markers, and comorbidities are predictive factors for facial nerve palsy (FNP) in patients with malignant otitis externa (MOE).

Study Design: Retrospective analysis using TriNetX.

Setting: Academic and non-academic.

**Patients:** A total of 12,751 patients with MOE (F:48.91%, M:46.88%; 68.8% not Hispanic or Latino (H/L), 13.02% H/L) and 719 patients with MOE and FNP (F:35.05%, M:62.86%; 67.74% Not H/L, 17.66% H/L).

#### Interventions: N/A

Main Outcome Measures: This study examines the predictive factors for FNP, including demographics, biochemical markers and comorbidities.

**Results:** Statistical analyses revealed a significant association between male and FNP ( $p \approx 4.65e-15$ ). 13.02% of the MOEonly group were H/L, compared to 17.66% in the MOE and FNP group, indicating a significant association (z-score = 3.19, p = 0.0014. Additionally, biochemical markers such as calcium, creatinine, glucose, urea nitrogen, albumin, aPTT, iron, ESR, and lactate were identified as statistically significant, with albumin and urea nitrogen emerging as the most notable ( $p < 10^{-32}$ ). Hypertension (odds ratio [OR] = 3.72,  $p = 6.95 \times 10^{-55}$ ) and chronic kidney disease (OR = 3.12,  $p = 1.44 \times 10^{-49}$ ) were more prevalent in patients with FNP. Electrolyte imbalances (OR = 2.59,  $p = 4.29 \times 10^{-36}$ ), malnutrition (OR = 3.44,  $p = 1.61 \times 10^{-35}$ ), and altered mental status (OR = 2.34,  $p = 7.34 \times 10^{-15}$ ) were significant comorbidities. While dizziness was also significant (OR = 1.58,  $p = 3.99 \times 10^{-8}$ ), migraine and headaches did not show statistically significant differences.

**Conclusions:** FNP was noted in 6% of MOEs. Male and H/L is a predictive factor. Monitoring blood glucose, albumin levels, and ESR may aid in predicting FNP in MOE patients. Comorbidities such as hypertension and kidney disease may be associated with higher risk for FNP.

**Professional Practice Gap & Educational Need:** Understanding predictive factors for facial nerve palsy in MOE can enhance clinical assessments and guide management strategies, particularly in patients with comorbidities.

Learning Objective: To identify key predictive factors for facial nerve palsy in patients with MOE and to explore the associated comorbidities that may inform clinical outcome.

**Desired Result:** By recognizing the predictive factors and associated comorbidities in patients with MOE, healthcare providers can develop targeted strategies for monitoring and intervention, potentially reducing the incidence of facial nerve palsy.

Level of Evidence: Level IV

#### Music Perception in Children with Cochlear Implants: A Systematic Review and Meta-Analysis

Lauren R. McCray, BS; Erin E. Briggs, BS; Shaun A. Nguyen, MD Robert F. Labadie, MD, PhD; Clarice S. Clemmens, MD; David R. White, MD

**Objective:** Our goal is to assess quantitative measures of music perception in the pediatric cochlear implant (CI) population compared to children with normal hearing.

**Data sources:** CINAHL, Cochrane Library, PubMed, and SCOPUS were searched for English-language studies published from inception through September 11<sup>th</sup>, 2024, with the following keywords: cochlear implant, hearing aid, and music.

**Study selection:** Cohort and cross-sectional studies related to music perception in pediatric CI patients under 18 years old were included. Studies involving hearing aids, adult patients, or qualitative data only were excluded.

**Data extraction:** Two authors extracted and reviewed data, and disagreements were resolved with a third party if needed. The risk of bias was assessed according to the Risk of Bias in Non-randomized Studies - of Exposure for cohort studies and the Joanna Briggs Institute critical appraisal checklist for cross-sectional studies.

**Data synthesis:** Primary outcome measures included continuous measures (mean) and proportions (%) with 95% confidence intervals (CI).

**Conclusions:** Twenty-two studies (n = 758) pertaining to music perception in the pediatric CI population were included. The mean age was 9.3 for the CI group and 8.9 for the control group. The average age of implantation was 3.2 years, with an average of 5.9 years' experience. There were significant differences in accuracy with identifying music emotion (72.9% vs. 77.3%; p = 0.04) and melody recognition (62.3% vs. 88.8%; p < 0.0001) in CI users compared to controls. Average accuracy for timbre recognition (37.3% vs. 64.6%) and rhythm recognition (55.4% vs. 94.8%) were also reported for children with CIs and the control population, respectively; however, there was only one study that measured these outcomes for the control group. Thus, we recommend further research on this topic and patient counseling regarding these findings.

**Professional Practice Gap & Educational Need:** It is important to counsel patients and their families regarding music perception with a CI.

Learning Objective: To describe the differences in music perception in pediatric CI users compared to children with normal hearing.

**Desired Result:** Our aim is to improve quality of life in the pediatric CI population by increasing awareness of music perception among otolaryngologists and audiologists interacting with these patients.

Level of Evidence: Level III

# Exploring Otological Comorbidities of Tinnitus in the U.S. Population

Sunil Shenoy, BA; Cynthia Tsang, BS; Romina Mirshahi, MD; Saharnaz Nedjat, MD, PhD Mehdi Abouzari, MD, PhD; Hamid R. Djalilian, MD

**Objective:** To document presence and extent of otological comorbidities in patients with tinnitus.

**Methods:** Retrospective analysis of demographic, otological symptoms, and audiometric data from the National Health and Nutrition Examination Survey (NHANES) Database between 1999 and 2004.

**Results:** A total of n=6,509 patients were included with a mean age of 53.9 and 50.2% female. Among demographic measurements, participants who reported having tinnitus were significantly older than healthy individuals (OR=1.26, 95% CI: 1.12-1.42, p<0.001), and men were more likely than women to suffer from tinnitus (OR=1.18, 95% CI: 1.04-1.33, p=0.007). No significant difference in BMI was evident (p=0.069). Major hearing loss (OR=4.0, 95% CI: 3.08-5.23, p<0.001) and dizziness (OR=3.06, 95% CI: 2.66-3.53, p<0.001) had the strongest associations with tinnitus among the otological symptoms assessed. Neck pain (OR=1.93, 95% CI: 1.69-2.22, p<0.001) and migraine (OR=1.45, 95% CI: 1.25-1.68, p<0.001) demonstrated a comparatively milder increased likelihood of tinnitus presence. Among a subpopulation of the cohort (n=3,022), those with tinnitus were more likely to endorse a recent sinus problem (p<0.001) and recent otalgia (p<0.001) compared to non-tinnitus patients. Otoscopy exam data among this subset also identified collapsing ear canal (p=0.031) as a significant factor in tinnitus presence, while cerumen impaction (p=0.796) was not significant.

**Conclusion:** Several otological symptoms including major hearing loss, dizziness, neck pain, and migraine are significant comorbidities in tinnitus patients. These findings provide a basis of potential etiologies of tinnitus and therapeutic targets for patients.

**Define Professional Practice Gap & Educational Need:** The pathophysiology and etiologies of tinnitus are not fully understood, with most cases being subjective. Identifying comorbidities allows for a better understanding of risk factors and potential causes of tinnitus. Further, these associations can help clinicians provide broader, comprehensive treatment strategies for patients' symptoms.

Learning Objective: To identify demographic factors and otological symptoms that impact presence of tinnitus in the United States population.

**Desired Result:** Informing otologists of tinnitus comorbidities to improve symptom management and identify patient populations at risk of tinnitus development.

Level of Evidence – III

#### Differences in Audiologic Healthcare Utilization by Race

Roy W. Qu, MD; Helen Xu, MD; Baishakhi Choudhury, MD

**Objective:** To identify patterns of audiologic healthcare utilization by race and subsequently identify barriers for patient populations with poor utilization in the United States.

**Study Design:** Cross-sectional study of the National Health and Nutrition Examination Survey (NHANES) from 2011 - 2012, 2015 - 2016, and 2017 - 2020.

Setting: Community-based setting in the United States.

Patients: Adults in the United States aged 20 years and older.

Main Outcome Measures: Hearing loss, time to last hearing test by a hearing specialist

**Results:** 11,120 participants aged 20 years and older, of which 9,206 had audiograms, were included for analysis. The cohort was 48.2% male, 15.4% Hispanic, 11.8% Black, 5.8% Asian, and 67.0% White and had an average age of 47.43 years. Whites were more likely to have hearing loss (22.0%, p < 0.001) compared to racial minorities: 13.4% in Hispanics, 12.7% in Blacks, and 14.5% in Asians. However, only blacks had lower odds of hearing loss (OR 0.44, p = 0.035) compared to whites after controlling for age, gender, health insurance, education, income-to-poverty ratio, access to routine healthcare, and length of time in the United States.

We assessed how recently participants had their hearing tested by a specialist. Hispanics (OR 2.06, p < 0.001) and Asians (OR 3.06, p < 0.001) had longer intervals since their last hearing test compared to whites. Blacks were more likely to have a recent hearing test compared to whites (OR 0.780, p = 0.003). On multivariate ordinal regression, less severe hearing loss (p = 0.003), better self-perceived hearing (p < 0.001), and shorter time in the United States (p < 0.001) were associated with a longer interval since their last hearing test. However, despite correcting for multiple confounders, Asians had a longer time since their last hearing test of whites (OR = 1.64, p = 0.004). Next, we identified factors associated with a longer time since the last hearing test in Blacks (p = 0.015) and Hispanics (p = 0.006), but hearing loss severity was not (Black, p = 0.433; Hispanic, p = 0.790). Lower hearing loss severity (p = 0.021), better self-perceived hearing (p < 0.001) and speaking a non-English language for most of the time in the household (OR 1.372, p = 0.007) were independently associated with a longer time to last hearing test for Asians. Speaking mostly Spanish at home was not associated with time to last hearing test for Asians. Speaking mostly Spanish at home was not associated with time to last hearing test for Asians.

**Conclusions:** Despite adjustments for hearing loss and other confounders, the time since last hearing test still differed by race, namely for Asian Americans. Addressing factors associated with seeing a hearing specialist, such as discordance between objective and self-perceived hearing loss and language barriers, may improve hearing health for racial minorities.

**Professional Practice Gap & Educational Need:** Data on audiologic healthcare utilization in racial minorities is underreported. Further knowledge on behaviors associated with differences in utilization may inform interventions to improve the rate of audiologic testing within each racial minority group.

Learning Objective: To identify factors associated with hearing testing in racial minorities.

**Desired Result:** Provide knowledge on differential audiologic healthcare utilization in racial minorities. Healthcare providers will be more aware of characteristics that affect rates of audiologic testing within each racial minority group. This will also encourage future research to explain the forces driving these differences.

Level of Evidence – Level IV

# Factors Influencing Emergency Department Revisits in Patients with Otologic Diagnoses

Joshua K. Kim, BS; Nathan G. Sattah, BA; Vincent M. D'Anniballe, MS; Eric J. Formeister, MD, MS

**Objective:** To investigate factors leading to revisits in patients presenting to the emergency department (ED) with otologic diagnoses.

Study Design: Retrospective cohort study.

Setting: Level I academic trauma center.

**Patients:** Patients who presented to the ED with otologic diagnoses (ICD 10 codes H60-H67, H70-H75) excluding dizziness or vertigo between January 2015 and June 2024. Patients were only included if the otolaryngology service was consulted during ED visit or admission.

Main Outcome Measures: Revisit to the emergency department within 30 days of initial presentation.

**Results:** In total, 971 patients were included with 523 (53.9%) males, a mean age ( $\pm$  S.D.) of 34.4 $\pm$ 26.6 years at diagnosis, and 853 (87.8%) English-speakers. Overall, 394 (40.6%) patients presented with suppurative or nonspecific otitis media, 271 (27.9%) with otitis externa, and 163 (16.8%) with mastoiditis or mastoiditis with complication. One-hundred fifty-three (5.8%) patients revisited the ED within 30 days. Bivariate analysis revealed that race, need for admission, total length of stay at index presentation, Elixhauser comorbidity burden, and smoking status correlated with ED revisit (all p<0.05). Patients with a higher comorbidity burden (OR=1.06, 95% CI=1.01-1.12, p=0.014) and current smokers (OR=2.20, 95% CI=1.32-3.66, p=0.002) were more likely to revisit. Of note, longer initial admission was associated with a lower risk of revisit (OR=0.95, 95% CI=0.90-0.98, p=0.018).

**Conclusions:** Patients who smoke and patients with a higher comorbidity burden were more likely to revisit the ED for otologic conditions, while longer stays following their initial presentation reduced revisits. Otologists consulting in the ED should be especially vigilant when treating smokers with complex medical histories, as these patients are at higher risk for complications and revisits.

**Professional Practice Gap & Educational Need:** Current smokers and patients with a high comorbidity index are not only more susceptible to otologic conditions but also require more complex follow-up and continued care. Studies are needed that investigate clinical and patient factors contributing to poorer outcomes in patients with otologic diagnoses.

**Learning Objective:** The audience will learn to risk stratify patients presenting to the ED with otologic conditions and to identify those at risk for ED revisit following otolaryngology evaluation.

**Desired Result:** Readers will gain insight into patient factors necessitating closer follow-up and more intensive interventions for otologic diagnoses.

Level of Evidence – Level III.

Indicate IRB or IACUC: Duke Health IRB, Determined Exempt Pro00116404.

## Postoperative Complications Related to Bone Conduction Hearing Devices: A Comprehensive Evaluation at a Single Institution

Ina A. Lee, MS; Ankita Patro, MD, MS; Michael W. Canfarotta, MD; Elizabeth L. Perkins, MD Kareem O. Tawfik, MD; David S. Haynes, MD; Marc L. Bennett, MD

**Objective:** 1) To comprehensively report our experience with postoperative complications from bone conduction hearing devices (BCHDs), and 2) to identify preoperative patient-related factors that differ among BCHDs.

Study Design: Retrospective cohort.

Setting: Tertiary academic practice.

Patients: 187 patients (114 adults, 73 children) who met criteria for BCHD.

**Intervention(s)**: Implantation with BAHA Attract (n=40), BAHA Connect (n=40), Osia (n=64), Ponto (n=17), or Bonebridge (n=26) between January 2018 and April 2024.

Main Outcome Measures: Postoperative complications, operative time, demographics, preoperative pure-tone average.

**Results:** Median age at implantation was lower for the Ponto (9y, IQR 7—67) and Osia (18y, IQR 12—47) compared to the Attract (33y, IQR 8—52), Connect (47y, IQR 15—60), and Bonebridge (49y, IQR 26—60). Gender, type of hearing loss, and preoperative air- and bone-conduction thresholds were equivalent among the devices (p>0.05). Postoperative infections were highest for the Connect (68%), followed by the Attract (45%), Osia (33%), Ponto (29%), and Bonebridge (8%) (p<0.001). Skin overgrowth was most prevalent with the Connect (25%) (p=0.002). Difficulties with magnet retention were more likely with the Bonebdrige (12%) and Osia (8%) than the Attract (0%) (p=0.012). Patient complaints of pain, bleeding, and decreased hearing were similar among the BCHDs (p>0.05). Of 10 BCHDs that were revised, 6 converted from Connect or Attract to Bonebridge or Osia; 1 converted from Osia to Bonebridge; and 3 were replaced with the same device. Median operative time was similar between the Osia and Bonebridge (p>0.05).

**Conclusions:** Despite issues with poor magnetization, active transcutaneous BCHDs had relatively lower rates of infection. Patients that underwent revision surgery were more likely to convert from a percutaneous to transcutaneous device.

**Professional Practice Gap & Educational Need:** While studies have compared postoperative complications with two BCHDs, a comprehensive assessment of all implants has not been reported. Moreover, we sought to assess if there were demographic differences that could steer patients and physicians to use of one device over another.

Learning Objective: To identify differences in preoperative characteristics and postoperative complications among BCHD.

**Desired Result:** Providers will have knowledge of the potential postoperative complications among multiple BCHDs which can help with patient counseling and identification of which BCHD may be the best fit for them.

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

Indicate IRB or IACUC: IRB Approved (230221, Vanderbilt University, approved on 2/2/2023)

#### The Evaluation of Cochlear Implantation Usage, Complications, and Speech Perception Outcomes in a Rural, Elderly Population

Austin B. Rue, BA; Gautham H. Budaraju, MEng; Hope E. Scherger, BS Gerhard W. Hill III, MD

**Objective:** Cochlear implantation (CI) is generally well tolerated in elderly populations. However, studies have shown that elderly patients may not experience speech perception improvements as dramatically as younger populations. Additionally, elderly patients may be at an increased risk of postoperative complications. Few studies have researched these topics in patients older than 80 years of age, and studies that have investigated this population have provided inconsistent results. The goal of this study is to investigate the audiologic outcomes, comorbidities, and usage of CI in patients aged 80 years and older, particularly in rural patient populations.

Study Design: Retrospective chart review.

Setting: Tertiary referral center that serves a large, rural population.

**Patients:** There were 127 participants in this study, which included all cochlear implant recipients aged 70 years or older who underwent CI at a tertiary referral center between 2/21/2014 and 4/3/2024.

**Interventions:** Data reflecting preoperative and postoperative speech perception scores, comorbidities, body mass index, postoperative complications, usage of cochlear implants, and years of life after surgery were extracted from the charts of participants. Data was analyzed as a whole, and data was compared between the age groups of 70 - 79 and over 80 years.

**Main Outcome Measures:** Improvements in CNC and AzBio scores, years of life after surgery, postoperative complications, rates of emergency department (ED) visits within 1 month of surgery, rates of explantation, and usage of cochlear implants at last follow-up visit.

**Results:** Patients aged 80 years or older had a lower increase in AzBio scores at 3 months after surgery (p < 0.01) but had similar improvements in speech perception scores 6 to 12 months after surgery when compared to those aged 70 to 79 years. Patients over the age of 80 years had a 1-year mortality of 7.7%, while patients aged 70 to 79 had a 1-year mortality of 1.25%, although this difference was insignificant. Rates of non-users at the last postoperative appointment and rates of complications were not different between the age groups. Patients aged 80 years or older were less likely to follow up after 1 year when compared to those aged 70 to 79 years (p < 0.01). Those over the age of 80 were also more likely to undergo explantation (p = 0.057) and to visit the ED after surgery (p = 0.070), but these results only approached significance. In all patients over the age of 70, those with a history of cardiovascular disease were more likely to visit the ED or need explantation (p < 0.05). Additionally, some comorbidities, such as cardiovascular disease, lung disease, and kidney disease predisposed patients of both age groups to smaller speech perception score improvements.

**Conclusions:** Many outcomes of CI were similar between age groups. However, special considerations must be made for patients over the age of 80, as results showed significantly decreased 1-year follow-up rates and near significant increases in 1-year mortality, explanation, and ED visits. Although CI enhances speech perception and provide patients with improved quality of life, elderly patients may require more comprehensive preoperative CI evaluation and counseling.

**Professional Practice Gap & Educational Need:** As the cochlear implant candidate population ages, more research is needed to identify risk factors and outcomes that are unique to elderly populations considering CI.

Learning Objective: Identify considerations for CI in rural, elderly populations that could influence preoperative evaluations and counseling.

**Desired Result:** Improved provider to patient communication about specific considerations for CI in the elderly population. Identify areas of potential improvement in CI outcomes in the elderly.

Level of Evidence – Level IV Indicate IRB or IACUC: IRB 024-333 approved by Baylor Scott & White Research Institute.
#### Changes in Patient-Reported Dizziness after Simultaneous Endolymphatic Sac Decompression and Cochlear Implantation in Patients with Meniere's Disease

Eric E. Babajanian, MD; Karl R. Khandalavala, MD; John P. Marinelli, MD; Brennan G. Olson, MD, PhD Christine M. Lohse, MS; Brian A. Neff, MD; James R. Dornhoffer, MD

**Objective:** To evaluate the impact of simultaneous cochlear implantation and endolymphatic sac decompression (ELSD) on dizziness in patients with advanced Meniere's disease.

Study Design: Historical cohort.

Setting: Tertiary academic medical center.

Patients: Patients with a preoperative diagnosis of Meniere's disease who underwent cochlear implantation from 2000 to 2024.

Interventions: Cochlear implantation, ELSD.

Main Outcome Measures: Patient-reported changes in dizziness severity and frequency compared between those who did and did not undergo simultaneous ELSD.

**Results:** 125 patients with preoperative dizziness secondary to Meniere's disease were eligible for study, including 19 (15%) who underwent simultaneous ELSD. In total, 17 (89%) and 2 (11%) of the 19 patients with simultaneous ELSD reported improvement and stability in dizziness severity, respectively; in comparison, 29 (27%), 57 (54%), and 20 (19%) of the 106 patients without any dizziness intervention reported improvement, stability, and worsening in dizziness severity, respectively (p<0.001). Likewise, 17 (89%) and 2 (11%) of the patients with simultaneous ELSD reported improvement and stability in dizziness frequency, respectively, whereas 25 (24%), 60 (57%), and 21 (20%) of patients without any intervention reported improvement, stability, and worsening in dizziness frequency, respectively, respectively (p<0.001).

**Conclusions:** In patients with Meniere's disease who experience ongoing dizziness but meet criteria for cochlear implantation, consideration of simultaneous ELSD may allow for improvements in dizziness severity and frequency.

**Professional Practice Gap & Educational Need:** Given the historical controversy surrounding the utility of ELSD in medically refractory Meniere's disease, and its more recent widespread adoption due to studies showing high rates of vertigo control, there is a need to better understand its impact on dizziness severity and frequency when performed concurrently with cochlear implantation.

Learning Objective: To describe dizziness-related outcomes after simultaneous cochlear implantation and ELSD in patients with Meniere's disease.

**Desired Result:** To provide guidance on patient counseling regarding the utility of simultaneous ELSD and cochlear implantation in the setting of advanced Meniere's disease.

Level of Evidence: III

Indicate IRB: Mayo Clinic IRB #22-000183

#### Audiometric Predictability of Photon-Counting Computed Tomography Findings in Otosclerosis

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**Objective:** To examine correlation between baseline audiometric data and surgical outcome with extent of otosclerotic plaque using preoperative high-resolution photon-counting computed tomography (PCCT).

Study Design: Retrospective cohort.

Setting: Large academic center.

Patients: Patients with otosclerosis who completed preoperative PCCT imaging.

Interventions: Observation, surgery.

Main Outcome Measures: Radiologic disease extent, pre- and postoperative audiometric data.

**Results:** 53 ears met inclusion criteria and were included in the analysis. The mean age at PCCT was 51 years (SD 14). The radial degrees of oval window involvement was not significantly associated with air-bone gap (p=0.3) or magnitude of the Carhart notch (p=0.8). Likewise, oval window plaque depth was not significantly associated with air-bone gap (p=0.2) or magnitude of the Carhart notch (p=0.6). Following CT, 22 ears underwent surgery. In this subset, extent of oval window involvement measured in angular degrees and plaque depth was not significantly associated with the postoperative change in air-bone gap or high-frequency thresholds.

**Conclusions:** Despite enhanced visualization of subtle abnormalities with PCCT imaging, extent of oval window otosclerotic plaque, measured in angular degrees and thickness, does not predict preoperative hearing or postoperative audiologic changes in patients with otosclerosis.

**Professional Practice Gap & Educational Need:** With the advent of high-resolution PCCT imaging, we need to better understand the potential audiometric impact of the degree of radiologically visualized disease.

Learning Objective: To describe the association of otosclerosis findings on high-resolution PCCT imaging with audiometry.

**Desired Result:** To provide guidance on the predictability of pre- and postoperative audiometrics based on high-resolution radiologic otosclerotic disease extent.

Level of Evidence: III

Indicate IRB: Mayo Clinic IRB #23-012204 (exempt from formal review)

## Advances in Retrieval Augmented Generation and Large Language Models for Diagnosing Vestibular Disorders

Alexandra T. Bourdillon, MD; Soraya Fereydooni, BS; Song Cheng, MD

**Objective:** Large language models (LLMs) such as ChatGPT can integrate vast amounts of data, and Retrieval Augmented Generation (RAG) is a method to customize LLMs to harness domain-specific knowledge to improve responses. Our aim is to design, implement and characterize the diagnostic utility of advanced RAG-based LLMs in assessing vestibular clinical vignettes.

Study Design: Qualitative Study

Setting: Tertiary referral center

Patients: Published case reports of patients with common vestibular disorders.

**Interventions:** Our institutional secure instance of ChatGPT-4 (called Versa) was compared to a scripted otology-specific RAG LLM supplied with Bárány society consensus documents of vestibular and other otologic conditions. Both models were prompted with clinical vignettes drawn from case reports capturing various conditions: superior semicircular canal dehiscence (SSCD), otosclerosis, Meniere's disease, benign paroxysmal positional vertigo (BPPV), vestibular migraine, and vestibular neuritis. Each model was asked to build a differential diagnosis and grade the likelihood of each diagnosis using a 10-point grading rubric.

**Main Outcome Measures:** Model performance (ChatGPT-4 versus RAG LLM) was assessed by the accuracy of the differential diagnosis and concordance between the two models in their grading of the diagnoses.

**Results:** Both models accurately diagnosed each of the 6 clinical vignettes. The RAG generated a more complete differential diagnosis that spanned more varied conditions beyond typical vestibular disorders. Furthermore, the standard model demonstrated more skew by assigning more confidence (higher scores) to the most likely diagnosis and less confidences (fewer points) to the remaining diagnoses. Generally, there was high concordance in grading schemes between the two LLMs in their ordering of the diagnoses.

**Conclusions:** RAG LLMs have improved differential diagnosis building and can weigh the nuances of various vestibular conditions with more complexity. Assessing the confidence of LLM responses using a scoring rubric is a valuable way to characterize the quality of these tools for counselling patients or augmenting clinical workflows.

**Professional Practice Gap & Educational Need:** Assessments of generative large language models are needed as they advance in quality and popularity.

Learning Objective: Understanding critical concepts for designing and evaluating the performance of LLMs

Desired Result: Examining the diagnostic capacity of LLMs using a paradigm of a scoring rubric

**Level of Evidence -** NA

Indicate IRB or IACUC: Exempt.

#### Piezoelectric Device for Canal Wall Reconstruction Tympanomastoidectomy: A Cadaveric Study

Joshua S. Lin, MD; Sahiti Vemula, BS; Dorothy W. Pan, MD, PhD Seiji B. Shibata, MD, PhD

**Objective:** Evaluate whether piezoelectric devices are safe and effective for canal wall reconstruction (CWR) tympanomastoidectomy.

Study Design: Cadaveric study

Setting: Temporal bone lab

Patients: 5 donor formalin-fixed temporal bones

**Interventions:** Piezoelectric devices that utilize bone-specific ultrasonic frequencies to achieve tissue-selective cutting were used to perform posterior canal wall (PCW) osteotomies in CWR tympanomastoidectomy.

Main Outcome Measures: Time required to complete the PCW osteotomies by piezoelectric devices. Selectivity for bonecutting over soft tissue by examining the surrounding soft tissue integrity.

**Results:** Following complete mastoidectomy and extended facial recess, a piezoelectric device was used for en-block removal of the PCW to optimize middle ear visualization, particularly sinus tympani exposure, as would typically be performed in a CWR tympanomastoidectomy. A neurotology fellow and attending performed the PCW osteotomies. The mean osteotomy time was 9.67 minutes (range=[5-14]), with repetition decreasing total osteotomy time by as much as 50%. The resultant PCW bone grafts remained intact with seamless fit back into the canal. Surrounding soft tissue also remained intact with osteotomies performed with straight (0.4mm-thickness) and curved (0.35mm-thickness) inserts. Contact of the piezoelectric saw with soft tissue produced different tactile feedback compared to that of bone. Brief contact of the device with crucial structures, including the facial nerve and tegmen dura, did not cause any notable damage, although continued targeted device application did eventually lacerate these structures.

**Conclusions:** Piezoelectric devices can efficiently and effectively perform PCW osteotomies for a CWR tympanomastoidectomy. Osteotomy time decreased from 14 minutes to 5 minutes with repetition and familiarity of the device. There is also versatility of angles and cuts with various inserts in the piezoelectric device, overall proposing a potentially safer, more attractive tool for these osteotomies compared with the microsagittal oscillating saw.

**Professional Practice Gap & Educational Need:** Piezoelectric devices use ultrasonic frequencies to provide bone-selective cutting over soft tissue structures. It has been widely used in specialties such as facial plastics and craniofacial surgery, but is not routinely used for otologic surgery. Due to the small space and important structures such as the facial nerve and tegmen dura in close proximity to the PCW, using a microsagittal saw when performing the osteotomies for CWR tympanomastoidectomy can be formidable. Therefore, using the piezoelectric device instead of microsagittal oscillating saw can provide some level of protection when performing this procedure.

**Learning Objective:** Piezoelectric device is an efficient, effective, and safe alternative to microsagital oscillating saw in performing PCW osteotomies for CWR. While the microsagittal saw requires less time to perform the osteotomy cuts, familiarity with the piezoelectric device led to shorter osteotomy time.

**Desired Result:** CWR tympanomastoidectomy provides elements of canal wall down and canal wall up procedures to optimize surgical exposure and effectively treat chronic ear disease. Since PCW osteotomies require regular use of the microsagittal oscillating saw, some surgeons may be reluctant to perform CWR tympanomastoidectomy. Surgeons can consider using piezoelectric devices, an equally effective and potentially safer alternative due to relative soft tissue protection, for performing this procedure.

Level of Evidence - Level V Indicate IRB or IACUC : Exempt

#### Effects of the Concentration of Intratympanic Dexamethasone in the Treatment of Idiopathic Sudden Sensorineural Hearing Loss

Lee M. Bauter, MD; Alyssa L. Damon, DO; Michelle P. Nixon, PhD J. Scott Greene, MD Arun K. Gadre, MD; W. James Azeredo, MD

**Objective:** Compare the efficacy of the two concentrations of intratympanic dexamethasone referenced by The American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS) for the treatment of Idiopathic Sudden Sensorineural Hearing loss (ISSNHL).

Study Design: Retrospective cohort study

Setting: Academic otolaryngology clinic over a 10-year period

Patients: Age eighteen and over who presented with ISSNHL and underwent intratympanic dexamethasone injections.

Interventions: Intratympanic dexamethasone injections with 10 mg/mL or 24 mg/mL concentrations.

**Main Outcome Measures:** We compare changes in pre- and post-treatment subjective and audiometric data between 10 mg/mL and 24 mg/mL cohorts- namely, pure-tone average (PTAs), speech reception threshold (SRT), word recognition score (WRS), and subjective improvement in hearing.

**Results:** In our standardized groups, there are no differences in the degree of change between pre-treatment and post-treatment PTA (dB) (p-value: 0.735), SRT (dB) (p-value: 0.133), or WRS (%) (p-value: 0.355). There is no difference in the number of patients who experience a subjective improvement in hearing between treatment groups (p-value: 0.335). For both the 10mg/mL and the 24mg/mL treatment group, there is an approximately 10% improvement PTA after treatment (p-value: 0.004 and p-value: <0.001 respectively).

**Conclusions:** There does not appear to be a significant difference in the subjective and audiometric outcomes in patients treated with either 10 mg/mL or 24 mg/mL intratympanic dexamethasone injections in our patient population. There does appear to be objective improvement of PTAs in both cohorts.

**Professional Practice Gap & Educational Need:** Inconsistency in the treatment of ISSNHL. Need for resource allocation when compounding 24mg/mL dexamethasone solution.

Learning Objective: Discuss the treatment of ISSNHL and compare the treatment outcomes for the referenced concentrations of intratympanic dexamethasone.

**Desired Result:** Applicable comparison of the described doses of intratympanic dexamethasone for the treatment of ISSNHL.

Level of Evidence - IV

Indicate IRB or IACUC: IRB number: 2024-0786. IRB exemption: 9/26/2024.

#### Patient Selection and Outcomes for Eustachian Tube Dilation in Cholesteatoma Surgery

Ana Marija Sola, MD; Tiffany Husman, BS; Charles J. Limb, MD

**Objective:** To report patient selection and outcomes for eustachian tube dilation (ETD) in patients with primary acquired cholesteatoma and compare these factors in a subset of case-matched patients undergoing surgery with or without ETD.

Study Design: Retrospective cohort study; case-control sub-analysis.

Setting: Tertiary academic center.

**Patients:** Thirty-six patients >18 years with primary acquired cholesteatoma. Twelve cases undergoing primary canal-wall-up cholesteatoma resection were 1:1 control-matched for age, gender, extent/location of cholesteatoma, ossicular chain reconstruction (OCR), type of OCR, and degree of pre-operative hearing loss.

**Interventions:** Patients undergoing surgery for removal of cholesteatoma with contemporaneous ETD. For case-control subanalysis, cases underwent cholesteatoma removal and ETD while controls underwent removal alone.

**Main Outcome Measures:** Main outcomes measures were postoperative change in conductive hearing loss (CHL), change from Type B or C to type A tympanogram, and cholesteatoma recurrence.

**Results:** All patients undergoing ETD had at least 2 characteristics of obstructive eustachian tube dysfunction (OETD): audiogram findings, symptoms, and physical exam findings. Mean follow up was 30.2 months (median: 31.2). Postoperative audiograms occurred on average 9 months post-operation. The rate of cholesteatoma recurrence in this cohort was 16.7% (6/36). Patients who underwent mastoidectomy in addition to cholesteatoma resection and ETD reported an average improvement in conductive hearing loss of 6.43 dB, compared to a worsening by 3.5 dB in patients who did not undergo mastoidectomy (p=0.04). On case-control sub-analysis, patients selected for ETD more frequently reported symptoms of OETD (odds ratio: 7.0, p=0.045) and had contralateral disease (odds ratio: 7.0, p=0.045). Average improvement of CHL was 4.3 dB (standard deviation (SD)=8.12) in the ETD group compared to 1.3 dB (SD=9.28) in the control group, although this did not reach statistical significance. In addition, the rate of conversion to Type A tympanogram post-surgery was higher in the ETD group (33%, 4/12 vs 8.3%, 1/12), although this analysis also did not reach statistical significance. There was no difference in rate of cholesteatoma recurrence between cases and controls (16.7%, 2/12 in both groups).

**Conclusions:** Patients undergoing ETD with cholesteatoma surgery have cholesteatoma recurrence rates within the average reported ranges and may show improved hearing outcomes with mastoidectomy. No adverse outcomes related to ETD were reported. The likelihood of patients with similar disease characteristics and pre-operative hearing being selected for ETD with cholesteatoma surgery is increased when there are symptoms of OETD and contralateral disease. Overall, ETD alongside cholesteatoma resection is safe and may confer a hearing and eustachian tube functional benefit—although a larger cohort may be required to further characterize this effect.

**Professional Practice Gap & Educational Need:** Obstructive eustachian tube dysfunction (OETD) can manifest as effusion, otitis media (OM), and/or cholesteatoma. While several studies have focused on the role of ETD in management of OM, there is limited research related to ETD in cholesteatoma surgery.

Learning Objective: To describe characteristics of patients undergoing ETD with cholesteatoma surgery and identify potential relationships between patient characteristics and outcomes.

Desired Result: To provide information on patient selection and outcomes related to ETD and cholesteatoma surgery.

Level of Evidence: IV

Indicate IRB or IACUC: UCSF:24-42636

#### Complete Insertion Rates and Insertion Depth with versus without Image Guided Cochlear Implant Electrode Selection Software

James C. Campbell, MD; Amanda Rago, AuD; Abhinav R. Ettyreddy, MD Douglas A. Chen, MD; Todd A. Hillman, MD

**Objective:** Report rates of full insertion before and after standardized utilization of image guided cochlear implant electrode selection (IGCIES), tradename OTOPLAN, for patients electing to receive a MED-EL cochlear implant.

Study Design: Retrospective Cohort Study

Setting: Tertiary care neurotology practice.

**Patients:** Adult patients presenting between 7/2021-27/2024 found to be cochlear implant candidates that chose a MED-EL device.

Interventions: Standardized utilization of IGCIES in 3/2023

Main Outcome Measures: Full insertion rates, frequency of longer electrode use, and maintenance of low frequency hearing (either  $\leq$ 65dB or  $\leq$ 85dB at 125, 250, or 500 Hz).

**Results:** 61 adults (36 female, median age 66) underwent implantation without IGCIES and 56 adults with IGCIES (35 female, median age 64). Complete insertion was more likely with IGCIES (100% vs 93%, p=0.02), as was use of a 31mm vs 28mm electrode (50% 33mm use vs 26%, p=0.01). IGCIES did not alter low frequency hearing preservation  $\leq$ 65dB (45% vs 34% preservation, p=0.46) or low frequency hearing preservation  $\leq$ 85dB (55% vs 49%, p=0.58).

**Conclusions:** After standardized utilization of IGCIES, increases in complete insertions and longer electrodes were observed, with no change in low frequency hearing preservation rates.

**Professional Practice Gap & Educational Need:** Image guided electrode selection is a new tool available to cochlear implant surgeons. How might this affect the amount of longer electrodes and full insertions that a surgeon achieves?

**Learning Objective:** Review our practice's results since using image guided electrode selection for all patients electing to receive a MED-EL device, with a control cohort of patients receiving MED-EL electrodes prior to this new tool's availability for comparison.

Desired Result: Provide data for surgeons on where image guided electrode selection may or may not improve their practice.

Level of Evidence – Level III

Indicate IRB or IACUC: Exempt

# Characterizing Middle Ear Carcinoid Tumors: A Population-Based Study

Lulia A. Kana, MD, MS; Masanari G. Kato, MD; Seilesh C. Babu, MD

Objective: Describe clinical characteristics and survival outcomes of middle ear carcinoid tumors

Study Design: Retrospective cohort study

Setting: Surveillance, Epidemiology, and End Results Database of the National Cancer Institute

Patients: All cases of histopathologically confirmed carcinoid tumors of the middle ear as primary location.

Main Outcome Measures: Patient features, tumor characteristics, treatment patterns, and survival outcomes

**Results:** Twenty-seven patients with middle ear carcinoid tumors were identified. The median age was 39 years (range, 21-68). There was nearly equal distribution between males and females (48% and 52%, respectively) and the majority were white (69%). The median follow-up duration was 13 years (range, 0-21). The median tumor size was 9 mm (range, 2-11). Seventeen presented with local (94.4%) and one with regional disease (5.6%). No patient experienced distant disease. Nearly all patients underwent surgery (92.6%) with one also undergoing adjuvant radiation. Five and ten-year overall and five and ten-year disease-specific survivals were 100%.

**Conclusions:** Middle ear carcinoid tumors are extremely rare entities with low metastatic potential. The favored treatment modality appears to be surgical resection with infrequent adjuvant radiation. While located in a complex anatomic location, the tumor portends a much favorable prognosis overall.

**Professional Practice Gap & Educational Need:** Studies on patient and tumor characteristics of middle ear carcinoid tumors is limited in the current literature.

Learning Objective: To understand clinical characteristics and survival outcomes of patients with middle ear carcinoid tumors.

Desired Result: To be able to describe tumor characteristics and clinical outcomes of middle ear carcinoid tumors.

Level of Evidence – Level  $\rm V$ 

Indicate IRB or IACUC: Exempt

#### Early Outcomes of Round Window Drill-Out for Otosclerosis Causing Round Window Obliteration

Kaitlyn A. Brooks, MD; Jeffrey T. Vrabec, MD

**Objective:** To discuss the effect of round window drill-out on otosclerosis cases with radiographic evidence of round window obliteration.

Study Design: Retrospective case series.

Setting: Single institution tertiary care referral center.

**Patients:** Four adult patients (5 ears) were included with audiometric findings of mixed hearing loss and radiographic evidence of otosclerosis causing round window obliteration. Three (75%) patients were female and median age at time of surgery was 64 years old.

**Interventions:** Round window obliterative disease was addressed with a formal round window drill-out (RWD) by opening the lumen of the basal turn of the cochlea with a micro drill. The opening was then reconstructed with fascia to create a two-window system.

**Main Outcome Measures:** Number and percent of patients with decrease in air-bone gap pure-tone average thresholds (ABG-PTA) calculated using 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz pure-tone thresholds.

**Results:** Two ears (same patient) underwent stapedectomy with successful RWD achieving ABG-PTA improvements of 27.5 dB (left) and 47.5 dB (right). One ear underwent stapedectomy alone with a residual ABG-PTA of 15 dB. One ear with RWD alone and one ear with revision stapedectomy and unsuccessful RWD did not show significant benefit. No ear was worse.

**Conclusions:** For patients suffering from mixed hearing loss with substantial residual hearing due to round window involving otosclerosis, formal RWD may be beneficial for hearing outcomes by reestablishing a two-window system.

**Professional Practice Gap & Educational Need:** Otosclerosis with inner ear and round window involvement is particularly challenging, especially when that patient has significant residual hearing and does not feel ready or qualify for cochlear implantation. Discussion of alternative surgical strategies is needed.

Learning Objective: Present our patient selection, technique, and outcomes of round window drill-out in applicable otosclerosis cases.

**Desired Result:** To foster further discussion regarding surgical techniques and outcomes in otosclerosis cases with round window obliterative disease.

Level of Evidence – Level  $\rm V$ 

Indicate IRB or IACUC: Houston Methodist Hospital IRB #38485-1

#### The Current State of Temporal Bone Education in the United States

Daniel E. Bestourous, MD; Mana Espahbodi, MD; Neil S. Patel, MD Matthew L. Carlson, MD; Richard K. Gurgel, MD, MSCI

**Hypothesis:** There is wide variability in how temporal bone lab education is delivered which may affect resident competency with otologic surgery.

**Background:** Otologic surgery is first learned by trainees in the temporal bone lab, which is a required component of ACGME-accredited residency programs. Despite this, no specific guidelines or standardization of education is provided. The purpose of this study is to evaluate the current state of temporal bone education across the United States through a survey of ACGME-accredited otolaryngology programs.

**Methods:** A cross-sectional evaluation of otolaryngology residency programs was conducted. An anonymous survey was distributed to program directors and coordinators and neurotology fellowship directors at each ACGME Accredited Otolaryngology Residency Program in the United States. Survey responses were compiled and analyzed using R Statistical Software (Vienna, Austria).

**Results:** A total of 37 responses were obtained from the 131 accredited otolaryngology programs in the United States (29.0%). Fifteen programs (39.5%) had accredited neurotology fellowship programs. Ten programs (26.3%) did not have a dedicated otology rotation for residents. Twenty-five programs had annual or biannual dissection courses, and 15 programs had monthly or weekly temporal bone dissection courses. Thirty programs (81.1%) used a dissection manual, the most common of which was the Ralph Nelson House Dissection Manual (n=28, 93.3%). Sixteen programs had at least as many drilling stations as they had residents (13.5%), and on average programs had 9 more residents than drilling stations. The average age of temporal bone laboratories across all programs was 13 years, with the oldest having been built in 1985 and the newest in 2024. Only 16 programs (43.2%) had a metric of measuring resident performance in the temporal bone lab, and of those 16, thirteen programs used a grading rubric developed by their own institution. The ratio of drilling stations to residents ( $\beta = -0.74$ , p =0.004) and the presence of a dedicated otology rotation ( $\beta = 0.41$ , p = 0.020) were strongly associated with residents pursuing neurotology fellowships by logistic regression.

**Conclusions:** There is variability in temporal bone education, resources, and time spent in the lab across US otolaryngology residency programs. Development of a more universal model for education may help to standardize educational practices an improve trainee preparedness for otologic surgery.

**Professional Practice Gap & Educational Need:** Otologic surgery is among the most technically and anatomically difficult subspecialties within otolaryngology and can be associated with significant morbidities. Previous studies have illustrated high variability in resident self-reported comfort with temporal bone surgery, but to date, no comprehensive evaluation of how temporal bone education is delivered has been performed.

**Learning Objective:** Review differences in temporal bone education models, resources, facilities, and instruments among otolaryngology programs and analyze factors that may influence resident comfort with otologic surgery

**Desired Result:** To highlight variability among otologic education and provide insight into possibilities for standardization of education.

Level of Evidence - V

Indicate IRB or IACUC: Exempt

# Benefits of Early Cochlear Implantation in Children with Single-Sided Deafness (SSD)

Piotr H. Skarzynski Prof.; Artur Lorens, Prof.; Anita Obrycka, PhD Anna Ratuszniak, PhD; Dorota Pastuszak, MSc; Henryk Skarzynski Prof.

**Objective:** To objectively assess the spatial hearing benefits after cochlear implantation (CI) and the daily device usage time in children with congenital/perinatal single-sided deafness (SSD) early implanted. This study described also surgical procedure used for this populations.

Study Design: The retrospective study was conducted to assess benefits of early cochlear implantation in SSD children.

Setting: Tertiary referral center.

**Patients:** Thirty-two children with congenital/perinatal SSD treated with CI participated in the study before age two and a half. The mean age and implantation was 18 months (SD = 6).

Interventions: Minimally invasive cochlear implantation via round window.

**Main Outcome Measures:** Their spatial hearing benefit with CI was measured using age-appropriate speech discrimination in noise tests. Daily processor usage time was obtained from two sources: parent interviews and datalogging technology.

**Results:** For speech discrimination in noise, children experienced the advantages of the head-shadow effect (4.3 dB SNR). The mean daily processor usage time was reported to be 9.5 hours/day according to parents, compared to 7.4 hours/day as recorded by datalogging.

Conclusions: Cochlear implantation is an effective treatment for children with congenital SSD.

**Professional Practice Gap & Educational Need:** Current SSD treatment options for young children are limited in effectiveness and not always can be used. The need for more data on long-term outcomes of SSD treatment options, is essential for guiding clinical practice.

Learning Objective: To evaluate the effectiveness of cochlear implants in children with SSD.

**Desired Result:** Clinicians will be better informed about cochlear implants, leading to improved treatment choices for SSD children.

Level of Evidence - III

**Indicate IRB or IACUC:** The study was approved by the Bioethics Committee of the Institute of Physiology and Pathology of Hearing (KB.IFPS:1/2019).

# Influence of Insertion Speed on Cochlear Implant Hearing Preservation

Piotr Henryk Skarzynski, Prof.; Artur Lorens, Prof.; Marek Polak, PhD Adam Walkowiak, PhD; Anita Obrycka; Henryk Skarzynski, Prof.

**Objective:** To evaluate the course of electrode insertion time and evaluate possible influence on cochlear implant hearing preservation.

Study Design: The retrospective study included adult patients with profound hearing loss who underwent cochlear implantation.

Setting: Tertiary referral center.

Patients: Twenty-six patients were implanted with Flex electrodes according to anatomical and audiological considerations.

Interventions: Minimally invasive cochlear implantation via round window.

**Main Outcome Measures**: Preoperative computed tomographic imaging (CT) and audiogram was performed within 1 month before the surgical intervention. The electrode location of the intracochlear electrode contacts was estimated and cochlea parameters were measured by the Otoplan v 3.1 software. The electrodes were selected to achieve minimum insertion depth of 450 degree of electrode insertion and to overcome any anatomical gap meaning that tip of the array reached acoustic region of each cochlea. After implantation, postoperative CT and audiogram at 3 months postoperatively were obtained. The electrode location of the intracochlear electrode contacts and cochlea parameters were measured.

**Results:** All subjects had partial or complete hearing preservation. Among this group 9 subjects had complete hearing preservation. Duration of electrode insertion varied from 47 to 276 seconds. For subjects with complete hearing preservation insertion speed was not linear, but it varied. Typically, insertion speed was faster at the beginning and up to 3 times slower towards the end of the insertion. This corresponded to the estimation of 5 degree of insertion per second.

**Conclusions:** Several surgically related implicated findings could be found. The speed of the electrode insertion is an important factor during the surgery. Study suggest that speed of the electrode insertion is nonlinear and may be estimated by degree of insertion per second.

Professional Practice Gap & Educational Need: No defined guidelines for electrode insertion speed.

Learning Objective: Influence of insertion speed on cochlear implant hearing preservation.

Desired Result: It is therefore mandatory to better comprehend the impact of the implant on cochlear health.

Level of Evidence - III

**Indicate IRB or IACUC:** The study was approved by Bioethics Committee of the Institute of Physiology and Pathology of Hearing (KB.IFPS/16/2021).

#### Barriers to Hearing Healthcare in the Northern US: A Comparison of Rural and Urban Residents

Catherine L. Kennedy, MD; Nivedita Sabarinathan; August Richter Meredith E. Adams, MD, MS

**Objective:** To compare awareness of hearing loss and barriers to hearing healthcare between rural and urban residents 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

**Patients:** Adults  $\geq$  18 years attending the Minnesota State Fair

Interventions: In-person survey, otoscopy, and audiometric screening at 25 dB across four frequencies.

Main Outcome Measures: Descriptive analysis of sociodemographics, awareness of hearing loss and healthcare, and Brief Health Literacy Screening (BHLS). Hearing loss (HL) was defined as failing at least 1 frequency in 1 ear.

**Results:** There were 211 participants, mean age 48.4 years (18-86), 63.5% female, 86.7% white, 70.6% urban residents, 29.4% rural residents, 93.8% insured. Health literacy was adequate (mean urban BHLS 14.3 [95% CI 11.7-16.9], rural 13.9 [10.7 to 17.1], p=0.05). Similar proportions of urban and rural residents reported subjective HL (30.9% and 40.3%, p=0.186) and audiometric HL (44.7% and 50.9%, p=0.743). Urban residents demonstrated lower concordance between perception of HL and the results of screening (50.9% vs. 44.4%, p=0.018). Both groups had low rates of hearing testing within 5 years (urban 28.8% vs. rural 33.8%, p=0.471) and discussing hearing testing with their PCPs (urban 7.7% vs. rural 14.3%, p=0.180). Urban residents reported that location of hearing testing was a significant barrier (25.7% vs. 11.3%, p=0.02); both reported financial concerns as a barrier. Rural residents had lower awareness of normal hearing levels (6.6% vs. 20.8%, p=0.012). Both groups had low awareness of state healthcare benefits (rural 29.5% vs. urban 27.5%, p=0.771).

**Conclusions:** Urban and rural residents experience similar barriers in access to hearing healthcare. Both would benefit from public health initiatives to educate PCPs and increase awareness of state benefits.

**Professional Practice Gap & Educational Need:** This study aims to identify barriers to hearing healthcare for residents of the Northern US, where public insurance benefits afford greater coverage than in other previously described rural US regions. In spite of excellent insurance coverage and access to hearing healthcare, patients in Northern 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:

To determine prevalence of hearing loss and participant awareness of hearing loss and rehabilitative options. To identify public awareness of healthcare benefits in a state with excellent public insurance hearing healthcare coverage. To compare barriers in access to hearing healthcare for residents of rural and urban communities.

**Desired Result:** To recognize new pathways to overcome barriers to hearing healthcare in Northern US rural and urban communities.

Level of Evidence: Level V

Indicate IRB or IACUC: IRB Study # 00019167, University of Minnesota (June 22, 2023).

#### Video High Impulse Testing Provides Insight into Patient Reported Outcome Measures and Falls in Patients with and without Unilateral Vestibular Hypofunction

Harrison J. Smith, MD, MSCI; Jennifer Kelly, DPT; Yoav Gimmon, PhD Anat V. Lubetzky, PT, PhD; Maura K. Cosetti, MD

**Objective:** To assess the relationship between Video High Impulse Testing (vHIT), caloric weakness, falls, and patient reported outcome measures (Dizziness handicap Inventory, DHI), in patients with and without unilateral vestibular hypofunction (UVH)

Study Design: Cross-sectional

Setting: Academic tertiary referral center

Patients: 23 adults with UVH, mean age 62 (range 32-82) 39 controls, mean age 52 (range 22-78)

Interventions: Diagnostic vestibular testing (vHIT, caloric function); DHI, falls

Main Outcome Measures: vHIT: affected ear gain, saccades

**Results:** Measured gains and number of saccades correlated with DHI (r=-0.63; r= 0.66 respectively) Patients with overt saccades had higher DHI (MD = 17, 95% CI:  $5.5*10^{-5} - 33$ , p < .001) and patients with covert saccades had higher DHI (MD = 26 95% CI: 16 - 36, p < .001). Of the 10 patients with falls (n = 3 control, n = 7 UVH), 7 patients demonstrated saccades, 6 patients demonstrated overt saccades, and 5 patients demonstrated covert saccades (p>.05). Lateral gains in patients with falls were not different than those without falls (MD = -.11, 95% CI: -.28 - .02, p = .09). Caloric weakness correlated with DHI and patients with falls had greater unilateral weakness (r = .69, MD = 21 95%: CI: 5 - 42, p = .009).

**Conclusions:** Analysis of vHIT data suggests both gain and saccades correlate with DHI. Patients with falls had high frequency of saccades on vHIT and lower gains. This data suggests that vHIT can provide objective corroboration of patient reported outcomes. While caloric testing is the gold standard, vHIT may provide insight into patient handicap without provoking patient symptoms.

**Professional Practice Gap & Educational Need:** vHIT data and relationship to dizziness handicap and clinical function have been minimally investigated. This study aims to understand the relation between objective and subjective data in dizziness testing.

Learning Objective: To recognize the relationship between vHIT data and patient reported handicap and falls in patients.

Desired Result: Use vHIT data for the diagnosis and treatment of vestibular hypofunction.

**Level of Evidence** – Level 3

**Indicate IRB or IACUC:** Approved by the Biomedical Research Alliance of New York LLC Institutional Review Board (BRANY IRB, study #20-02-278-05) on 9/15/21

# Pupil Diameter as an Indicator of Task Load during Simulated Mastoidectomies

Oren Wei, BS; Andy S. Ding, MD, MSE; Nimesh Nagururu, MSE; Adnan Munawar, PhD Manish Sahu, PhD; Russell H. Taylor, PhD; Francis X. Creighton, MD

Hypothesis: Pupil diameter is a viable indicator of task demand among surgeons performing mastoidectomies.

**Background:** Temporal bone surgery requires significant cognitive effort to perform. Quantifying this demand is important for surgical training to assess procedural proficiency and identify phases which are particularly challenging. We sought to improve upon traditional evaluation methods by examining pupil diameter–a higher resolution and continuously monitored metric–as a surrogate for task demand in a simulated environment with limited confounders.

**Methods:** Operators at a single tertiary care institution performed mastoidectomies on a virtual-reality surgical simulator developed in our lab. Operators were divided into experts (fellow or attending) and nonexperts (medical student or resident). Continuous pupil measurements were recorded using a pupil tracking device (Core by Pupil Labs). Operators then completed a NASA Task Load Index (TLX) questionnaire–a well-validated quantifier of task demand–after each mastoidectomy. Spearman correlation and linear regression were used to assess relationships between pupil metrics and TLX responses. T-tests were used to assess differences between groups.

**Results:** Thirteen operators (3 experts, 10 nonexperts) performed a total of 86 mastoidectomies across 10 different temporal bone anatomies. Pupil diameter (in pixels) correlated positively with task mental demand (p=0.04), physical demand (p=0.002), temporal demand (p=0.0001), and self-rated performance (p=0.002). Temporal demand contributed significantly to increased pupil diameter (p=0.003) while frustration contributed significantly to decreased diameter (p=0.002). Both average pupil diameter (22.3 vs. 19.2 pixels, p=0.0009) and average diameter standard deviation (3.7 vs. 3.2, p=2E-7) were larger in experts than in nonexperts, signaling increased cognitive demand.

**Conclusions:** Pupil diameter correlates significantly with various metrics of task demand during a simulated mastoidectomy. Future studies will investigate additional pupil and gaze characteristics throughout specific phases of surgery.

**Professional Practice Gap & Educational Need:** Understanding task load of various surgical procedures is important for surgical education, where operator demand can impact performance both positively and negatively. Current methods for evaluating task load are often subjective and static. Pupillometry represents a new assessment platform that can provide more targeted feedback during surgical training, especially in a simulated environment. Validating this platform is important for improving current training practices.

**Learning Objective:** To introduce otolaryngologists to pupillometry as an intraoperative assessment platform and to provide insights into the validity of pupil diameter as an indicator of surgical task load.

**Desired Result:** Readers will become familiar with pupillometry and gain an understanding of its applications in assessing task demand.

Level of Evidence - V

Indicate IRB or IACUC: Johns Hopkins University School of Medicine IRB00264318

## Pitfalls of the Current Temporal Bone Fracture Classification System

Jumah G. Ahmad, MD; Nathaniel Hunter, BS; Ahmad Abdelhadi, BS Aidan Wright, BS; David Z. Allen, MD; Vivian F. Kaul, MD

**Objective:** To evaluate the utility of the current classification system in predicting outcomes of patients with temporal bone fractures and propose alternative imaging findings that are associated with outcomes.

Study Design: Retrospective study.

Setting: Tertiary referral center.

**Patients:** Consecutive patients with traumatic temporal bone fractures (TBF) confirmed via CT between 10/8/2019 and 03/22/2024.

Interventions: Diagnostic evaluation.

**Main Outcome Measures:** Association of TBF type (longitudinal vs transverse, otic capsule sparing vs involving) with clinical outcomes (facial nerve paresis (FNP), hearing loss (HL)) and the presence of imaging findings associated with FNP and HL.

**Results:** Among 598 temporal bone fractures, 74% were longitudinal and 26% were transverse. Longitudinal fractures had a higher rate of ossicular chain discontinuity (15% v 6%, p < 0.05) and transverse fractures were more likely to be otic capsule involving (59% v 20%, p = 0.006). There were no significant differences in development of FNP or HL. Patients with otic capsule involving fractures were no more likely to develop FNP or HL than patients with otic capsule sparing fractures. Univariate analysis elicited a higher rate of FNP in patients who had ossicular discontinuity (19% vs. 5%, p < 0.01), carotid canal fractures (27% vs. 12.5%, p < 0.05), and vascular injury (26% vs. 12.7%, p < 0.05) on imaging. Multivariate analysis identified ossicular discontinuity as the sole predictor of FNP (OR = 3.28, 95% CI: 1.08-8.9, p = 0.0253).

**Conclusions:** The current TBF classification system does not provide clinically prognostic value in this patient cohort. A new classification system that incorporates alternative imaging features of the middle ear and carotid artery may provide more clinically useful associations when it pertains to FNP.

**Professional Practice Gap & Educational Need:** The current TBF classification system is not consistent in providing clinically meaningful prognostic value. We assessed its utility in our patient cohort and suggested alternative imaging findings to be incorporated into a more effective classification system.

**Learning Objective:** To realize the pitfalls and limitations of the current TBF classification system and explore alternative imaging findings that could provide clinically useful associations with patient outcomes.

Desired Result: Improve the clinical value of the current classification system used for patients with TBF.

Level of Evidence - Level IV.

Indicate IRB or IACUC: UTHealth Houston HSC-MS-24-0358.

# Artificial Intelligence and Over-The-Counter Hearing Devices: A Scoping Review

Sameer H. Siddiqui, BS; Vivian F. Kaul, MD

**Objective:** To characterize the marketplace for commercially available, over the counter (OTC) hearing augmentation devices that utilize artificial intelligence (AI).

Study Design: Scoping review

**Methods:** A Google search for "OTC AI hearing devices" was conducted to find OTC hearing devices that incorporate AI. Manufacturer websites were accessed to search for product features, price ranges, and targeted symptoms.

**Results:** Our search yielded 35 devices, with 4 devices meeting the criteria of OTC hearing augmentation devices incorporating AI. For OTC hearing devices with AI, the prices ranged from \$399 to \$2,950, whereas OTC devices without AI ranged from \$99 to \$1,995. Non-OTC hearing device pricing varies based on patient insurance. In non-OTC AI hearing devices, private insurance and Medicaid generally provide coverage depending on individual plans. However, Medicare users, whose age range places them in a population that utilizes hearing devices often, are not provided coverage for hearing care. AI devices primarily target improvements in noise reduction and speech clarity. These OTC AI devices were all indicated for mild-to-moderate hearing loss, unlike IYO Audio, which can address mild-to-moderate hearing loss, but is not indicated as a medical device.

**Conclusions:** In the growing markets for AI and OTC hearing devices, the implementation of AI and accessibility to this state of the-art equipment has dramatically increased. AI hearing devices emphasize personalization of hearing profiles in real time, focusing on controlling noise spontaneously. While this new technology for hearing loss is exciting, future studies must be conducted to determine a difference in impact on health outcomes with the implementation of AI into hearing augmentation devices.

**Professional Practice Gap & Educational Need:** Growing prevalence of advanced AI technology in the OTC hearing device market changes how clinicians may inform patients of their intervention options. Therefore, awareness of the market available to patients is crucial for medical decision making.

**Learning Objective:** To improve awareness of devices available on the market for OTC hearing devices and develop an understanding of the features provided by implementing AI into these devices.

**Desired Result:** We hope clinicians can gain a deeper understanding of AI hearing devices available OTC to patients to best guide them in finding an audiologic intervention that suits their hearing needs.

**Level of Evidence** – N/A

Indicate IRB or IACUC: Exempt.

# Magnetic Resonance Imaging (MRI) Markers of Temporal Bone Pneumatization

Mana Espahbodi, MD; Heather J. Smith, BM; Melissa Shuhui Lee MBBS Jason L. Steele, BS; Richard K. Gurgel, MD, MSCI Richard H. Wiggins, MD; Neil S. Patel, MD

**Objective:** Computed tomography (CT) imaging of the temporal bones is often obtained prior to routine otologic and cochlear implant surgery to assess surgical anatomy. However, magnetic resonance imaging (MRI) is often required in cochlear implant candidates for indications such as asymmetric hearing and evaluation of cochlear fluid signal. Obtaining both studies prior to a routine case is costly and inefficient. The objective of this study is to identify markers on MRI that correlate with temporal bone pneumatization assessed by CT and may obviate the need for CT in anatomically typical, unoperated ears.

Study Design: Retrospective review.

Setting: Tertiary academic referral center.

**Patients:** Fifty-two adult subjects (92 ears) who underwent both contrast-enhanced MRI brain and CT temporal bone without contrast from 2013-2022. Twelve ears were excluded due to prior temporal bone surgery or temporal bone pathology interfering with imaging measurements.

Interventions: Contrast-enhanced MRI brain and CT temporal bone without contrast.

**Main Outcome Measures:** Volume of pneumatized temporal bone on CT and MRI linear measurements in the axial and coronal planes were assessed using Horos software. Statistical analyses were performed with SPSS version 29. Pearson correlations between medical student and neurotologist/neuroradiologist measurements were 0.89 or greater (p<0.05).

**Results:** Laterality was 48% right and 52% left. Median volume of pneumatized temporal bone was 11.33 (interquartile range [IQR] 8.24 – 15.25) cm<sup>3</sup>. Median MRI linear measurements were the following: sigmoid to mastoid cortex 7.11 mm (IQR 5.55-8.50 mm), sigmoid to external auditory canal (EAC) 14.70 mm (IQR 12.36-17.59 mm), EAC to temporal lobe 5.85 mm (IQR 4.76-6.98 mm), and jugular bulb to internal auditory canal (IAC) 6.68 mm (IQR 5.51-8.26 mm). On univariable, binary logistic regression analysis, distance from the sigmoid to mastoid cortex, sigmoid to EAC, and EAC to temporal lobe were associated with volume of pneumatized temporal bone  $\geq 12$  cm<sup>3</sup>, while jugular bulb to IAC was not. On multivariable binary logistic regression analysis, the following remained associated with volume of pneumatized temporal bone  $\geq 12$  cm<sup>3</sup>, while jugular bulb to IAC was not. On multivariable binary logistic regression analysis, the following remained associated with volume of pneumatized temporal bone  $\geq 12$  cm<sup>3</sup>, while jugular bulb to IAC was not. On multivariable binary logistic regression analysis, the following remained associated with volume of pneumatized temporal bone  $\geq 12$  cm<sup>3</sup>: distance from the sigmoid to mastoid cortex (odds ratio: 1.45, 95% confidence interval (CI): 1.05-2.00; median (IQR) of 5.87 mm (4.94-7.24 mm) with volume < 12 cm<sup>3</sup> and 8.48 mm (7.06-9.97 mm) with volume  $\geq 12$  cm<sup>3</sup> and 6.92 mm (5.94-7.43 mm) with volume  $\geq 12$  cm<sup>3</sup>).

**Conclusions:** A minimum sigmoid to mastoid cortex distance of 8 mm and EAC to temporal lobe distance of 7 mm are highly correlated with a well-pneumatized temporal bone. These clinically useful measurements provide insight into the pneumatization of the temporal bone that may obviate the need for CT in routine cases.

**Professional Practice Gap & Educational Need:** MRI markers associated with temporal bone pneumatization are unknown. Identification of these markers may preclude the need for CT in uncomplicated cases.

Learning Objective: To determine the MRI makers that correlate with temporal bone pneumatization assessed by CT.

**Desired Result:** Increase understanding of MRI markers that are correlated with temporal bone pneumatization that may obviate the need for CT in anatomically typical, unoperated ears.

Level of Evidence – IV

Indicate IRB or IACUC: IRB 00045048; University of Utah

# Sleep Quality of Service Members and Veterans with and without Reports of Dizziness

Erica S. Rich, MD; Carrie W. Hoppes, PT, PhD; Samrita Thapa, MPH; Karen H. Lambert, PT Matthew S. Brock, MD; Isaac D. Erbele, MD; Kelly M. Reavis, PhD, MPH

**Objective:** Sleep management may exacerbate dizziness symptoms and worsen patient fall risk. The purpose of this study was to evaluate the sleep quality of active-duty service members (ADSM) and Veterans with and without reports of dizziness.

Study Design: Cross-sectional study.

Setting: Multi-institutional tertiary care.

Patients: ADSM and Veterans (n=1,524) enrolled in the Noise Outcomes In Servicemembers Epidemiology (NOISE) study.

Interventions: Survey.

Main Outcome Measures: Sleep disorder and Epworth Sleepiness Scale scores.

**Results:** Self-reported dizziness was found in 27% of the sample. Common symptoms included "Feeling faint or light-headed" (40%), "Loss of balance" (27%), and "Spinning sensations" (24%). Those with dizziness were 1.7 (95% CI: 1.3, 2.2) times more likely to have a sleep disorder and 1.6 (95% CI: 1.2, 2.2) times more likely to experience excessive daytime sleepiness than those without dizziness.

**Conclusions:** Patients with self-reported dizziness were more likely to have poor sleep quality. More work is needed to determine if poor sleep is an independent risk factor for dizziness, or alternatively, a factor for worsening better-established causes of vestibular insults and compensation. Management of sleep disorders should be considered in patients being evaluated for dizziness, and physical therapists may also consider integrating sleep hygiene education into vestibular therapy.

**Professional Practice Gap & Educational Need:** Current practice patterns often overlook the connection between dizziness and sleep disorders, despite evidence that poor sleep quality exacerbates dizziness symptoms and increases fall risk. Routine screening for sleep disturbances is not consistently performed, leading to suboptimal patient outcomes. Addressing this gap can enhance the comprehensive care of individuals with dizziness, particularly within the military and veteran populations.

Learning Objective: Understand the relationship between dizziness and sleep quality in service members and Veterans; Incorporate sleep disorder screening into clinical practice.

**Desired Result:** Increase awareness of the prevalence of sleep disorders in patients with dizziness, leading to better screening, management, and patient outcomes.

#### Level of Evidence: Level III

**Indicate IRB or IACUC:** Joint VA Portland Health Care System/Oregon Health and Science University (#3159/9495 and #4655/22488) and 59th Medical Wing/Joint Base San Antonio Military Healthcare System (#FWH20180143H)

#### Anatomy-Specific Virtual Safety Barriers for Cooperative Control Robotic Temporal Bone Surgery

Andy S. Ding, MD MSE; Hisashi Ishida, MSE; Nimesh V. Nagururu, MSE Adnan Munawar, PhD; Manish Sahu, PhD; Russell H. Taylor, PhD Francis X. Creighton, MD

**Hypothesis:** Virtual safety barriers can be enforced in cooperatively controlled robotic mastoidectomies with submillimeter accuracy to prevent damage to critical structures.

**Background:** Temporal bone surgery is technically challenging, with complex anatomy and landmarks often encased in bone. Cooperatively controlled robots (CCRs), in which a surgeon and robot manipulate an instrument simultaneously, can improve the accuracy and safety of this surgical domain. These systems allow for robotic precision while leveraging the surgeon's technical expertise. As an added safety measure, CCRs can implement virtual safety barriers around relevant anatomy to prevent intraoperative damage. This study assesses the feasibility and accuracy of anatomy-specific CCR-enforced safety barriers for temporal bone surgery.

**Methods:** The CCR used in this study consists of a 5-degrees-of-freedom gantry arm that carries an optically tracked surgical drill. Three cadaveric temporal bone specimens were registered to this CCR. Preoperative CT images were segmented to identify relevant anatomy (e.g., ossicles, inner ear, facial nerve, chorda, sigmoid sinus). A safety barrier of 0.5mm was set along all structures, and the robot was programmed to provide resistance scaled by the proximity of the drill to the closest anatomy. Robot-assisted mastoidectomies were performed by the senior author, with deliberate effort to skeletonize the facial nerve and expose the sigmoid sinus. Postoperative CT scans were obtained and compared against preoperative segmentations.

**Results:** Mastoidectomies were successfully completed for all specimens without violation of critical structures. Distance (mean $\pm$ SD) from the drilled mastoid cavity and the facial nerve and sigmoid sinus were 0.285 $\pm$ 0.461mm and 0.587 $\pm$ 0.966mm, respectively.

**Conclusions:** This study shows the feasibility of anatomy-aware virtual safety barriers in robot-assisted temporal bone surgery. Future studies will investigate replacing optical tracking with computer vision-based instrument tracking.

**Professional Practice Gap & Educational Need:** Although previous studies describe the use of robotic guidance in performing mastoidectomy, prior work has focused on autonomous designs. Our work in developing a CCR for surgery, in which the surgeon and robot work together to manipulate the surgical instrument, demonstrates a semi-autonomous method which allows the system to benefit from the surgeon's inherent skill and knowledge, while providing increased safety. To our knowledge, this is the first assessment of anatomy-specific CCR-enforced virtual barriers for temporal bone surgery reported in a clinical venue.

**Learning Objective:** The learning objectives were to examine the efficacy of using a cooperatively controlled robotic system for temporal bone surgery and to determine the accuracy of robot-enforced virtual safety barriers around relevant anatomy.

**Desired Result:** We hope our study will highlight the role of robotics in otology and will spark discussion of methods to improve this technology in the future.

**Level of Evidence** – Level V

Indicate IRB or IACUC: Johns Hopkins School of Medicine IRB00264318

#### Association between Cigarette, E-Cigarette, and Marijuana Use and Eustachian Tube Dysfunction

Kaitlin Hori, BS; Tyler Gallagher, BS; Janet S. Choi, MD, MPH

**Objective:** To evaluate the association between cigarette, E-cigarette and marijuana use and obstructive eustachian tube dysfunction (OETD) in US adults.

Study Design: Cross-sectional

Methods: Multivariable regression analysis of National Health and Nutrition Examination Survey (2015-2018)

**Patients**: Participants ( $\geq 18$  years) with data on tympanometry, pure-tone audiometry, and drug and smoking questionnaires (n=18,383).

Interventions: Cigarette, E-cigarette and marijuana use were evaluated based on never, former or current use.

Main Outcome Measures: OETD was defined as middle ear pressure < -100 decapascals (daPa).

**Results:** 5.9% of US adults [95%CI 4.9%-7.2%] had OETD. When accounting for demographics and other drug use, current cigarette use was significantly associated with OETD (OR2.6, 95%CI 1.5-4.0), while former use was not (OR1.2, 95%CI 0.6-2.6). For E-cigarettes, 6% [95%CI 5.2%-6.7%] were current users and 16.1% [95%CI 14.6%-17.6%] were former users. When accounting for demographic factors, former e-cigarette use was significantly associated with OETD (OR2.0, 95%CI 0.9-4.2). When additionally adjusting for cigarette smoking, there was no significant association between former or current e-cigarette use and OETD. For marijuana, 14.1% [95%CI 12.2%-16.4%] were current users and 26.1% [95%CI 24.0%-28.5%] were former users. When accounting for demographic factors, current marijuana use was significantly associated with OETD (OR2.3, 95%CI 1.3-4.3), while former use was not (OR0.8, 95%CI 0.4-1.4). When adjusting for cigarette smoking, former or current marijuana use was not associated with OETD. A subgroup analysis among never cigarette smokers found no significant associations between independent e-cigarette or marijuana use and OETD.

**Conclusions**: In this national cohort, traditional cigarette smoking was independently associated with OETD, while e-cigarette and marijuana use was not. Further studies can explore the independent and combinatorial impact of e-cigarette and marijuana use on OETD.

**Professional Practice Gap & Educational Need:** There lacks current consensus on the association between E-cigarette and marijuana use and obstructive eustachian tube dysfunction. This study provides preliminary insight into the relationship between the use of these drugs and OETD.

Learning Objective: To explore the relationship between cigarette, E-cigarette and marijuana use and OETD in a national sample.

**Desired Result:** To recognize that cigarette, E-cigarette and marijuana use can be associated with OETD. However, future research needs to explore the discrete and additive effects of these drugs on the development of OETD.

**Level of Evidence** – Level 3

Indicate IRB or IACUC: Exempt

#### Eustachian Tube Dysfunction following LeFort I Orthognathic Surgery: A Prospective Cohort Study

Cameron B. Lindemann, DO; Avori Bastemeyer MSIV; Claudia Mondragon, MD Ethan McGann, MD; Michael Eliason, MD

**Objective:** To prospectively evaluate the incidence of eustachian tube dysfunction following LeFort I orthognathic surgery.

**Study Design:** We conducted a prospective cohort study to evaluate the occurrence of new-onset ETD following LeFort I orthognathic surgery.

Setting: A single, tertiary-care, military treatment facility.

Patients: Adult patients undergoing LeFort I orthognathic surgery.

**Interventions:** The validated Eustachian Tube Dysfunction Questionnaire 7 (ETDQ-7) was administered to patients undergoing LeFort I orthognathic surgery, The same questionnaire was administered 3 months following surgery.

**Main Outcome Measures:** ETDQ-7 total score and mean item score following LeFort I surgery. Multivariate analysis was performed to stratify the data based on age, race, and gender.

**Results:** Preliminary analysis suggests no significant change in incidence of ETD following LeFort I surgery. Pre-operative mean item score average was 1.97; total score 13.8, with postoperative mean item score average being 1.79; total score 12.5, an overall decrease, not reaching statistical significance. As the study is ongoing, multivariate analysis has been postponed as further data is collected.

**Conclusions:** LeFort I osteotomes are commonly performed to improve dental occlusal abnormalities. Major anatomic shifts of the mid face may result in many unintended physiologic changes. We hypothesized that advancing the maxilla relative to the skull base could theoretically change the orientation of the eustachian tube, and thus, decrease its functionality. However, our preliminary results do not support this. Further data should be collected in this realm to adequately analyze this relationship, allowing for proper patient counseling.

**Professional Practice Gap & Educational Need:** Eustachian tube dysfunction has not been described as a complication of LeFort I orthognathic surgery to our knowledge. This represents an anatomically interesting surgical complication which is not discussed by surgeons when counseling patients.

**Learning Objective:** To 1) review the muscular and skeletal anatomy of the eustachian tube as it relates to LeFort orthognathic surgery and 2) discuss the impact of this surgery on the physiology of the eustachian tube and its relevance to peri-operative counseling.

**Desired Result:** To further characterize the impact of LeFort orthognathic surgery on the structure and function of the eustachian tube.

Level of Evidence - Level III

Indicate IRB or IACUC: Navy Medical Readiness and Training Command - Portsmouth IRB 0072

# ENTGPT: A Large Language Model for Automated Data Extraction in Otolaryngology

Akash Kapoor, BS; Joshua Fuller, BS; Michael A. Hewitt, BA Ana H. Kim, MD; Anil K. Lalwani, MD

Hypothesis: We hypothesized that a large language model (LLM) can accurately extract data from otolaryngology charts.

**Background:** Manual chart review is time-intensive yet essential for clinical research. While LLMs show promise in automating data extraction, their potential in otolaryngology remains unexplored. In this study, we compare an LLM's performance in extracting clinical data to a manual chart review.

**Methods:** We extracted de-identified clinical notes from 40 patients previously reviewed by research fellows for a published study. ENTGPT (built with GPT-40) was given notes from multiple providers, specialties, and time points and asked to extract study variables. Variables were categorized as "discrete" (e.g. implanted ear), "calculated" (e.g. pre-operative puretone average), and "clinical judgement" (e.g. hearing loss etiology). For clinical judgment variables, the model provided both discrete answers and descriptive summaries. A negative control (patient height), absent from the notes, was also requested. Accuracy was calculated and verified by a board-certified otolaryngologist.

**Results:** The model achieved 100% accuracy in extracting discrete variables (95% CI: 0.98-1.0) and correctly identified the absence of the negative control variable (95% CI: 0.91-1.0). For variables requiring calculation, accuracy was 98% (95% CI: 0.96-0.99). For descriptive variables, the LLM's discrete answer had a concordance of 63% (95% CI: 0.54-0.71) with the manually extracted data. However, the descriptive summaries were medically accurate 100% of the time (95% CI: 0.97-1.0) as determined by physician review.

**Conclusions:** ENTGPT reliably extracted clinical variables from complex charts without hallucination, performing best on discrete and calculated variables. For variables requiring clinical judgement, descriptive summaries were accurate and useful. LLMs have the potential to transform retrospective clinical studies, by streamlining data extraction and saving significant time for researchers.

**Professional Practice Gap & Educational Need:** Otolaryngology is a complex surgical subspecialty with diverse patient presentations, making chart review heterogeneous and challenging to automate. Manual chart review is time-intensive and often essential for clinical research and trial enrollment. Limited literature is available evaluating the efficacy of LLMs in otolaryngological data extraction.

**Learning Objective:** To review the application and limitations of large language models in clinical data extraction, assess the accuracy of a large language model on a heterogenous set of otolaryngology data, and provide a blueprint for use of this tool in otolaryngology.

**Desired Result:** This study supports the potential role of Large Language Models as tools to streamline data extraction and saves significant time for researchers to ask more clinical questions and derive insights from patient charts.

**Level of Evidence** – N/A

Indicate IRB or IACUC: IRB approved, IRB #AAAV4730

#### Evaluation of Electrode Placement and Cochlear Implantation Results in Incomplete Partition Type I

Anna K. Piecuch, MD; Piotr H. Skarzynski, Prof; Henryk Skarzynski; Prof

**Objective:** Evaluation of cochlear implant electrode position in a cystic cochlea lacking modiolus and spiral lamina and auditory assessment of early and long-term results of cochlear implantation in incomplete partition type I.

Study Design: Retrospective case review.

Setting: Tertiary referral center; ambulatory and hospital.

**Patients:** The study group included 6 patients (3 males and 3 females) with a congenital inner ear defect of cystic cochleovestibular malformation (IP I), bilateral (n=5), IP I with another inner ear defect in the opposite ear (n=1). Cochlear implant (CI) for IP I defect was implanted in 6 patients, 2 of them bilaterally (8 ears with CI). The mean age at first cochlear implantation was 12 years 4 months (range: 11 months - 38 years).

Interventions: Diagnostic, therapeutic, and rehabilitative.

**Main Outcome Measures:** Assessment of straight electrode position using CT images. Post-implantation effects were assessed with the following tests: behavioural observation audiometry (BOA) and visual reinforced audiometry (VRA) in children, free-field threshold audiometry and adaptive auditory speech test in adolescents and adults.

**Results:** Average CI implant electrode position in a cystic cochlea lacking a modiolus and spiral lamina (IP I): 523.33 degrees. CI implant effects: early - children's BOA test and VRA mean 67.17dB (n=3) after 4 months, early - adaptive auditory speech test 20% in quiet, 15% in noise (n=1) after 1 year. Late effects: free-field threshold audiometry mean 34.44dB (n=3) at 5, 8 and 10 years, adaptive auditory speech test 50% in quiet, 20% in noise (n=1) at 12 years after implantation.

**Conclusions:** It is possible to effectively stimulate the auditory nerve in a cochlea without a modiolus by stimulating the cochlear wall region. The distal effects of cochlear implantation in patients with IP I can be satisfactory but depend on the age of implantation and the length of rehabilitation.

**Professional Practice Gap & Educational Need:** Lack of knowledge about the indications for cochlear implantation and the locations of auditory nerve fibre stimulation in a type I incompletely partitioned cochlea without a miodiolus.

**Learning Objective:** Education and indications on cochlear implantation for IP I and the need for preoperative diagnostic imaging to select an appropriate electrode in a cochlea without a modiolus (straight).

**Desired Result:** Patients with IP I are suitable candidates for cochlear implantation and can achieve satisfactory results with CI after a long period of rehabilitation.

**Level of Evidence -** Level V

Indicate IRB or IACUC: Exempt.

## Pain Medication Prescribing Trends Among Otologists and Neurotologists

Zachary Buxo, MD; Masanari Kato, MD; Lulia Kana, MD; Robert S. Hong, MD, PhD

**Objective:** Describe pain medication prescribing patterns of otologists and neurotologists.

Study Design: Retrospective cohort study.

**Method:** Otologists and neurotologists were identified through the National Plan and Provider Enumeration System National Provider Identifier Registry between 2013-2022 and their respective pain medication claims data through the Medicare Part D Prescribers by Provider and Drug database. Prescribing patterns were then evaluated over time.

**Results:** 195 prescribers were included annually on average ( $\pm 10.4$ ). Opioids were consistently prescribed more frequently than non-opioids. Hydrocodone-acetaminophen was the most prescribed pain medication by volume, totaling 3806 claims by 75.4% of surgeons in 2013 down-trending to 3200 claims by 54.5% of surgeons in 2022. Negative trends by percent of active prescribers were observed in most combination opioids and positive trends in non-combination opioids with oxycodone demonstrating the greatest increase in percent prescribers over time (+9.9%) and hydrocodone-acetaminophen the greatest decrease (-20.9%). Among non-opioids, gabapentin was the most frequently prescribed, accounting for 174 total claims by 3.7% of surgeons in 2013, growing to 1361 claims by 11.5% of surgeons in 2022. Either static or positive trends were observed in non-opioids with gabapentin experiencing the greatest increase in active prescribers over time (+7.8%). On linear regression, absolute claim counts for opioids decreased (-39.7/year) while non-opioids increased (+198.9/year).

**Conclusions:** Opioids consistently remain the most prescribed pain medications among otologist and neurotologists, although steady changes are observed in the profile of medications utilized. Non-opioids appear to be increasingly adopted in practice.

**Professional Practice Gap & Educational Need:** Prescribing patterns of pain medications by otologists and neurotologists are not well-characterized.

Learning Objective: Understand recent trends and underlying rationales in opioid and non-opioid prescribing patterns among otologists and neurotologists.

Desired Result: Increase awareness of appropriate pain medication prescribing practices amongst otologists and neurotologists.

Level of Evidence: Level V

Indicate IRB or IACUC: Exempt

#### Association of Chronic Otitis Media with Rhinologic and Otologic Variations: A High-Resolution Computed Tomography Study

Nazneen Liaqat, MBBS, MRCS-ENT; Israr Ud Din, MBBS, FCPS; Ihtisham Ul Haq, MBBS, FCPS Shakir Ullah, MBBS, FCPS; Zeeshan Ali, MBBS

**Objective:** To compare anatomical variations between diseased and healthy sides of the skull of patients with unilateral chronic otitis media (COM).

Study Design: With-in-subject case-control study

Setting: Department of ENT of Khyber Teaching Hospital, Peshawar, Pakistan

Patients: 50 adult patients with unilateral COM

Interventions: High-resolution computed tomography scans of temporal bone and paranasal sinuses.

**Main Outcome Measures:** Prevalence of rhinologic and otologic anatomical variants in the COM and healthy sides. Statistical comparison using McNemar's test for categorical variables and paired t-tests for continuous variables. Effect sizes (Cohen's d for continuous variables, Cramér's V for categorical variables) and odds ratios (OR) for significant findings.

**Results:** Among rhinologic variants, a deviated nasal septum was more frequent on the COM side compared to the healthy side (19 vs 8; p = 0.05, OR = 2.37), and the angle of septal deviation was significantly larger on the COM side (1.89 ± 2.66 vs 0.46 ± 1.13; p = 0.003, Cohen's d = 0.44). Concha bullosa was more common on the COM side (18 vs 9; p = 0.04, OR = 3.25). Sinus opacification and turbinate hypertrophy showed no statistically significant discordance between the two sides (p > 0.05). Among otologic variants, the mastoid was less pneumatized (4 vs 20) and more frequently sclerotic on the COM side (39 vs 12; p < 0.01, Cramér's V = 0.54). The prevalence and thickness of the Korner septum were similar on both sides (p > 0.05). Eustachian tube lengths were comparable between sides, but the Eustachian tube angle was narrower on the COM side (22.09 ± 1.80 vs 22.90 ± 1.76; p = 0.01, Cohen's d = 0.34). The tubotympanic angle was wider (148.86 ± 3.57 vs 144.76 ± 2.15; p < 0.001, Cohen's d = 0.96), and the pretympanic diameter was smaller on the COM side (3.30 ± 0.77 vs 3.91 ± 0.56; p < 0.001, Cohen's d = 1.01).

**Conclusions:** Significant anatomical differences were observed between the diseased and healthy sides of the skull in patients with unilateral chronic otitis media, particularly in the nasal septum, concha bullosa, mastoid pneumatization, and Eustachian tube anatomy.

**Professional Practice Gap & Educational Need:** There is a lack of awareness regarding the anatomical variants associated with unilateral chronic otitis media, and their potential role in disease pathogenesis. Educating clinicians on identifying and considering these variants could enhance diagnostic accuracy and treatment outcomes in patients with COM.

Learning Objective: To understand the anatomical disparities between the COM-affected and healthy sides in patients with unilateral chronic otitis media, and how these findings may influence clinical decision-making and treatment strategies.

**Desired Result:** Clinicians will improve their understanding of the anatomical factors contributing to chronic otitis media, enabling more precise diagnostic evaluations and personalized treatment plans that address these underlying anatomical issues.

Level of Evidence - Level III

Indicate IRB or IACUC: 495/DME/KMC

# The Upside-Down Approach with a Lazy-S Incision for Osia Implantation

# David Shimunov MD; Huseyin Isildak, MD

**Objective:** To introduce and evaluate the efficacy of an alternative "upside-down" approach with a "lazy-S" incision for the implantation of the OSIA300 bone conduction hearing system, aimed at improving patient comfort, sound localization, and cosmetic outcomes.

**Study Design:** A descriptive case study evaluating surgical outcomes and improvements associated with the modified OSIA300 implantation technique.

Setting: Tertiary care center.

**Patients:** Patients indicated for OSIA300 bone conduction hearing implants, particularly those transitioning from traditional bone-anchored hearing systems (BAHA).

**Interventions:** The intervention involves an "upside-down" approach for OSIA300 implantation, repositioning the actuator and coil for enhanced performance, alongside a "lazy-S" incision to reduce skin tension and improve cosmetic outcomes.

Main Outcome Measures: The main outcomes measured include the absence of surgical and post-operative complications, improved sound localization, and enhanced patient comfort, especially with headwear.

**Results:** The modified technique resulted in successful implantations without complications. Sound localization was improved by positioning the coil closer to the ear canal, and patient comfort was enhanced, particularly in relation to headwear.

**Conclusions:** The "upside-down" approach with a "lazy-S" incision presents several advantages over traditional OSIA300 implantation techniques, offering improved patient comfort, sound localization, and cosmetic outcomes, while simplifying the surgical process. This method is especially beneficial for patients transitioning from BAHA systems.

**Professional Practice Gap & Educational Need:** There is a need for improved surgical techniques that enhance patient outcomes, specifically regarding ease of surgery, comfort in OSIA300 implantation, and transition to OSIA from BAHA system.

Learning Objective: To understand the surgical technique and benefits of the "upside-down" approach with a "lazy-S" incision for OSIA300 implantation.

**Desired Result:** The application of this technique should result in improved patient comfort, better sound localization, and reduced complications.

**Level of Evidence -** Level V

Indicate IRB or IACUC: Exempt.

# Audiologic Outcomes in Temporal Bone Trauma Patients

Nina Gallo, MD; Ashley Kraft, MD; Anna Rawls, BS; Zahide Fang, MD; Rahul Mehta, MD

**Objective:** To evaluate the audiologic outcomes in patients sustaining temporal bone fractures by comparing hearing loss on the ipsilateral side to the contralateral side and to assess the implications for clinical management and patient care.

#### Study Design: Retrospective chart review

Setting: Data was collected from a tertiary medical center.

**Patients:** The study cohort consisted of 431 patients diagnosed with temporal bone fractures between January 2010 and December 2020. Of these, 147 patients had detailed audiologic assessments available for analysis.

**Interventions:** Audiologic data, including pure tone averages (PTA), speech reception thresholds (SRT), and word recognition scores (WRS), were collected and analyzed for each patient. The ipsilateral ear (fractured side) was compared to the contralateral ear (non-fractured side).

Main Outcome Measures: The primary outcomes assessed were PTA, SRT, and WRS in both fractured and non-fractured ears, as well as the impact of facial nerve paralysis on hearing outcomes.

**Results:** The mean PTA was  $36\pm28$  dB on the fractured side versus  $20\pm13$  dB on the non-fractured side. The mean SRT was  $28\pm22$  dB on the fractured side versus  $18\pm12$  dB on the non-fractured side. The mean WRS was  $86\pm26\%$  on the fractured side and  $96\pm10\%$  on the non-fractured side. 77% of fractured ears exhibited serviceable hearing (PTA <50 dB and WRS >50%) compared to 96% in non-fractured ears. Patients with complete facial nerve paralysis demonstrated significantly poorer audiologic outcomes (PTA:  $68\pm38$  dB, WRS:  $58\pm34\%$ ) compared to patients with incomplete paralysis (PTA:  $25\pm15$  dB, WRS:  $94\pm8\%$ ). Higher follow-up rates were observed among patients presenting with subjective hearing loss, vertigo, and cerebrospinal fluid (CSF) leaks.

**Conclusions:** Temporal bone fractures have a considerable impact on hearing outcomes, with significant audiologic differences between fractured and non-fractured ears. Early and targeted audiologic rehabilitation is crucial for optimizing long-term auditory outcomes.

**Professional Practice Gap & Educational Need:** There is a clear need to increase awareness of the audiologic complications associated with temporal bone fractures and to implement early diagnostic and rehabilitative interventions, including routine hearing assessments and tailored rehabilitation strategies.

**Learning Objective:** To understand the impact of temporal bone fractures on audiologic outcomes and recognize the importance of early diagnosis and treatment to optimize hearing recovery.

**Desired Result:** Improved long-term patient outcomes through enhanced follow-up care, targeted audiologic interventions, and better patient education on the risks of hearing loss after temporal bone trauma. Level of Evidence - III

**Indicate IRB or IACUC:** IRB approval was obtained from LSUHSC-New Orleans, University Medical Center New Orleans, and Our Lady of the Lake Baton Rouge (IRB #367428).

#### Decreasing Medicare Reimbursement for Facility-Performed Neurotology Procedures from 2000 to 2024

Julia J. Shi, BA; Rance J. T. Fujiwara, MD; Lisa M. Punnen Hitomi Sakano, MD; Brandon Isaacson, MD

**Objective:** To understand trends in Medicare reimbursement for neurotology procedures from 2000 through 2024.

**Study Design:** The Physician Fee Schedule (PFS) Look-Up Tool from the Center for Medicare and Medicaid Services was utilized to assess reimbursement data for relevant otologic/neurotologic Current Procedural Terminology (CPT) codes from 2000 through 2024. All monetary data were adjusted to 2024 U.S. Dollars using the U.S. Bureau of Labor Statistics Consumer Price Index. Percent changes in reimbursement were calculated.

Setting: Center for Medicare and Medicaid Services

Patients: Not applicable.

Interventions: Not applicable.

Main Outcome Measures: Nominal and inflation-adjusted reimbursement for selected otology and neurotology procedures.

**Results:** The average nominal value of reimbursement for all procedures from 2000 to 2024 increased from \$1400.54 (SD \$714.52) to \$1557.38 (SD \$796.26), representing a 11.2% increase from 2000 to 2024. However, after adjusting for inflation, the average Medicare reimbursement decreased by 33.52% from \$2576.99 (SD \$1314.72) to \$1713.12 (SD \$875.88). Changes in inflation-adjusted reimbursement ranged from -66.43% for CPT code 69714 (osseointegrated implant) to +43.43% for CPT code 61798 (gamma knife radiosurgery). An increase in reimbursement for all CPT codes occurred only in 2024. This increase was associated with the calendar year 2024 PFS final rule, which came into effect on March 9 and increased the PFS conversion factor from \$32.7442 to \$33.2875. From 2000 to 2024, the PFS conversion factor decreased from \$36.6137 to \$33.2875.

**Conclusions:** From 2000 to 2023, Medicare reimbursements for otologic and neurotologic procedures decreased after adjusting for inflation. The only year with an increase in reimbursement was 2024, which saw an increase to the PFS conversion factor. These trends highlight the need for greater awareness of, and agreement on, neurotology reimbursement models amongst surgeons, policy makers, and facility administrators.

**Professional Practice Gap & Educational Need:** Several studies have described temporal trends in Medicare reimbursement rates in otolaryngology, including various subspecialties. No prior studies to our knowledge have described these trends in the otologic and neurotologic setting.

Learning Objective: To understand changes in Medicare reimbursement rates for otologic and neurotologic procedures, differences between nominal and inflation-adjusted values, and how policy changes have impacted reimbursement rates

**Desired Result:** To raise awareness of discrepancies between nominal and inflation-adjusted reimbursement rates and provide evidence for future policy initiatives

**Level of Evidence** – N/A

Indicate IRB or IACUC: Exempt

# 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. All of the AOS grant awards may involve research on any topic related to ear disorders. 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, 2025

If you would like to submit a grant for consideration of funding in the next cycle, 2026-2027, in ONE PDF, include a LETTER OF INTENT and PI BIOSKETCH (NIH template), including details regarding other existing support, and any potential overlap with your mentor(s) must be submitted by November 1st of the year prior to funding. The letter of intent must state the desired grant mechanism for the proposal (CSA, Fellowship grant, Clinical Investigation, or Research grant), the Principal Investigator, and Institution(s), a working title, with an abstract and Specific Aims (2-page limit on abstract and aims). See website for additional formatting instructions. 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 in 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

# A HUGE thanks to the members of the 2024-25 AOS Research Advisory Board

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The Research Advisory Board (RAB) is comprised of seven AOS members, each serving a 7-year term and three consultants, each serving a 5-year term. These individuals are among the most highly respected researchers in our field. The expertise and dedication of the RAB are critical to the success of the mission of the AOS Research Foundation.

Additional information may be obtained from the following: Andrea Vambutas, MD, Executive Secretary, Research Fund of the American Otological Society Email: avambuta@northwell.edu

Kristen Bordignon, AOS Research Fund Administrator Email: <u>administrator@americanotologicalsociety.org</u>

# **COMING SOON!**

A new grant mechanism for Senior investigators/AOS members!

# AOS GRANT PROGRESS REPORTS - FUNDING CYCLE JULY 1, 2024 - JUNE 30, 2025

American Otological Society Fellowship Grant – Progress Report

Progress Report Period: 07/01/2024 - 02/10/2025

Principal Investigator: Aray Adylkhan

Mentor: Xiaowei Lu

**Project Title:** Mechanisms of phospho-regulation of PCDH15 in hair bundle morphogenesis and function **Background:** 

The V-shaped hair bundle atop auditory hair cells is essential for mechanotransduction (MET) of sound. Extracellular filaments, including kinociliary links and tip-inks, are crucial for hair bundle development and function. PCDH15, an important component of multiple extracellular links in the developing and mature hair bundle, exists in three alternatively spliced variants (CD1, CD2, and CD3), each characterized by a unique cytoplasmic domain. PCDH15-CD2 (referred to as CD2 hereafter) is a key component of both kinociliary links during development and tip-links in mature hair cells<sup>1,2</sup>. While mutations in PCDH15 cause Usher syndrome with congenital deafness and blindness<sup>3,4</sup>, the regulatory mechanisms controlling PCDH15-containing links remain poorly understood. Our lab recently discovered that Wnt/G protein signaling regulates hair bundle morphogenesis through effector kinases including AKT, PAK and GSK3β<sup>5</sup>. We hypothesize that phosphorylation of PCDH15-CD2's C-terminal tail by these kinases influences hair bundle development and function. Using immunoprecipitation (IP) followed by mass spectrometry analysis, we discovered three potential phosphorylation sites within the cytoplasmic domain of PCDH15-CD2 when expressed in heterologous cells. Our biochemical studies in HEK293 cells showed that these phosphorylations affect how CD2 interacts with its known binding partner. This study aims to explore this further and investigate the physiological relevance of PCDH15-CD2 phosphorylation.

**Aim 1:** Determine the role of phospho-regulation of PCDH15-CD2 in hair bundle morphogenesis *in vivo*.

We hypothesize that the phosphorylation of CD2 is important for maintaining stable kinociliary links and guiding proper hair bundle development. To test this, we have generated knock-in mouse models with specific phosphorylation site mutations in PCDH15-CD2 using CRISPR/Cas9 gene editing (Fig.1). We examined hair bundle morphology at postnatal day 0 (P0) using immunofluorescence microscopy and determined precise PCDH15-CD2 subcellular distribution patterns using super-resolution imaging techniques.



Figure 2. (A, C) Kinocilium positioning in control (A), and CD2<sup>AAAA</sup>(C). Arrowheads indicate an off-center kinocilium; (B, D) Quantification of the kinocilium index in control and (B) CD2<sup>5177651776D</sup> and (D) CD2<sup>AAAA</sup> knock-in mice. Mean ± s.d.: One-way ANOVA with Tukey's Post-test. <u>Progress:</u> Our analysis of kinocilium positioning and hair bundle orientation revealed distinct phenotypes across

multiple CD2 phosphomutants. CD2<sup>AA/AA</sup> and CD2<sup>S1776D/S1776D</sup> subtle but statistically significant kinocilium positioning defects, as quantified by kinocilium positioning index measurements in both inner and outer hair cells at P0 without significant hair bundle misorientation (Fig.2). In contrast, initial analysis of CD2<sup>4A/AA</sup> showed that there are no significant alterations in kinocilium position, but there is a mild hair bundle

misorientation (Fig. 3). Based on our biochemical studies, we initially

predicted that the CD2<sup>4A/4A</sup> mutation would result in severe developmental defects comparable to CD2 knockout mice. However, our analysis at P0 revealed surprisingly mild phenotypes, which suggests that CD2 phosphorylation plays a minor role in hair bundle development than initially predicted. Analysis of CD2 expression in phosphodeficient mice at postnatal day 0 (P0) using deconvolution microscopy revealed significant alterations in protein distribution in CD2<sup>4A/4A</sup> mutants. (Fig.4A) Preliminary quantification showed that CD2 signal intensity, when normalized to F-actin levels, was reduced by 30% in phosphodeficient mutants compared to wild-type controls (Fig.4B). Beyond changes in intensity, we observed distinct differences in both the spatial distribution and organizational patterns of CD2 staining in the mutants. To better characterize these changes, we employed tau-STED microscopy for detailed structural analysis of CD2 localization relative to



Figure 1. Sequencing data from WT and knock-in mice carrying phospho-mimetic and phospho-deficient mutations in PCDH15-CD2.

A CO2 \*\*\* CO2

Figure 3. (A) Kinocilium positioning and HB orientation in control and CD2<sup>4A4A</sup>. Arrowheads indicate an off-center kinocilium; (B) Quantification of the kinocilium index and (C) HB angle in control and CD2<sup>4A4A</sup> knock-in mice. Mean ± s.d.: Mean ± s.d.: One-way ANOVA with Tukey's Post-test

kinocilium. Our analysis revealed that in phosphodeficient CD2<sup>4A/4A</sup> mutants, CD2 showed reduced coverage, decreased signal intensity, and more diffuse distribution at P0, suggesting phosphorylation affects CD2's targeting to hair bundle (Fig. 4C, D). Ongoing experiments are aimed to optimize staining conditions for CD2 localization at later developmental stages (P6 and P15) using TSTED microscopy to assess CD2 distribution in tip links after the onset of mechanotransduction (MET). This work will be completed during the spring semester.

**Aim 2:** Evaluate hearing function in PCDH15-CD2 phospho-mutant mice.

We hypothesize that phosphorylation of PCDH15-CD2 can influence tip-link tension and

mechanotransduction in mature hair cells, thereby affecting the hearing function. To evaluate hearing

CD2 4MA CD2

Figure 4. (A) Deconvolution microscope images of CD2<sup>44/4A</sup> and CD2<sup>WT</sup>stained with CD2, F-actin and acetylated tubulin at P0. (B) Preliminary quantification of CD2 intensity in hair bundle normalized to F-actin in control and CD2<sup>44/4A</sup> using images taken with Deconvolution microscope. Mean  $\pm$  s.d.: Mann-Whitney test. (C) CD2 localization to the tips of stereocilia and the kinocilium using  $\tau$ STED mice at P0 and (D) corresponding zoomed-in images of the Outer Hair Cells. Scale bar: 5 µm.

function over time, we performed auditory brainstem response (ABR) testing at 1, 2-2.5, and 4-4.5 months of age (Fig. 5). The analysis revealed elevated ABR thresholds in CD2<sup>4A/4A</sup> mutants, particularly at high frequencies (22 kHz and 32 kHz). The high-frequency hearing impairment starts at 1 month of age and persists through 5 months. These results suggest that the phosphorylation of CD2 may play a role in auditory function in mature hair cells, particularly in the mechanotransduction process. The increase in thresholds may indicate

a decrease in tip-link tension due to disrupted interactions of CD2 in lower tip-link densities.

To further address this aim, we will quantitatively assess how phosphorylation affects CD2's molecular interactions by measuring binding affinities between CD2 phosphopeptides and their protein partners



using a Fluorescence Polarization assay. Second, in collaboration with Ulrich Mueller's lab we plan to analyze mechanotransduction currents in CD2 phosphomutants using electrophysiological assays and finally examine hair bundle ultrastructure in adult mutants using scanning electron microscopy. These experiments will be performed in the spring semester.

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#### American Otological Society-Fellowship grant. Six-month progress report: July 10, 2024- January 10, 2025. Principal investigator: Isabel Aristizabal-Ramirez. Mentor: Gregory I. Frolenkov. Title: Molecular Mechanisms Mediating Activation of the Mechano-Electrical Transduction Channel in Mammalian Auditory Hair Cells

Mammalian auditory hair cells detect sounds with the frequencies higher than 20 kHz [1], which means that their mechano-electrical transduction (MET) channels must open in 10µs or less. However, it is unclear how exactly the tip-link force is conveyed to the MET channel on such a fast time scale. The activity of ion channels is often modulated by accessory subunits and/or local stretch of the plasma membrane. The Calcium and Integrin-Binding protein 2 (CIB2) is an accessory subunit of the MET channel and its absence in the auditory hair cells causes loss of mechanotransduction [2, 3]. In contrast to the auditory hair cells, vestibular hair cells express both CIB2 and CIB3. Since CIB3 rescues MET current amplitude in  $Cib2^{-/-}$  auditory hair cells, and only the absence of both, CIB2 and CIB3 results in vestibular abnormalities, these two proteins are thought to be redundant. However, it is yet unknown why the auditory hair cells express only CIB2. Deafness-related mutations in *Cib2* cause mis-localization of BAIAP2L2 [4, 5], a membrane-associated protein, and, as we recently showed, result in slow MET channel activation in auditory hair cells [5]. Therefore, the overall hypothesis of this project is that *CIB2 confers faster MET complex kinetics than CIB3 by differential recruitment or retention of membrane*.

associated proteins to the stereocilia tips.

## **Progress:**

In the past six months, considerable progress has been made. For Aim 1, we acquired an ultra-fast patch clamp amplifier with bandwidth of >250 kHz and I successfully integrated it into my setup. Aim 2 is near completion as described below.

Study 2.1: Determine the effects of BAIAP2L2 in MET current kinetics: Whole-cell patch-clamp experiments were used to record MET currents elicited by fast deflections of the stereocilia bundle ( $\sim 5\mu s$ ) in wildtype outer hair cells (OHCs) after mis-localization of BAIAP2L2 by blocking MET channels with tubocurarine (Fig. 1A). To prevent rapid recovery of BAIAP2L2 to the stereocilia tips, I kept the organ of Corti in tubocurarine and perfuse HBSS to individual hair bundles to unblock the MET channels and record MET currents (Fig. 1B). The control group was incubated for two hours in supplemented media without tubocurarine.





<u>Results:</u> Local perfusion with fresh HBSS effectively unblocks transduction channels as evidenced by individual MET current traces (Fig. 1B) and comparable MET current amplitudes in control and tubocurarine- treated OHCs were obtained (Fig. 1C). Time constants of MET current activation were calculated through a single-Boltzmann fit. These calculations showed that tubocurarine-treated cells had significantly slower MET current activation are compared to control OHCs (Fig. 1D). It is worth mentioning that these differences in MET current activation are

not a consequence of small MET currents (Fig. 1C). Thus, the loss of BAIAP2L2 from MET complexes in wild type OHCs decreases the efficiency of channel gating, presumably through local mechanical changes in the plasma membrane. However, the loss of BAIAP2L2 from MET complexes does not affect the relationship between MET current amplitude and hair bundle displacement (I-X curve) (Fig. 1E). Although these results are still preliminary and more data collection is still needed, one possibly interpretation is that the membrane-associated protein BAIAP2L2 is needed for fast channel gating but does not change the intrinsic sensitivity of the channel to sustained tip-link tension. To further explore the local plasma membrane effects of mis-localizing BAIAP2L2 from the stereocilia, I will label PIP2, known to regulate MET current properties [6], after tubocurarine incubation.

*Study 2.2: explore the differences in CIB2 and CIB3 interactions with membrane-associated protein BAIAP2L2:* There is limited evidence suggesting direct interactions between CIB2 and BAIAP2L2 [4]. Therefore, it is still unclear how mutations in *Cib2* could result in abnormal localization of BAIAP2L2. In addition, whether CIB3 can interact with BAIAP2L2 has not been studied. To explore this, we are using fluorescence polarization (FP) assays where purified CIB2, CIB2 p.R186W or CIB3 are incubated with a fluorescently tagged BAIAP2L2 peptide containing the predicted interacting region with CIBS (based on AlphaFold simulations provided by Dr. Craig Vander Kooi at the University of Florida). The FP index is directly proportional to the amount of BAIAP2L2 peptide interacting with CIB protein in solution. Since CIB proteins have Ca<sup>2+</sup>-binding domains, I also measured the FP index at high or low Ca<sup>2+</sup> concentrations (5mM CaCI or 5 mM EDTA respectively) to evaluate if Ca<sup>2+</sup> mediates CIB2-BAIAP2L2 interactions.

Results: The data shows higher FP indexes with 5mM EDTA, suggesting more robust CIB2-BAIAP2L2 binding at low Ca<sup>2+</sup> concentrations (Fig. 2A). This result may be physiologically relevant considering the stereocilia Ca2+ concentration is ~12 µM according to our estimates. The following experiments were conducted using 5mM EDTA. Increased polarization indexes were achieved with greater concentrations of both CIB2 and CIB2 p.R186W. However, the wildtype CIB2-BAIAP2L2 samples had higher FP indexes than CIB2 p.R186W-BAIAP2L2, suggesting that the R186 residue of CIB2 may be involved in binding BAIAP2L2 (Fig. 2B). My next step is to repeat these experiments but using purified



Figure 2: In-vitro interactions between CIB2, CIB2 p.R186W and CIB3 and BAIAP2L2. Polarized light was measured as an indicator of protein interactions in constant concentration (1:500) of fluorescently tagged Nterminus BAIAP2L2 after: A) Increasing concentrations of CIB2 (0.02-50  $\mu$ M) in 5mM EDTA (black circles) or 5mM CaCl (blue triangles). B) Same concentrations of BAIAP2L2 peptide and EDTA as in A) at increasing concentrations of CIB2 and CIB2 p.R186W (0.02-50  $\mu$ M). C) Agarose gel containing purified CIB3 after affinity and size exclusion chromatography (right and middle lane) and loading control (left lane).

CIB3 (Fig. 2C) and BAIAP2L2 to compare qualitatively the affinity of CIB2 and CIB3 interactions with BAIAP2L2. I will also use Differential Scanning Fluorimetry (DSF) assays to validate the above mentioned results.

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# AOS RESEARCH GRANT: PROGRESS REPORT

# BACKGROUND

Since cochlear implantation was approved for treatment of single-sided deafness (SSD) in 2019, a rapidly growing body of work has supported its use to optimize performance on tasks of binaural hearing<sup>1–12</sup>, including speech perception in noise<sup>2,12</sup>, the ability to perceive spatially separate speech stimuli<sup>13,14</sup>, and localization of sounds in space<sup>1,7,15–18</sup>. Several individual studies<sup>15,19–21</sup> and recent meta-analyses<sup>22–28</sup> propose cochlear implants (CI) for SSD may improve understanding in background noise; however, limited data on non-users shows similar gain on clinical speech tests between implant users and non-users<sup>29</sup>, suggesting improvements demonstrated on research tasks may not accurately reflect real-world benefit. Systematic reviews investigating the magnitude of benefit for localization have demonstrated similar conclusions<sup>23</sup>, but the strength of the results has been limited by both the heterogeneity of the study methods and the subject performance variability. The challenge of interpreting these results is compounded by the artificial nature of traditional audiometric evaluation and the need for a novel approach to assessment of suprathreshold binaural hearing performance.



Figure 1. Mean absolute error by signal-to-noise ratio for normal hearing and SSD subjects during complex speech localization task. Repeated measures ANOVA, to compare SSD with and without CI, revealed a significant effect of CI status [F=4140, p<0.001] and SNR [F=19.0, p<0.001].

head movements in subjects with SSD by comparing performance both with and without CI to individuals with normal hearing (Aim 2a) and describe the resulting acoustical cues (Aim 2b). Taken together, the results will lead to better understanding of how behavioral adaptations due to SSD change the acoustical information arriving at each ear and impact the availability of binaural cues to effect complex binaural task performance.

AIM1. Localization Accuracy. We will employ multiple metrics of localization accuracy (including mean absolute error. localization function slope and regression analysis, and circular statistics) to compare localization of speech in background noise with non-salient

Here, we propose a study to characterize compensatory head movements and resulting binaural acoustical cues for patients with single-sided deafness during localization testing and a complex and novel speech-in-noise task. The overall objective of this proposal is to evaluate the effects of cochlear implant use on ecologically valid speech localization performance and examine the resulting behavioral adaptations of individuals with unilateral deafness.

To accomplish this objective, subjects will participate in a novel speech-in-noise task with stimuli presented from random locations along an azimuthal array during and which they are allowed to move their heads. A radiofrequency tracking system will be used to capture head position and ear-level probe microphones will measure acoustical cue input to each ear. We will first compare localization performance between speech and non-speech stimuli for subjects with SSD and normal hearing (Aim 1a) and measure the effect of cochlear implant use (Aim 1b). Next, we will characterize compensatory



broadband and narrowband stimuli. Progress: We have completed data collection for the planned cohorts (normal hearing, n=28 and SSD with and without CI, n=12), with additional data collected for 8 SSD subjects using bone conduction implants and 10 traditional CI candidates with bilateral implants. Analysis of localization by absolute error (Figure 1) and slope (Figure 2) by performance group are presented with speech performance in noise data (Figure 3) in two manuscripts (one accepted to Otolaryngology—Head and Neck Surgery and one submitted). A third manuscript evaluating the impact of acute plugging in normal hearing subjects (a secondary project) has also been submitted. Data analysis for a fourth manuscript in preparation comparing the metrics (mean absolute error, localization function slope and regression analysis, and circular statistics) is being completed with anticipated submission before the end of the academic year.

AIM2. Head Movement and Ear-Level Acoustical Cues. We will complete granular assessment of head movement patterns by quantifying movement delay, response time, and absolute displacement, then measure the resulting impact of head positioning on ear-level acoustical cues.



Figure 3. Speech performance by SNR for all groups (A) and by presentation direction for unaided (B) and aided (C) SSD subjects. Error bars represent the SEM.



Figure 4. Head movement data by SNR and target azimuth, corrected for side of deafness (positive values indicate targets to the normal hearing ear).



Figure 5. Interaural time and level differences extracted from ear-level microphone data, overlayed on head position in degrees azimuth, demonstrating the ability of acoustical measurements to predict head position.

Progress: Data has been collected and analyzed for the same groups as in AIM1, with submitted manuscripts as detailed above. In examining absolute head displacement, NH subjects were proportional relative to the target source, while SSD subjects demonstrated less variability, with no significant difference between displacements toward the deaf or hearing ear. NH subjects initiate head movement shortly after stimulus onset, while SSD subjects waited longer, in some cases until after stimulus presentation. SSD subjects also demonstrated reduced overall response time. Analysis of microphone data is underway, with early results demonstrating systematic cue change commiserate with head movement.

Data collected here will provide the foundation for development of more ecologically valid, clinical tasks of binaural hearing that will be used both to assist clinicians in *identifying and counseling optimal* surgical candidates and to allow SSD patients to realize the best possible hearing performance outcomes.
## Accomplishments – Fellow Grant – Kevin TA Booth, PhD – 6 Month Progress Report – Feb. 2025

Proper variant interpretation is fundamental to precision medicine. Misclassification can lead to missed or incorrect diagnoses, resulting in inappropriate clinical management. In hearing loss, where genetic testing is standard of care, accurate variant classification informs diagnosis, intervention decisions, and syndromic surveillance. Most critically, it determines patient eligibility for gene therapy trials, where distinguishing individuals who may benefit from treatment is paramount.

A key but underrecognized contributor to genetic disease is RNA splicing defects. Pathogenic variants can disrupt splicing, leading to nonsense-mediated decay (null alleles) or the production of aberrant proteins with dominant-negative, gain-of-function, or loss-of-function effects. Identifying these variants is essential not only for accurate classification but also for developing targeted therapeutics. Splicing defects are increasingly viewed as treatable through antisense oligonucleotides (ASOs), small molecules, or CRISPR-based approaches.

Despite their importance, splicing defects remain difficult to predict. Current variant interpretation pipelines rely heavily on in silico predictors, which often yield conflicting results. Experimental validation is necessary but traditionally relies on minigene assays or patient-derived transcript analysis—methods that are slow, low-throughput, and impractical for large-scale variant assessment. Given the growing number of variants identified through genetic testing, a high-throughput, scalable assay for experimentally assessing splicing effects is urgently needed.

This project develops a massively parallel assay to assess the impact of thousands of variants on RNA splicing simultaneously. Unlike the conventional variant-by-variant approach, which is labor-intensive and lacks scalability, this method employs barcoded minigene constructs to systematically evaluate splicing alterations across thousands of variants. Insights gained will enhance variant classification, improve splicing prediction tools, and guide the development of novel computational models for splicing prediction.

### **Progress to Date**

In the first six months of the funding period, we have successfully designed and optimized a scalable cloning and barcoding strategy to assess variant impact on RNA splicing, with a focus on the *OTOF* gene. Key achievements include:

**Library Construction**: We have successfully generated four variant libraries, each comprising approximately 500 variants. Each variant is represented by >5 independent barcodes, ensuring robust coverage and technical replicability in downstream analyses.

**Expanded Analysis Window**: While initially we proposed to focus on exonic variants, we have expanded our analysis window to include regions spanning ±20 base pairs of the exon-intron boundary. This enables the identification of intronic variants that impact RNA-splicing, which are frequently overlooked in clinical interpretation, but captured in most genetic testing pipelines.

**Optimization of Data Processing Pipelines**: We have developed a computational pipeline to analyze highthroughput sequencing data from our splicing assay, allowing for the quantification of exon inclusion/exclusion events and identification of aberrant splicing products.



Figure 1. Barcode Count Distribution for Nucleotide Substitutions in Exon 3. The plot represents barcode counts for nucleotide substitutions at various positions within Exon 3. The x-axis denotes the wildtype nucleotide, while the y-axis represents barcode count. Different nucleotide substitutions are color-coded and shape-coded: T (red Xs), A (blue circles), G (purple triangles), and C (green squares). The exon structure is illustrated at the bottom, with an increasing positional scale from left to right. This figure highlights the variability barcode in counts associated with different nucleotide changes within the exon.

# **Future Directions**

Moving forward, we plan to:

- Scale Up Variant Testing: Expand the assay to additional hearing loss-associated genes, with an emphasis on syndromic and non-syndromic genes with high clinical testing rates.
- Correlation with Clinical Data: Compare experimentally derived splicing effects with clinical classification data to refine interpretation frameworks.
- Integration with Splicing Prediction Models: Use assay results to evaluate the accuracy of commonly used in silico prediction tools and inform the development of next-generation computational models.



**Figure 2. Distribution of CADD Scores and SpliceAl Predictions by Classification.** (Top) Violin plot of CADD scores across variant classifications. (Bottom) Scatter plots comparing SpliceAl-predicted donor (DL vs. DG) and acceptor (AL vs. AG) effects. Points are colored by classification: benign (blue), pathogenic (orange), and VUS (gray).

The AOS Fellow Award has been instrumental in providing the preliminary data necessary to expand this research. The progress made thus far has directly contributed to several competitive grant applications: The Showalter Trust Award – Submitted to Indiana University School of Medicine (currently under review), MIRA R35 Grant Proposal – Submitted to the NIGMS (currently under review), and an R01 Grant Proposal – In preparation for submission to the NIDCD (anticipated submission date: June 2025). The data generated from this project have laid a strong foundation for future work, and I am eager to continue developing this research program, made possible through the generous support of the AOS Fellow Award. The ongoing work will not only advance our understanding of splicing defects in hearing loss but will also contribute to broader efforts in precision medicine by establishing a scalable framework for experimental variant classification.

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 <u>overriding goal</u> 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 8<sup>th</sup> 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 31 participants for Aim 1 and have an additional 15 participants targeted for enrollment this year. Participants have been 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. Uniformity in array (CI 632) allows comparison of eCAP and CIM measures without confounding elements related to array specific differences (e.g. electrode contact size and spacing).

Since the last report, we have unblinded the initial phase of this trial and identified a clear diverging trend of impedance change in standard vs "Dex" CI recipients. "4-point" bipolar impedances are influenced by local, electrode-adjacent changes, including neo-ossification and fibrosis. **Figure 1** demonstrates a gradual increase

in basal- and mid-implant electrode contact impedances in the standard group, as compared to relatively stable and lower impedance measures across all electrodes in the "Dex" CI group. A similar trend is seen in other complex impedance measures, including access resistance (not pictured). Interestingly, standard CI impedance values show continued change at 12 months post-CI (in the standard CI group). These results suggest (1) post-CI fibrosis and neo-ossification continues to increase in the cochlear base until



**Figure 1.** Plot of 4-point impedance values across electrode pairs, measured at activation, 6- and 12 months-post CI. Control (black) CI show initial low impedance at activation with a persistent rise, most predominant at basal electrode pairs. Dex (red) CI show stable, low impedance values across timepoints.

at least 12 months post-CI and (2) dexamethasone-eluting Cis may significantly and durably mitigate the post-CI tissue response. Preliminary analysis (not pictured) of PCCT images at 1- and 12-months post-CI show increased scala tympani volume intensity over time in the standard CI group, suggestive of progressive fibrosis and neo-ossification, whereas Dex-CI scala tympani volume intensity is relatively stable over time.

# 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 neoossification and classify it according to established osteogenic processes. Further, we planned to broadly explore the role of neo-angiogenesis in cochlear neo-ossification and identify relevant osteogenic signaling pathways and precursor cellular populations.

We have observed a mosaic pattern of neo-ossification in the post-CI mouse cochlea that is characterized by cartilage intermediates, which begin mineralizing by day 21-28 days post-CI (**Figure 2C**). Multiple observations suggest post-CI cochlear neo-ossification predominantly forms through endochondral ossification (as opposed to direct endosteal extension): 1) Bone formation is preceded by cartilage intermediates on Movat's Pentachrome staining 2) An influx of Sox9+ cells (chondroblast markers) precedes an influx of Runx2+ cells (osteoblast marker), consistent with a process of osteogenic differentiation of chondroblasts (**Figure 2 A,B**).

Endochondral ossification is often associated with hypoxic signaling processes and neo-angiogenesis. We have utilized a PECAM1-GFP reporter mouse to track neo-angiogenesis post-CI. Platelet endothelial cell adhesion molecule-1 (PECAM1; CD31) is a marker for endothelial cells and neo-angiogenesis. We have observed a process of scala tympani neo-angiogenesis starting post-op day 5, peaking near post-op day 10, but persisting out to 21 days post-CI (**Figure 2D-F**). We hypothesize the baseline hypoxic and acellular nature of the central scala tympani provides a hypoxic stimulus driving neo-angiogenesis and neo-ossification. Last report, we described the effect of macrophage suppression post-CI has on decreasing neo-ossification. We hypothesize macrophage tissue remodeling may enable fibrin clearance to allow the neo-angiogenesis permissive for neo-ossification; with macrophage suppression, excessive fibrin deposition blocks this process.

# **Future Directions:**

For Aim 1, we project exceeding our recruitment target of 40 patients by the end of year 2. eCAP and PCCT scan data are currently being analyzed to compliment impedance data (Figure 1). We anticipate the final results of this aim will (1) demonstrate the time course of post-CI neo-ossification (2) define the clinical significant of post-CI neo-ossification and (3) provide an assessment of the sensitivity of CIM and eCAP derived measures in detecting post-CI neo-ossification.

For Aim2, we have documented endochondral ossification occurring after CI and hypothesize macrophage activity facilitates this process partially through tissue-remodeling permissive of neo-angiogenesis. Moving forward, we are planning single-cell RNAseq investigations in the mouse CI model, aiming to (1) identify cochlear precursor cells of neo-ossification through



Figure 2. (A-E) Yellow dashed lines outline basal scala tympani in mid-modiolar mouse cochlear sections. (A) 21 days post-CI: infiltration of Runx2+ osteoblasts corresponding to neo-ossification. (B) 10 days post-CI: infiltration of Sox9+ chondroblasts corresponding to cartilage formation as part of endochondral ossification. (C) 28 days post-CI: Movat's Pentachrome stain demonstrating cartilage formation (yellow "C") and neo-ossification (blue "B") adjacent to CI tract (red "CI"). 10 days post-CI implanted (D) and control (E) cochleae with PECAM-GFP marking neo-angiogenesis. (F) Neo-angiogenesis quantified as volume of PECAM-GFP+ staining peaks 10 days post-CI in the basal scala tympani, "STB", and at 21 days in the basal lateral wall, "LWB", in implanted left, "Lt", cochleae, with near-zero neo-angiogenesis seen in non-implanted right, "Rt", cochleae.

trajectory analysis and (2) further interrogate signaling pathways critical to neo-ossification, including those involved in hypoxic signaling and neo-angiogenesis.

American Otological Society Clinical Investigations Grant Funding Period: 07/10/24-06/30/25 PI/PD: Daniel Romano, MD Mentors: Keiko Hirose, MD and Sid Puram, MD PhD Title: Single-Cell RNA Sequencing Analysis of Cholesteatoma Pathogenesis

## **OVERVIEW**:

Cholesteatoma is an otologic disease defined by the abnormal presence of keratinizing stratified squamous epithelium in the middle ear and/or mastoid bone, with complications ranging from hearing loss to facial nerve injury, and even potentially life-threatening intracranial extension and infection. Complete surgical removal is the exclusive available treatment for cholesteatomas, with published 5-year recurrence rates of 21-38%. Cholesteatoma management is especially important and challenging in children because: 1) 5-year recurrence rates in children < 16 years-old are twice as high as those in adults; 2) repeated surgeries are disruptive and stressful for children and families; 3) cross-sectional imaging performed for diagnosis and operative planning exposes children to ionizing radiation and sometimes sedation; and 4) even a mild, transient, or unilateral hearing impairment can seriously impact the academic outcomes, behavioral performance, and speech-and-language development of children. Novel therapies could decrease the morbidity that is associated with cholesteatoma management in children. However, the development of new treatments will require a greater understanding of cholesteatoma pathogenesis. Here, we hope to significantly improve understanding of the molecular mechanisms underlying cholesteatoma pathogenesis and recurrence in children with single-cell RNA-seq).

### ACCOMPLISHMENTS:

- 1. Developed an optimized single-cell dissociation protocol for scRNA-seq of human cholesteatoma tissue, with:
  - a. An ability to obtain adequate numbers of single cells from tissues as small as 25 mg
  - b. Cell viability consistently greater than 80%, and greater than 90% for most samples
- 2. Generated high-quality, single-cell suspensions and single-cell cDNA libraries for surgical cholesteatoma samples from n = 9 patients with the assistance of the Washington University Genome Technology Access Center (WashU GTAC) at the McDonnell Genome Institute, with:
  - a. Feature barcode matrices obtained for n = 7 samples thus far
  - b. Preliminary scRNA-seq analysis completed for n = 5 samples thus far
  - c. n = 2 samples currently awaiting sequencing
- 3. Collected n = 37 cholesteatoma samples from patients for histology, immunohistochemistry, and spatial expression studies (i.e., Visium HD)
- 4. Collected n = 29 cholesteatoma samples from patients in RNALater for traditional RNA sequencing
- 5. Submitted an abstract on this project for the AOS meeting at COSM 2025 and invited to present at a podium session

**AIM 1:** <u>Characterize the inter- and intracellular signaling pathways associated with cholesteatoma keratinocyte</u> proliferation in the pediatric age-group and compare these pathways to those in post-auricular skin.

Background: Traditional molecular techniques have shown that cholesteatomas are not simply ectopic growth of normal skin tissue. Numerous cytokines and growth factors are overexpressed in cholesteatomas, and some are associated with ossicular erosion. complications, and recurrence. Cholesteatomas demonstrate dysregulation of JAK/STAT signaling, and previous research supports a model in which paracrine signaling from the perimatrix (the outer subepithelial layer of a cholesteatoma) stimulates the uncontrolled proliferation of cholesteatoma keratinocytes. However, the specific details remain elusive, and there is a



Figure 1: (A) An acridine orange and propidium iodide (AO/PI)-labeled single-cell suspension generated from a surgical cholesteatoma specimen, as visualized on a Luna-FL cell counter. Live cells are green, with red denoting cells with compromised cell membrane integrity (i.e., dead or dying). (B) Single cell quality data from n = 13 specimens dissociated using our optimized protocol (Note: n = 1 sample is not included because of low viability attributed to incubator malfunction and specimen overheating).

need for research that clarifies: 1) the driver genes of uncontrolled keratinocyte proliferation in cholesteatomas, 2) the upstream autocrine and paracrine messenger molecules, and 3) the regulatory networks and signaling pathways involved in cholesteatoma pathogenesis. scRNA-seq provides the single-cell and tissue-level resolution necessary to begin elucidating these mechanisms. Ultimately, an improved understanding of the underlying mechanisms of cholesteatoma pathogenesis may allow for the identification of potential target molecules for alternative or adjuvant medical therapies.

Progress: Here, we proposed performing scRNA-seg on human cholesteatoma tissue to elucidate the molecular mechanisms underlying cholesteatoma keratinocyte proliferation in children. At the suggestion of the reviewers, we have included adult patients in the scRNA-seg studies too. To date, we have enrolled n = 87 patients who underwent surgery for a clinical diagnosis of cholesteatoma, resulting in inclusion of n = 68 patients with an intraoperatively confirmed cholesteatoma diagnosis and enough tissue for collection and/or processing (n = 19 patients were consented for sample collection based on clinical history and imaging, but without cholesteatoma present at the time of surgery). Some samples were not able to be used for single cell studies due to time of day and the hours of operation of WashU GTAC and/or inadequate sample size for single cell processing and were preserved for other experiments. We have preserved n = 29 surgical cholesteatoma samples in RNALater for traditional RNA sequencing, and formalin fixed and paraffin embedded (FFPE) another n = 37 samples for future high-resolution spatial transcriptomics. We used samples from n = 16 patients to validate and optimize a single-cell dissociation protocol for human cholesteatoma tissue, testing a variety of digestion enzymes, durations and additives. Our current protocol for the dissociation of cholesteatoma into single cells yields an average of  $1.07 \times 10^4$  (range =  $2.96 \times 10^2 - 5.71 \times 10^4$ ) live cells /mg tissue, with an average viability of 95.1  $\pm$  5.2% (S.D.) (Fig 1). With this, we have now performed scRNA-seq on n = 9 cholesteatoma samples. Analysis is ongoing as we continue to acquire and process more samples. An interim analysis of scRNA-seg datasets from n = 5 patients shows a rich array of cell types, including pericytes, neutrophils, melanocytes, keratinocytes, mononuclear phagocytes (e.g., monocytes, macrophages), and endothelial, dendritic, Schwann, mucosal, plasma, and mast cells in both adult and pediatric cholesteatoma samples, with some cell types (e.g., neutrophils in pediatric) noticeably more abundant in one group or the other (Fig 2). Preliminary differential expression analysis has revealed a number of significantly down- and upregulated genes in pediatric vs adult cholesteatoma cells.



Figure 2: UMAP plot of 36,792 cells from n = 5 patients, (A) colored by cell type and (B) study group.

#### AIM 2: Determine molecular correlates of age in pediatric cholesteatoma specimens.

*Background:* Age is an important predictor of postsurgical cholesteatoma recurrence: 5-year recurrence rates in children < 16-years-old are over two times as high as those in adults, and increase with each year younger than 16 years by 7% /year. However, whether molecular factors contribute to the increased recidivism in younger children remains unknown. Although KGF/KGFR double-positivity and Ki-67 labeling index have both been associated with postsurgical cholesteatoma recurrence, the exact roles of these genes in recurrence – and whether they are related to clinical risk factors such as age – are not well-understood. Identification of single genes that correlate with patient age may provide insights into the molecular mechanism(s) of recurrence. Ultimately, an improved understanding of the molecular factors involved in postsurgical cholesteatoma recurrence may allow for the identification of molecular predictors of recurrence.

*Progress:* Here, we proposed using scRNA-seq to determine cholesteatoma transcriptional signatures that are significantly associated with age. We have now performed scRNA-seq on n = 9 cholesteatoma samples. We plan to perform this analysis when we have a larger number of scRNA-seq samples.

# American Otological Society, Research Grant – Progress report – Funding period 07/01/2024-06/30/2025

# Principal investigator: Philippe Vincent, PhD

# Functional assessment of regenerated synapses in vitro between inner ear hair cells and sensory neuron progenitors.

Background: Ribbon synapses between inner hair cells (IHCs) and type-I spiral ganglion neurons (SGNs) are responsible for sound encoding in the inner ear. Mechanical sound waves trigger action potentials on type-I SGNs that are conveyed to the brain. However, in response to noise exposure, the excessive release of glutamate from IHCs often leads to ribbon synapse damage and to the retraction of SGN endings from IHCs and sometimes to SGN death. Although no therapeutics are available to restore those synapses in humans, one promising regenerative strategy currently developed is the engraftment of sensory neuronal progenitors (NPs), derived from human induced pluripotent stem cells (hiPSCs), into the cochlear nerve trunk to replace damaged SGNs. This approach has demonstrated that engrafted NPs do reach IHCs and tend to form new synapses, based on immunolabeling and measurement of auditory brainstem responses. However, the specific functional properties of these new synapses and their ability to encode sound signals have never been assessed. The goal of our study is therefore to compare the functional properties of regenerated IHC/NP synapses with the encoding properties of native IHC/SGN synapses to evaluate the regenerative potential of neuron progenitors in forming synapses suitable for sound encoding.

We recently published our article describing the *in vitro* co-culture method developed to assess the properties of regenerated IHCs/SGN synapses (Vincent et al., 2024; DOI: <u>https://doi.org/10.1073/pnas.2315599121</u>). In this research article, we highlight how this co-culture approach along with the EPSC deconvolution analysis can be used to identify newly formed synapses and characterize their encoding properties.

# Aim 1. Assessment of functional properties of regenerated synapses between IHCs and sensory NPs

Here, we propose to use an in vitro coculture model in which denervated Corti. expressing organs of channelrhodopsin in hair cells, are cocultured with otic neuronal progenitors (ONPs, **Fig.1**) to form new synapses with IHCs. In response to IHC optogenetic stimulation, we will record postsynaptic responses directly from ONP somata. The deconvolution



Figure 1. Timeline and *in vitro* co-culture conditions for testing the function of IHC/ONPs regenerated synapses (modified from Vincent et al., 2024).

analysis of postsynaptic currents allows us to test if ONPs form functional contacts with denervated IHCs with IHC-type synapse properties.



# Progress:

1) We are working with our collaborator Dr. Albert Edge (Mass. Eye and Ear, Boston, MA) to obtain labeled ONPs. His lab has extensive expertise in stem cells and in the generation of sensory progenitors as well as inner ear synapse regeneration. During the first six months of the award, efforts were focused on adjusting the differentiating protocol and checking its reliability to differentiate hiPSCs- $\alpha$ -tubulin-RFP (a gift from Dr. Karl Koehler, Harvard Medical School) into ONPs. Under the now optimized conditions, we now observe that ONPs send nerve projections in culture as needed for the experimental approach, also expressing RFP fluorescence (**Fig. 2**) and neurofilament markers (**data not** 

**Figure 2. Otic neuronal progenitors send projections in culture.** Nerve fibers can be observed in red via the native RFP fluorescence. DAPI staining (blue) indicates ONP nuclei. From Malvina Millet (PhD student, Albert Edge's lab), *unpublished data*.

**shown**). As mentioned above, fluorescent ONPs in live co-cultures are needed to trace labeled fibers back from newly formed synapses with hair cells to their somata for patch clamp recordings.

2) While ONPs are further characterized in Dr. Edge's lab, I also hired a master student, Sneha Ajay Sunitha, to work on this project. I have been teaching and training her for several months in tissue dissection and cell culture techniques, and she is now ready to perform larger experimental series.

3) The co-culture model that we are using in this project and that we recently published involves organs of Corti from immature prehearing animals between P4 and P11. This, as reviewers of this proposal had rightfully pointed out, could limit the interpretation of our results and the extrapolation towards a more adult scenario. For that reason, we have started to test the viability of organs of Corti dissected from 3-4-week-old hearing mice in culture. Figure 3 shows one example of a plated P30 organ of Corti, expressing ChR2-YFP in hair cells. We observed that the tissue survived in culture for up to 10 days (so far tested), based on the presence of ChR2-YFP positive IHCs (**Fig. 3A**) and based on IHC patch clamp recordings (**Fig. 3B-C**). We found that brief blue light stimulations depolarized IHCs (**Fig. 3B**) and triggered inward currents and vesicular exocytosis (**Fig. 3C**). These results indicate that organs of Corti excised from hearing animals can survive in culture for at least 10 days but also retain ChR2 expression so that vesicular release can be optogenetically triggered. It also suggests that more mature tissues could be co-cultured with ONPs to test their capacity to form new synapses, and this is what we will be also testing in a subset of our experiments during the remaining time of this award.



Figure 3. Organs of Corti excised from hearing animals survive in culture. A) The organ of Corti was dissected from P30 Gfi1<sup>Cre/+</sup>; Ai32-YFP<sup>fl/+</sup> hearing animals and plated on coated coverslips. Epifluorescent images were taken during incubation time from DIV1 (top image) to DIV10 (bottom image) to assess cell survival rate based on YFP signal (green). Note that outer hair cells do not resist to the dissection step. B) One representative example of a current clamp recording from a ChR2 positive IHC. 1 sec light pulse (blue line) was sufficient to trigger IHC membrane depolarization from its resting potential (V<sub>rest</sub> = -45 mV). C) Same protocol as in B but in voltage clamp. Light stimulation triggered large inward currents (top trace, black), and vesicular exocytosis as indicated by the jump of cell membrane capacitance (bottom, red line) after the light stimulation (double arrowhead). Similar time scale in B and C. Vincent et al., *unpublished data*.

### Future directions

The next step to be undertaken during the remaining time of the award will be to co-culture RFP expressing ONPs with immature (P4-P11) denervated organs of Corti. Patch clamp recordings will be performed from ONP somata that newly contact hair cells to test the presence and properties of synaptic currents in response to hair cell optogenetic stimulation. Synaptic currents will be analyzed by deconvolution to test for IHC-type synapse properties. Further immunolabeling will be performed to characterize the identity of the regenerated synapses in culture, especially with the use of antibody against glutamate receptors. Similar co-culture experiments but with denervated organs of Corti excised from hearing animals will be tested to investigate if more mature hair cells can promote synapse regeneration with ONPs.

After characterizing the synaptic properties of IHC/ONP synapses in control condition, we will move on and test if specific candidate compounds, like trophic factors (NT3, BDNF), improve the number of newly formed synapses and their encoding properties in culture as proposed in **Aim 2**. As already mentioned, **Aim 2** focuses on testing and trying to identify promising regenerative molecules that can improve the functional properties of regenerated synapses. Such compounds combined with the engraftment of ONPs, could be used as a therapeutic approach to replace damage SGNs in patients. In addition to NT3, we will focus on other candidates like Zoledronate (bisphosphonate), Amitriptyline, 7,8-dihydroxyflavone (TrK receptor agonists) or anti-RGMa (blocking the 'Repulsive Guidance Molecule a' (RGMa) that have shown regenerative properties *in vivo* and/or *in vitro*.

American Otological Society Medical Student Research Grant Progress report: January 2024 - 01/12/2025 PI: David Ahmadian with Nicholas A. Dewyer, MD Title: The Effect of Cochlear Implantation (CI) on Depressive Symptoms in Adults

# **Introduction**

Hearing loss is the fourth leading cause of disability worldwide, affecting hundreds of millions of individuals. Depression also presents a significant disease burden globally and has been shown to disproportionately impact individuals with hearing loss. Over the past several decades, cochlear implantation (CI) has emerged as the standard-of-care for patients with sensorineural hearing loss (SNHL) who no longer benefit from amplification (i.e. hearing aids). Despite this, there have been few and limited prospective studies assessing the impact of CI on depressive symptoms in the post-operative period. Thus, the aim of this multi-institutional study is to measure the prevalence of depressive symptoms in patients with SNHL, as well as the change in depressive symptoms following CI. We hypothesize that 1) depression is more prevalent in patients undergoing CI candidacy evaluation than in the general population and 2) treatment of SNHL with CI reduces depressive symptoms.

# **Specific Aims**

1.) Assess quality of life and prevalence and severity of depressive symptoms among adult patients with SNHL undergoing cochlear implantation candidacy evaluation.

**2.)** Determine how CI changes quality of life and depressive symptoms among these patients.

**3.)** Evaluate family and care providers' attitudes and beliefs towards how CI affected the patient's depression, quality of life, and social engagement.

# **Progress:**

In February 2024, we initiated clinical data collection of quality-of-life (QoL) patient-reported outcome measures (PROMs) from adult patients at our tertiary care center undergoing cochlear implantation (CI) for sensorineural hearing loss (SNHL). Our goal was to assess the impact of CI on mental health and overall QoL through a structured, longitudinal approach.

To date, we have significantly exceeded our initial projections for data collection. Based on our institution's CI clinical volume, we originally estimated enrolling 15–20 patients over a 12-month period. However, as of January 12, 2025, we have collected preoperative PROMs from 41 patients—more than double our initial estimate—and 6-month postoperative PROMs from 15 patients. As we approach the one-year mark since launching this initiative, we are preparing to collect 1-year postoperative PROMs, a critical endpoint in our study. Once an adequate sample of 1-year postoperative data is obtained, we will be positioned to conduct a comprehensive analysis of the impact of CI on depressive symptoms and QoL.

To ensure a multidimensional evaluation of mental health and QoL, we are utilizing a robust battery of validated survey instruments, including the CIQOL-35, mini-IPIP, and multiple PROMIS survey banks (depression, anxiety, fatigue, satisfaction with social roles and activities, ability to participate in social activities, and social isolation). This comprehensive approach will allow us to assess both the direct and indirect effects of CI on various psychosocial and emotional factors.

Thus far, we have nearly completed Aim 1 and Aim 2 of our study and anticipate their full completion within the next 6–12 months. Regarding Aim 3, we are actively developing a complementary set of survey questions designed for family members of CI recipients. This component will provide valuable insight into how CI influences not only the patients themselves but also their loved ones' perceptions of their health and well-being. We estimate that data collection for Aim 3 will be completed within the next 12 months as well.

Overall, our progress has outpaced expectations, and we remain on track to generate meaningful findings that will enhance our understanding of the broader psychosocial benefits of CI.

American Otological Society Research Grant–Medical Student Award Progress Report Progress Report Dates: 07/01/2024-01/01/2025 PI: Carolina Chu, MS, University of Iowa Carver College of Medicine Mentors: Dr. Douglas Bennion, MD/PhD and Dr. Marlan Hansen, MD Title: The Effect of Angiotensin Receptor Blockade via Losartan on Noise Induced Hearing Loss in a Murine Model

Introduction: Noise overexposure continues to be a major public health concern with audiometric evidence of noise-induced hearing loss (NIHL) in 1 in 4 adults with measurable hearing loss and in 1 in 5 adults without clinically significant hearing loss. Despite efforts to regulate and recommend "safe" levels of noise intensity and duration of exposure, NIHL continues to be high throughout the population. To date, there are no pharmacologic therapies that have been approved for the treatment of NIHL. Given the multitude of pathologies that may contribute to NIHL including oxidative damage, cellular excitotoxcity, vasculopathy, and inflammation, a potential therapeutic would be one whose effector mechanisms target multiple pathologic processes such as drugs targeting the renin angiotensin system (RAS). Previous studies in our lab querying the TriNetX database have found that patients with hypertension being treated with RAS blockers including angiotensin receptor blockers (ARBs), such as losartan, and ACE inhibitors to have decreased odds of hearing loss and cochlear implantation when compared to those being treated by any other anti-hypertensive. Moreover, preliminary experimental data in which losartan was administered to mice prior to mild noise exposure have shown a short-term otoprotective effect against significant temporary threshold shifts (TTS) along with significant protection against cochlear synaptopathy when compared to control mice at 14 days post-noise exposure. Therefore, we hypothesize that losartan may provide long term otoprotection against permanent threshold shifts (PTS) following moderate noise exposure through preservation of cochlear synapses and in turn spiral ganglion neurons. Our goal is to establish evidence showing losartan to be a promising candidate at the forefront of treating NIHL and shed light on the mechanism in which losartan may be providing protection against noise over-exposure.

**Specific Aim 1:** Determine the long-term effect of losartan at protecting hearing and preserving hair cells, synapses, and neurons after noise induced trauma.

In order to assess the long-term effect of losartan on otoprotection against noise overexposure, male and female CBA/J mice, age 8-10 weeks, were randomly and equally segregated into a group that received standard chow (n=8) and a group that received losartan-infused chow (n=9) (20 mg/kg/day, equivalent to ~100 mg daily dose in humans) starting 3 days prior to noise exposure until 14 days after noise exposure. Mice were exposed to two hours of 8-16 kHz octave band noise at 105 dB for males and 107.5 dB for females. ABR and DPOAE testing was done 1 day prior to noise exposure then repeated at 1, 7, 14, 30, and 90 days after noise exposure and continue to be currently followed. A separate subset of mice exposure for wholemount (n=6, 3 per group) was sacrificed 14 days after noise exposure for wholemount immunostaining with C-terminal binding protein 2 (CtBP2), post-synaptic density protein

95 (PSD95), and myosin 7A (myo7A) for cochlear synapse analysis. Following 180 days post-noise exposure, mice will be euthanized and cochleae harvested for wholemount immunostaining and cryosectioning to analyze cochlear synapses, hair cells, and spiral ganglion neurons.

# **Progress:**

# Audiometric Data

As of January 2025, we have followed the mice with ABRs and DPOAEs for 90 days post-noise exposure. At 24 hours post-noise exposure, the losartan treated group exhibited significantly (p<0.05) smaller ABR threshold shifts in response to stimuli at 16kHz (46.88 dB vs. 38.89 dB SPL shift). The protective effect of losartan persisted to 7 days at 8kHz (31.88 dB SPL vs 17.77 dB SPL shift, p<0.05) and 16kHz (40.63 dB SPL vs 28.89 dB SPL shift, p<0.05), to 14 days at 8 kHz (31.88 dB SPL vs 10.55 dB SPL shift, p<0.01), 16 kHz (44.38 dB SPL vs 23.33 dB SPL shift, p<0.05), and 32 kHz (40 dB SPL vs 26.66 dB SPL shift, p<0.01), and to 30 days at 8 kHz (30 dB SPL vs 19.52 dB SPL shift, p<0.05) and 16 kHz (42.5 dB SPL vs 30.28 dB SPL shift, p<0.05) (Figure 1A-C). When compared to a non-noise exposed control at 30 and 90 days, both noise exposed and losartan groups exhibited increased ABR thresholds compared to mice







exposure in control (n=8) versus losartan pretreatment (n=9) mice up to 90 days post-noise exposure at (A) 8 kHz, (B) 16 kHz, and (C) 32 kHz. *Future Directions:* We plan to continue following these mice with ABRs and DPOAEs every 30 days until 180 days after noise exposure.

# Immunostaining Data

As of January 2025, we have completed analysis of cochlear synapse and hair cell counts 14 days after noise exposure. At 14 days after noise exposure, there was a significantly higher number of preserved inner hair cell (IHC) ribbon synapses in the losartan treated group compared to the control group (12.63 ± 1.7 synapses/IHC vs. 8.7063 ± 0.7 synapses/IHC, p<0.02) (Figure 2A-C). There was no significant difference in IHC and OHC densities between the losartan treated group and the control group (Figure 2B-C).





Figure 2: Wholemount cochlear immunostaining and quantification of cochlear synapses following noise trauma in control (n=3) and losartan treated mice (n=3). (A) and (B) show representative sections of wholemount staining in the control and losartan treated mice respectively. (C) Quantification of synapse counts per IHC along with average number of inner hair cells (D) and outer hair cells (E) per 100  $\mu$ m arc-length in control (n=7) and losartan treated (n=4).

*Future Directions:* We plan to euthanize mice 180 days after noise exposure for wholemount immunostaining and cochlear cryosectioning to analyze cochlear synapses, hair cells, and spiral ganglion neuron counts between mice who were treated with losartan and those that were not.

We are very appreciative and grateful to the American Otological Society for their ongoing support.

### American Otological Society Research Grant

#### Intermediate Progress Report

**Title:** Loss of sensory transduction leads to synaptopathy: the role of hair cell membrane potential **PI:** Thibault Peineau, PhD **Mentor:** Gwenaelle Geleoc, PhD **Dates:** 7/1/2024- 2/1/25

#### Introduction:

Sensory transduction in the inner ear is carried by hair cells of the cochlea, the primary receptors of the ear, which convert mechanical stimulations induced by sound waves into electrical signals. These electrical signals trigger the release of glutamate via the hair cell ribbon synapse and excitation of spiral ganglion afferent nerve fibers. In this study, we investigate how lack of crucial proteins involved in sensory transduction affects the development of the hair cell synapse. We hypothesize that defects in this complex affect the hair cell resting potential thereby altering hair cells firing properties and calcium signal and leading to alterations in the development and maturation of ribbon synapses. To investigate this hypothesis, we proposed to assess hair cell properties and ribbon synapse morphology in genetic models that lack sensory transduction ( $Tmc1^{\Delta/2}$  and Tmie KO) using high magnification imaging with transmission electron microscopy and stimulated emission depletion microscopy. We then will assess how resting potential affects hair cell maturation, using compounds that can increase expression of Kir2.1 channels in hair cells, which will increase K+ efflux, thereby hyperpolarizing the cells. We hypothesize that overexpression of Kir2.1 channels will alter synapse maturation in WT mice mimicking alterations

associated with loss of sensory transduction. This work will help determine how loss of sensory transduction leads to synaptopathy and will provide crucial information for development of therapeutics for hearing loss associated with genetic and acquired forms of synaptopathy.

#### **Specific Aims:**

# Aim 1: Determine how loss of sensory transduction affects IHC resting potential, spontaneous and evoked firing in pre-hearing, post-hearing and adult stages.

For this aim, we have recorded resting membrane potential from Tmc mutant mice and control wild type mice at P12 (pre-hearing) and some at P21 (posthearing). To obtain a full picture, we added  $Tmc2^{\Delta/2}$  and *Tmc1*<sup>Δ/Δ</sup>*Tmc2*<sup>Δ/Δ</sup> mice which provide information. that respectively, from cells acquire sensory transduction at a later age (~one week later than WT) and cells that lack transduction entirely. At P12, we recorded from control IHCs (n=5),  $Tmc1^{\Delta/2}$  (n=3), *Tmc2*<sup> $\Delta/\Delta$ </sup> (n=5) and *Tmc1*<sup> $\Delta/\Delta$ </sup> *Tmc2*<sup> $\Delta/\Delta$ </sup> (n=7) IHCs. At P21,





we recorded resting membrane potentials from WT (n=10),  $Tmc1^{\Delta/4}$  (n=10) and  $Tmc2^{\Delta/4}$  (n=3) IHCs. At P12, we observed positively shifted resting membrane potential in  $Tmc1^{\Delta/4}Tmc2^{\Delta/4}$  IHCs while  $Tmc1^{\Delta/4}$  and  $Tmc2^{\Delta/4}$  did not show significant changes (Fig 1). After the onset of hearing,  $Tmc1^{\Delta/4}$  displayed positively shifted resting membrane potential (Fig 1). These preliminary results confirm that loss of sensory transduction affects the hair cells resting membrane potential.

We have performed initial assessment of hair cells firing activity in P12 WT,  $Tmc1^{\Delta/\Delta}$  and  $Tmc1^{\Delta/\Delta}Tmc2^{\Delta/\Delta}$  mice. Preliminary data show presence of spontaneous and evoked spiking activity in cells lacking sensory transduction ( $Tmc1^{\Delta/\Delta}Tmc2^{\Delta/\Delta}$ ), and presence of evoked spiking activity for  $Tmc1^{\Delta/\Delta}$  IHCs (Fig 1). Recording of resting membrane potentials for *Tmie* mice are expected to be done soon to complete the study.





We performed immunolabelling of the ribbon structures and Ca<sub>V</sub>1.3 channels of WT control and *Tmc* mutants IHCs at P12 (Fig 2B-C) and P21 (Fig 2D-E). Analysis of the colocalization between ribbon structures and Ca<sub>V</sub>1.3 channels showed that in WT mice at P12, 80% of the Ca<sub>V</sub>1.3 channels are colocalized with ribbon structures (Michanski et al., 2019). This colocalization dropped to 60% in *Tmc2*<sup> $\Delta/\Delta$ </sup> and 20% in *Tmc1*<sup> $\Delta/\Delta$ </sup> and *Tmc1*<sup> $\Delta/\Delta$ </sup> IHCs. At P21, colocalization was stable in WT and recovered in *Tmc2*<sup> $\Delta/\Delta$ </sup> IHCs at 80%. However, colocalization barely reached 50% for *Tmc1*<sup> $\Delta/\Delta$ </sup> and *Tmc1*<sup> $\Delta/\Delta$ </sup> IHCs. These results demonstrate that defects in sensory transduction affect the development and organization of the IHC synapse.

We have also acquired TEM images of the ribbon synapses in control WT and *Tmc* mutant mice (Fig3A). Analysis of the size of the ribbon in each genotype shows that they are elongated and surrounded by a well-organized ring of synaptic vesicle in WT and *Tmc2*<sup> $\Delta/\Delta$ </sup> mice. However, in *Tmc1*<sup> $\Delta/\Delta$ </sup> and *Tmc1*<sup> $\Delta/\Delta$ </sup> Tmc2<sup> $\Delta/\Delta$ </sup> IHCs, ribbons appear smaller, more spherical and synaptic vesicles are disorganized and more



heterogeneous. To confirm this observation, we have analyzed the volume of the ribbons from the immunostaining images previously acquired (Fig 2). This analysis shows that the volume of the ribbons in mutant *Tmc* IHCs is significantly reduced compared to the control WT (Fig. 3).

# Aim 3: Assess how constitutive hair cell hyperpolarization mimics loss of sensory transduction and affects ribbon synapses.

This last aim is the next step for our study. While we had proposed to generate a viral vector expressing Ki2.1, we opted to use a faster easier approach. We switched to the use of Zacopride, an agonist of the 5-HT<sub>4</sub> receptor and antagonist of 5-HT<sub>3</sub> receptors which has been shown to alter cardiomyocytes resting potentials by increasing IK<sub>1</sub> current (Liu et al., 2012). I plan to test this compound in *ex vivo* experiments in organ of Corti of WT mice and then perform neonatal injections of Zacopride through the utricle of the cochlea to observe *in vivo* effects.

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#### AOS Grant Progress Report Funding Period: October 1, 2024 – December 31, 2025

Report Date: January 13, 2025 Principal Investigator: Tarika Srinivasan, BSA, BA Mentor: Susan D. Emmett, MD, MPH Title: Expanding Access: Adapting a Novel School Hearing Protocol to Scale Across America

Childhood hearing loss significantly impacts children's linguistic development, educational outcomes, and future employment opportunities. Rural communities are particularly susceptible to disparities in childhood hearing loss, due in part to lack of infrastructure for annual school hearing screenings, as well as limited access to audiology and otolaryngology specialists for follow-up care. The Specialty Telemedicine Access for Referrals (STAR) Trials are two large NIH-funded cluster-randomized trials evaluating the effectiveness and implementation of enhanced mobile hearing screening and telehealth referral to address these disparities in eastern Kentucky (Appalachian STAR) and three regions of Alaska (North STAR). The enhanced mobile hearing screening process requires a self-contained training program; mobile unified equipment for pure-tone audiometry, tympanometry, and otoacoustic emissions testing; and a convenient user interface – all of which must be compatible with existing school health personnel and infrastructure in a variety of rural school districts. To that end, this sub-study involves a multistep implementation analysis and adaptation process of the enhanced mobile hearing screening component of STAR Trials

# Aim 1: Conduct an implementation evaluation of intervention personnel and key stakeholders in integration of a new school-based mobile hearing screening protocol across the Appalachian and North STAR Trials.

Progress: We conducted qualitative semi-structured interviews and focus groups with 21 screeners in eastern Kentucky and 10 screeners across the three participating regions of Alaska based on their experiences with STAR enhanced hearing screening over the 2023-24 school year. We identified several barriers and facilitators to enhanced hearing screening in the unique school contexts. Interview and focus group transcripts were coded using the Consolidated Framework for Implementation Research 2.0 (CFIR) by the primary investigator and other members of the study team. Perceived barriers at the intervention level included user error in tympanometry, duration of screening tests, and difficulty uploading results to school records systems. Facilitators included working in groups, conducting screening early in the year, and screeners' prior familiarity with ear/hearing health. Inner and outer setting factors affecting screening implementation included student absences/illness, difficulties connecting screening tablets to rural school Wi-Fi, and delays in obtaining student rosters from school districts prior to commencing screening. Screeners expressed a strong perception of fit regarding implementing the STAR model and equipment to improve ear/hearing health outcomes in rural school children. Findings from this aim pertaining to the Appalachian STAR trial have been disseminated at multiple regional conferences (see "Presentations").

# Aim 2: Adapt the screening process in Alaska and Kentucky schools based on the implementation evaluation from Aim 1 and describe the deliberate adaptation process that can be applied to other implementation efforts.

Progress: Based on the barriers and facilitators identified in Aim 1, we piloted data-driven adaptations to STAR model. The principal investigator and study team drafted action items to address barriers that could most easily be addressed by STAR model personnel and community screeners i.e., those in the intervention and inner setting domains of the CFIR framework. Such identified modifiable aspects of the STAR model encompassed *equipment (especially software interface), training, screening timing, technology support, and team communication.* The CFIR table of action items was reviewed and refined in an iterative fashion by the study team in de-brief meetings and with feedback from local Alaska and Kentucky community advisory boards (CABs). These adaptations were incorporated into a new version of enhanced hearing screening for rollout in 2024-25 school year.

# Aim 3: Conduct a secondary mixed-methods implementation analysis of data from screeners and stakeholders, eliciting successes and persistent challenges of the contextually adapted mobile hearing screening process from Aim 2.

Progress: The principal investigator conducted goal-directed site visits to several eastern Kentucky counties participating in the Appalachian STAR trial and schools within the Lower Yukon School District, the largest district participating in the North STAR trial by population and geographic area, which had the lowest regional rate of enhanced hearing screening over the 2023-24 year. In-person site visits were conducted to address two of the main barriers to adaptation: 1) to ensure connectivity of STAR enhanced hearing screening equipment to rural school WiFi networks and 2) to facilitate a new hybrid training program for screeners with direct, in-person feedback on otoacoustic emissions and tympanometry technique. The hybrid training program was tailored to provide background information on various hearing screening modalities to bolster the ability of lay screeners to troubleshoot testing in real-time. The principal investigator generated detailed notes on community participation, school conditions, and outcomes of training screening independently for the 2024-25 year.

Qualitative semi-structured interviews are currently being conducted to assess the feasibility of the adapted enhanced hearing screening protocol in each of the STAR trial settings. We anticipate a similar number of interviews and focus groups generated from Aim 1. Similarly, transcripts will be coded with respect to CFIR 2.0 domains to elicit the ultimate successes and challenges of scaling enhanced hearing screening in rural Alaska and Kentucky schools after a phased implementation adaptation. This data will be analyzed and disseminated over January through April 2025.



**Above:** Map of three participating school districts in North STAR Trial. The principal investigator conducted goaldirected site visits to schools within the Lower Yukon School District.

#### **Development Goals**

I have received continuous mentorship in the form of weekly meetings with Dr. Susan Emmett. I have achieved my goal of leading a community-engaged research project, having independently visited study sites to facilitate intervention deployment and overseeing collection and analysis of qualitative data from community partners. I have gained experience in research dissemination through first-author submission of a manuscript detailing the Appalachian STAR trial protocol, presentations of this work at regional conferences, and preparation of multiple manuscripts relevant to Aims 1-3 for publication over the next few months.

#### Presentations

- Srinivasan T, Bush ML. Optimizing school-based hearing screening: the App STAR Trial. Oral presentation. Kentucky Educators for the Deaf and Hard of Hearing Conference; June 2024; Richmond, KY.
- McGrath M, Leon J, Srinivasan T, Lane HG, Robler SK, Emmett SD, Bush ML. Deploying enhanced hearing screening in rural Kentucky schools: a qualitative implementation assessment of the Appalachian STAR trial. Oral presentation. Appalachian Translational Research Network Annual Health Summit; Jan 2025; Abingdon, VA



**Right:** Map of participating counties in Appalachian STAR trial. Blue denotes counties with schools receiving enhanced hearing screening. Stars denote location of partnering audiology clinic for telehealth component. The principal investigator conducted goal-directed site visits to several counties.

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Nancy M. Young, MD Chicago, Illinois Fellow

Daniel M. Zeitler, MD Seattle, Washington Fellow



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.



Dr. Michael M. Paparella Inducted to AOS in 1968 Passed: November 20, 2024



Dr. Bloyce Hill Britton Inducted to AOS in 1978 Passed: November 2, 2024



<u>Dr. Brenda L. Lonsbury-Martin</u> Inducted to AOS in 2000 Passed: September 2, 2024



Dr. Jose Antonio Rivas Inducted to AOS in 2009 Passed: August 17, 2024



Dr. Joseph Di Bartolomeo Inducted to AOS in 2015 Passed: July 27, 2024



<u>Dr. William (Bill) Lippy</u> Inducted to AOS in 1988 Passed: June 29, 2024