



PROGRAM and ABSTRACTS

of the

*One Hundred Fortieth
Annual Meeting*

**AMERICAN OTOLOGICAL
SOCIETY, INC.**

April 27-28, 2007

**Manchester Grand Hyatt
San Diego, California**

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The American Otological Society designates this educational activity for a maximum of 8 *AMA PRA Category 1 Credit(s)*TM. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Certificate of Attendance will be issued at the close of the meeting upon completion of the questionnaire required by us for the certifying organizations.

**AMERICAN OTOLOGICAL SOCIETY, INC.
MISSION STATEMENT**

The mission of the American Otological Society, Inc., shall be

- to advance and promote medical and surgical otology/neurotology and lateral skull base surgery in adult and pediatric patients including the rehabilitation of individuals with hearing and balance disorders.
- to encourage, promote, and sponsor research in otology/neurotology and lateral skull base surgery and related disciplines.
- to conduct an annual meeting of the members for the presentation and discussion of scientific papers and the transaction of business affairs of the Society.
- to publish the peer reviewed papers and discussions presented during the scientific program and the proceedings of the business meetings.

EDUCATIONAL MISSION STATEMENT

The Educational Mission of the American Otological Society is to foster dialog on, and dissemination of, information pertaining to advances in the understanding and management of otologic and neurotologic disorders. It is expected that the CME program of the AOS will enhance the competency of the participant in otology/neurotology and lateral skull base surgery.

Goals & Objectives: The overall goal of this course is to provide up-to-date information pertaining to advances in the understanding and management of otologic and neurotologic disorders. The **target audiences** are otologists, neurotologists, and otolaryngologists with specific interests in otologic and neurotologic disorders.

After attending this meeting, the participants will have a better understanding of:

- Auditory Brainstem Implants in Children
- Drug Delivery Systems for the Inner Ear
- Implantable Hearing Devices

resulting in more effective patient care to achieve improved hearing.

First Author/Presenter's signature on the following statements were required on all papers submitted to the American Otological Society. The author was advised that the submitted paper becomes the property of *Otology & Neurotology* and cannot be reprinted without permission of the Journal.

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PUBLICATION STATEMENT

The material in this abstract, (Name of Abstract), has not been submitted for publication, published, nor presented previously at another national or international meeting and is not under any consideration for presentation at another national or international meeting. The penalty for duplicate presentation/publication is prohibition of the author and co-authors from presenting at a COSM society meeting for a period of three years.

Submitting Author's Signature (required)

FACULTY DISCLOSURES

NOTES

The following faculty disclose

Jill B. Firszt, PhD—Advanced Bionics Corp - Advisory Board
Member - Cochlear Implant; Cochlear Corp - Advisory Board
Member - Cochlear Implants;
Research Grant Recipient- Cochlear Implants

Bruce J. Gantz, MD—Advanced Bionics Corp - Consultant -
Cochlear Implants;
Cochlear Corp - Consultant - Cochlear Implants

Jeffrey P. Harris, MD, PhD—Otoimmune - Ownership Interest

Brandon Isaacson, MD—Medtronic -Paid Speaker - Skull Base
Surgery

The following faculty have nothing to disclose

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Karen B. Teufert, MD
Frank M. Warren, MD
Andrea H. Yeung, MD
Guangwei Zhou, MD, ScD

FRIDAY, April 27, 2007

NOTES

Business Meeting – 7:00 am
Room: Elizabeth Ballroom FGH
(Restricted to Members)

Minutes of the Annual Meeting 2006

Introduction of New Members

Election of Nominating Committee

Report of the Secretary-Treasurer

Report of the Editor-Librarian

Scientific Program – 7:20 am
Room: Elizabeth Ballroom FGH
(Open to Non-Members)

7:20 **Remarks by the President**
Antonio De La Cruz, MD

Presidential Citation

Burt Brent, MD
Bob Shannon, MD
William E. Hitselberger, MD
William L. Lo, MD

7:25 **Introduction of Guest of Honor**
Fred H. Linthicum, Jr., MD

Moderators: Antonio De La Cruz, MD
Clough Shelton, MD

CI Basic/ABI in Children

7:30 **Basic Science Lecture: Speech Understanding
from Implants: Cochlear, Brainstem and
Midbrain**
Bob Shannon, MD

7:45 **Lecture: Assessing Results in Auditory Brain
Implants in Children**
Vittorio Colletti, MD

8:10 **Comprehensive Evaluation of a Child with
an Auditory Brainstem Implant**
Laurie S. Eisenberg, PhD
Karen C. Johnson, PhD
Amy S. Martinez, MA
Jean L. DesJardin, PhD
Carren Stika, PhD
Danielle Dzubak, AuD
Mandy Mahalak, AuD
Emily Rector, MS

8:20 **Assessing Parental Perceptions of Development in Relation to Language Development after Early Cochlear Implantation**
Frank R. Lin, MD
Nae-Yuh Wang, PhD
Nancy E. Fink, MPH
Alexandra L. Quittner, PhD
Laurie S. Eisenberg, PhD
Emily A. Tobey, PhD
John K. Niparko, MD
CDaCI Investigative Team

NOTES

8:30 **Speech Processor Frequency Mapping Influences Pitch Perception**
Bruce J. Gantz, MD
Lina A. J. Reiss
Christopher J. Turner, PhD

8:40 **Spectral Channels and Speech Recognition in Cochlear Implant Recipients Using HiRes 120 Sound Processing**
Jill B. Firszt, PhD
Laura K. Holden, MA
Ruth M. Reeder, MA
Margaret W. Skinner, PhD

8:50 **Discussion**

CI Clinical

8:55 **Reimplantation of Hybrid Cochlear Implant Users: From 10mm to 25mm Insertion Depth**
Matthew B. Fitzgerald, PhD
Elad Sagi, PhD
Michael Jackson, MS
William H. Shapiro, MS
J. Thomas Roland, MD
Susan B. Waltzman, PhD
Mario A. Svirsky, PhD

9:05 **Intra-operative Monitoring of Cochlear Function Permits Improved Hearing Preservation During Pediatric Cochlear Implantation**
Ross Tonini, AuD
Jamie Rasmus, AuD
Claudia Emery, AuD
Joann Haymond, MS
Jeffrey T. Vrabec, MD
Spiros Manolidis, MD
John S. Oghalai, MD

9:15 **Cochlear Implantation in Children with Congenital X-linked Deafness**
Konstantina M. Stankovic, MD, PhD
Annmarie Hennessey
Leila A. Mankariou, MD

- 9:25 **The "G-Flap" Incision for Cochlear Implantation**
 Ryan McCool, MD
 Frank M. Warren, MD
 Clough Shelton, MD
- 9:35 **Discussion**
- 9:40 **Break with Exhibitors**
- Sudden Hearing Loss/Meniere's Disease/SCC Dehiscence**
- 10:10 **Treatment of Idiopathic Sudden Sensorineural Hearing Loss (ISSNHL) with Intratympanic Dexamethasone and/or Prednisone Taper**
 Alex Battaglia, MD, PhD
 Roberto Cueva, MD
- 10:20 **Safety of High-dose Corticosteroids for the Treatment of Autoimmune Inner Ear Disease**
 Jeffrey P. Harris, MD, PhD
 Thomas H. Alexander, MD, MHS
 Michael H. Weisman, MD
 AIED Study Group
- 10:30 **Clinical and Diagnostic Characterization of Canal Dehiscence Syndrome: A Great Otologic Mimicker**
 Guangwei Zhou, MD ScD
 Quinton Gopen, MD
 Dennis S. Poe, MD
- 10:40 **Persistent Dizziness after Surgical Treatment of Vertigo: Prognostic Factors**
 Karen B. Teufert, MD
 Karen I. Berliner, PhD
 Antonio De La Cruz, MD
- 10:50 **Meniett Pump for Meniere's Disease: Use and Compliance at Two Years**
 Douglas E. Mattox, MD
 Mary Reichert, RN
- 11:00 **Use of Stacked ABR and CHAMP Analysis in the Evaluation of the Dizzy Patient**
 Andrea H. Yeung, MD
 Wileen Chang, MS, CCC-A
 Robert W. Sweetow, PhD
 Lawrence R. Lustig, MD
- 11:10 **Discussion**
- Pharmacology & Drug Delivery**
- 11:15 **ErbB and Nrg: Potential Molecular Targets for Vestibular Schwannoma Pharmacotherapy**
 Joni K. Doherty, MD, PhD

- 11:25 **Pharmacologic Prevention of Noise Induced Hearing Loss**
 Richard Kopke, MD
 Ben J. Balough, MD
 Brenda Lonsbury-Martin, PhD
 Martin Slade, PhD
 Laura Dreisbach, PhD
 Peter Torre III, PhD
 Ronald Jackson, PhD
 Alicia R. Sanderson, MD
 Peter Rabinowitz, MD
- 11:35 **Effectiveness of Combinations of Antioxidant Drugs in the Treatment of Acute Acoustic Trauma**
 Chul-Hee Choi, PhD
 Kejian Chen, MD, PhD
 Angelica Vasquez-Weldon, BS
 Ronald L. Jackson, PhD
 Robert A. Floyd, PhD
 Richard D. Kopke, MD
- 11:45 **Treatment of Inner Ear Diseases Using New Drug Delivery System**
 Juichi Ito, MD, PhD
 Takayuki Nakagawa, MD, PhD
 Tsuyoshi Endo, MD, PhD
- 11:55 **Discussion**
- 12:00 **Adjourn**
- 12:05 AOS Members Group Photograph (Location to be announced)
- 6:30 President's Reception & Dinner Dance (Members and Invited Guests Only)

NOTES

SATURDAY, April 28, 2007

NOTES

Business Meeting – 12:30 pm
Room: Elizabeth Ballroom FGH
(Restricted to Members)

REPORT OF THE

- A. Board of Trustees of the Research Fund
- B. American Board of Otolaryngology
- C. Award of Merit Committee
- D. American College of Surgeons
- E. American Academy of Otolaryngology-HNS

Report of the Audit Committee

Report of the Membership Development Committee

Report of the Nominating Committee

Unfinished Business

New Business

Scientific Program – 1:00 pm
Room: Elizabeth Ballroom FGH
(Open to Non-Members)

Moderators: Antonio De La Cruz, MD
Clough Shelton, MD

BAHA

- 1:00 **Patient Perceived Benefit Using the Bone Anchored Hearing Aid in Unilateral Deafness**
John W. House, MD
J. Walter Kutz, Jr., MD
- 1:10 **Single-stage BAHA Implantation: Is It Safe?**
Darius Kohan, MD
- 1:20 **Accelerational Stability of a Bone Anchored Electromechanical Transducer**
Travis J. Pfannenstiel, MD
Drew M. Horlbeck, MD
Jim Easter, MS, ME
David Basinger, BSEE
- 1:30 **Phase I Otologics Fully Implantable Hearing System: One Year Results**
Herman A. Jenkins, MD
James S. Atkins, MD
Drew Horlbeck, MD
Michael E. Hoffer, MD, CDR MC USN
Ben Balough, MD, CDR MC USN
Joseph V. Arigo, MD
George Alexiades, MD
William Garvis, MD

1:40 **Anatomy of the Round Window and Hook Region of the Cochlea with Implications for Cochlear Implantation and Other Surgical Procedures**
Peter M.M.C. Li, MD
Haobing Wang, MA
Clarinthra Northrop
Saumil Merchant, MD
Joseph B Nadol, Jr. MD

NOTES

1:50 **Hearing Restoration in Old Radical Cavities with the Round Window Implant**
Vittorio Colletti, MD
Marco Carner, MD
Liliana Colletti, PhD

2:00 **Discussion**

OAE/Molecular

2:05 **Transient and Distortion Product Evoked Otoacoustic Emissions in Normal Hearing Patients with and without Tinnitus**
Carlos A. Oliveira, MD, PhD
Ronaldo C. Granjeiro, MD, MSc
Helga M. Kehrle, MD, MSc
Roberta L. Bezerra, MD
Vanessa F. Almeida, MD, MSc
André L. L. Sampaio, MD

2:15 **Comparing Distortion Product Otoacoustic Emissions, Auditory Brainstem Response, and Electrocochleography for Intraoperative Monitoring of Auditory Function During Cerebello-pontine Angle Tumor Surgery**
Krzysztof F. Morawski, MD, PhD
Kazimierz Niemczyk, MD, PhD
Jorge Bohorquez, PhD
Fred F. Telischi, MEE, MD

2:25 **Molecular Pathogenesis of Otitis Media in a Mouse Model**
Jiang Ping Zhang, MD, PhD
Christopher M. McCarty
Heping Yu
Jill M. Giggey
Leah Rae B
Qing Yin Zheng

2:35 **Complications with Hydroxyapatite Cement for Mastoid Cavity Obliteration**
Janell S. Ridenour, PA-C
David W. Roberson, MD
Dennis S. Poe, MD

2:45 **Discussion**

2:50 **Break with Exhibitors**

NOTES

Oto/HA/COM

3:20 **Titanium Clip Piston Versus Platinum-Ribbon Teflon Piston: Piston and Fenestra Size Affect Air-Bone Gap**

Charles A. Mangham, Jr., MD, MS

3:30 **High Frequency Sensorineural Hearing Loss Following Stapedectomy**

Michele B. St. Martin, MD, MBA

Barry E. Hirsch, MD

3:40 **Investigation of the Mechanics of Type III Stapes Columella Tympanoplasty Using Laser Doppler Vibrometry**

Wade Chien, MD

John J. Rosowski, PhD

Saumil N. Merchant, MD

3:50 **Phylogeny of the Stapes Prosthesis**

Michael H. Fritsch, MD

Ilka C. Naumann, MD

4:00 **Bivalve Cartilage Inlay: A Short Simple Office Procedure for Closing Small and Medium Size Tympanic Membrane Perforations**

Ashkan Monfared, MD

Christopher Bergeron, MD

Justin Ortiz, MD

Howard Lee, PhD

Todd Dray, MD

Richard Gunsalus

4:10 **Long-Term Hearing Results after Ossiculoplasty in Comparison with Short-Term Results**

Yasuo Mishiro, MD

Masafumi Sakagami, MD, PhD

Tadashi Kitahara, MD

Takeshi Kubo, MD

4:20 **Discussion**

4:25 **Hyperventilation-Induced Nystagmus and Evaluation of the Dizzy Patient**

Angela G. Shoup, PhD

Peter S. Roland, MD

4:35 **Vestibular-Evoked Potentials in Bilateral Vestibulopathy**

Brandon Isaacson, MD

Emily Klerekoper Murphy, BA

Helen S. Cohen, EdD, OTR

4:45 **Discussion**
4:55 **Introduction of incoming AOS President**
Clough Shelton, MD
5:00 **Adjourn**

2007 Program Advisory Committee

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COSM 2008
141st AOS Annual Spring Meeting
May 2-3, 2008
JW Marriott Grande Lakes
Orlando, FL

Abstract Deadline: October 15, 2007

Abstract submission form
Website—www.americanotologicalsociety.org
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Journal Requirements

All abstract submissions must meet Journal requirements. To see those requirements, please consult “Instructions for Authors” in the printed Journal or online at www.otology-neurotology.org

Instructions to Authors/Presenters

Manuscripts must be submitted electronically to the O&N Journal no later than two weeks before the presentation. One copy of the manuscript (.pdf format) is to be submitted electronically to the AOS Administrative Office.

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1.

Comprehensive Evaluation of a Child with an Auditory Brainstem Implant

Laurie S. Eisenberg, PhD; Karen C. Johnson, PhD
Amy S. Martinez, MA; Jean L. DesJardin, PhD
Carren Stika, PhD; Danielle Dzubak, AuD
Mandy Mahalak, AuD; Emily Rector, MS

Objective: Auditory brainstem implants (ABI) in deaf children are gaining momentum in Europe, and protocols for clinical trials are being discussed in the United States. We recently evaluated a young boy with an ABI. In this presentation, we describe the multidisciplinary test protocol and discuss results.

Study design: Case study

Setting: Tertiary referral center

Patients: The child was 3 years, 11 months at time of testing in July, 2006. He was congenitally deaf from Goldenhar Syndrome and presented with auditory nerve agenesis. **Intervention:** Auditory brainstem implant

Main outcome measures: A battery of tests was compiled to assess performance in the domains of speech perception, language, behavior, cognition, quality of life, and parental perceptions.

Results: Following 5 weeks of consistent electrical stimulation, the child demonstrated detection of speech sounds, auditory pattern perception with visual cues, and inconsistent auditory-only vowel discrimination. The child was accepting of the ABI, showed awareness to sound and was increasing his vocalizations. Language age using signs was 20 months. The child had normal intelligence but exhibited attention deficits and difficulty completing tasks during a structured activity. The parents were counseled to make sign language a high priority and to increase structure in daily learning activities.

Conclusions: Pediatric ABI clinical trials are in the early stages of development in the United States. These trials should encompass a multidisciplinary approach in which children are evaluated in the context of the "whole child" in order to define the relevant variables and to quantify outcomes.

This research was conducted with support from the House Ear Institute and Cochlear Americas.
06-022

2.

Assessing Parental Perceptions of Development in Relation to Language Development after Early Cochlear Implantation

Frank R. Lin, MD; Nae-Yuh Wang, PhD
Nancy E. Fink, MPH; Alexandra L. Quittner, PhD
Laurie S. Eisenberg, PhD; Emily A. Tobey, PhD
John K. Niparko, MD
and the CDAI Investigative Team.

Objective: Early cochlear implantation allows for the development of verbal language and communication skills in deaf children that can provide the basis for optimal childhood development. We studied the use of two language measures, the MacArthur Communicative Development Inventory and the Reynell Developmental Language Scales, in relation to a measure of parental perceptions of their child's development. We hypothesized that language ability after CI should be reflected in and positively associated with parental perceptions of development.

Study design: Cross-sectional analysis

Setting: 6 academic cochlear implant centers

Patients: 188 deaf children (< 6 y.o.) one year after CI activation enrolled in the longitudinal Childhood Development after CI study

Main outcome measures: MacArthur Communicative Development Inventory, Reynell Developmental Language Scales, Parental perceptions of development quantified with a visual analog scale (VAS-development)

Methods: Nonparametric and parametric regression methods were used to model the relationship between language and VAS-development scores.

Results: Increasing language scores on both the MacArthur and Reynell were associated with more favorable parental perceptions of development in 4-6 y.o. children but not in 2-3 y.o. children. In 2-3 y.o. children, a threshold was reached at 15% of the total possible language score, after which further improvements in language ability were not reflected in higher VAS-development scores.

Comment: After early CI, increasing language ability manifests in more favorable parental perceptions of child development in older (> 4 y.o.) but not in younger (< 3 y.o.) children. In younger children, verbal language ability is not consistently associated with parental perceptions of development, and this relationship may be mediated by environmental/personal factors and evolving parental expectations. A conceptual framework for understanding outcome measures after CI and the need for additional metrics for young CI children are discussed.

This work was supported by grants from the NIDCD: R01 DC04797, T32 DC00027
IRB: Johns Hopkins Human Subject Assurance # FWA00005752.

3.

Speech Processor Frequency Mapping Influences Pitch Perception

Bruce J. Gantz, MD; Lina A. J. Reiss
Christopher J. Turner, PhD

Objective: It is assumed that electrical stimulation by a cochlear implant electrode evokes a pitch sensation similar to that of the normal auditory system. If true, electrodes must be advanced far into the cochlea to activate low frequency regions. However, deep insertion carries more risk to functioning auditory structures. The Iowa/Nucleus Hybrid Implant was originally developed to stimulate basal high frequency regions. However, speech perception tests using electric speech processing only suggests that low frequency information is being perceived with a 10mm electrode.

Study design: Subjects using the Hybrid implant for more than one year were studied to evaluate their ability to use electrical processing only. Pitch sensations of individual electrodes were also measured electrically through the implant and acoustically in the contralateral ear.

Setting: Tertiary Care Center

Results: Some individuals are able to achieve CNC word scores with electric only processing similar to combined electric plus acoustic processing. The changes observed occur slowly over time. Pitch perceptions obtained from individual electrodes in these subjects are closer to the frequency map assigned an electrode than that normally associated with a specific cochlear region.

Conclusions: These results suggest that pitch sensations may be more related to the implant map than cochlear location. This implies that the brain may adapt to spectral mismatches by re-mapping pitch. Changes in electric only speech perception and pitch sensation over time demonstrate that central processes, frequency assigned to an area of the cochlear, and experience have a greater influence on perceived pitch than previously imagined.

Acknowledgments:

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IRB:University of Iowa IRB Approved Number to follow

4.

Spectral Channels and Speech Recognition in Cochlear Implant Recipients Using HiRes 120 Sound Processing

Jill B. Firszt, PhD; Laura K. Holden, MA
Ruth M. Reeder, MA; Margaret W. Skinner, PhD

Objective: HiRes 120 is a new sound processing option that offers increased spectral resolution through the use of current steering. This within-subject study was designed to 1) evaluate speech recognition/music ratings in subjects using HiRes 120 sound processing compared to their performance with standard HiRes, 2) measure the number of spectral channels (or different pitches) that can be resolved using a psychophysical task, and 3) compare HiRes 120 results with spectral channel percepts in the same subjects.

Setting: Cochlear implant/tertiary referral center.

Subjects: Eight postlinguistically deafened adults implanted with an Advanced Bionics CII or HiRes 90K cochlear implant.

Study Design/Outcome Measures: Performance with standard HiRes and HiRes120 was assessed with a battery of measures including speech recognition in quiet and noise, and ratings of environmental sounds and musical passages. During another test session, the number of spectral channels was determined by stimulating two electrodes simultaneously with different proportions of current and identifying the number of discrete pitches perceived by each subject.

Results: Results showed a significant improvement in monosyllable word recognition, sentence recognition in noise, and music ratings with HiRes 120. In the same subjects, the average number of identified spectral channels was 74 (range 29-272). A relation between number of identified spectral channels and speech recognition/music rating scores within subjects was not evident.

Conclusions: HiRes 120 offers improved benefit to some patients. Novel outcome measures, such as music tests, are needed to further understand the benefits of HiRes 120.

Reference: Donaldson GS, Kreft HA, Litvak L. 2005. Place-pitch discrimination of single- versus dual-electrode stimuli by cochlear implant users. *J Acoust Soc Am*, 118, 623-626.

IRB:HSC Numbers 04-0198 and 05-0798.

5.

**Reimplantation of Hybrid Cochlear Implant Users:
From 10mm to 25mm Insertion Depth**

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Michael Jackson, MS; William H. Shapiro, MS
J. Thomas Roland, MD; Susan B. Waltzman, PhD
Mario A. Svirsky, PhD

Hypothesis: Pitch-scaling and word-recognition abilities of Nucleus 10mm Hybrid cochlear implant users will improve after reimplantation with a standard Nucleus 25mm array.

Background: While electroacoustic stimulation is a promising treatment for some hearing-impaired listeners, a small subset of electroacoustic listeners lose all residual hearing. It is not known how they will adapt after reimplantation with a standard 25mm array.

Methods: Before and after reimplantation, we measured on several occasions the ability of two reimplanted listeners to perform a pitch-scaling task with two different conditions, and their word-recognition ability. In the pitch-scaling task, we stimulated six electrodes in a pseudo-random order, and listeners assigned a pitch value to the sensation elicited by a given electrode. One condition employed six electrodes spread throughout the array; another used the six most basal electrodes. The word-recognition task consisted of two 50-word CNC lists.

Results: Initially, these listeners reliably scaled the pitches elicited by the six most basal electrodes, but not the pitches elicited by mid or apical electrodes. However, two months after reimplantation, one listener assigned distinct pitch values to electrodes positioned throughout the array. The other listener has yet to be retested. Regarding the word-recognition scores, both listeners performed better with the 25mm electrode than the 10mm electrode in several different conditions.

Conclusions: 1) Short-electrode (10 mm) cochlear implants may help preserve residual hearing but may also provide less information than traditional CI's. 2) Pitch percepts in response to electrical stimulation are plastic and may be modified by experience.

IRB Approval Number: 05-265

6.

**Intra-operative Monitoring of Cochlear Function Permits
Improved Hearing Preservation During Pediatric
Cochlear Implantation**

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Claudia Emery, AuD; Joann Haymond, MS
Jeffrey T. Vrabc, MD; Spiros Manolidis, MD
John S. Oghalai, MD

Objective: To determine if intra-operative auditory monitoring is feasible during cochlear implantation and whether this improves preservation of residual hearing.

Study design: Prospective non-randomized study

Setting: Pediatric tertiary referral hospital

Patients: 72 consecutive pediatric patients undergoing cochlear implantation that had measurable auditory thresholds pre-operatively were divided into two cohorts. The unmonitored cohort included the first 65 patients and the monitored cohort included the last 7 patients.

Intervention(s): Cochlear implantation

Main outcome measure(s): Pre-operative, intra-operative, and >1 month post-operative auditory thresholds.

Results: The average pre-operative PTA was 103 dB and 96 dB in the unmonitored and monitored cohorts, respectively. These were not statistically different (p>0.2). In the monitored cohort, we measured auditory steady state responses (ASSR) to assess cochlear function at multiple time points during the operation. Compared to baseline, thresholds were increased 3.6 dB after exposing the round window niche, 1.1 dB after opening the cochlea, and 8.6 dB after inserting the electrode array. In the 5/7 patients in which all hearing was not lost, the average threshold shift was only 2 dB intra-operatively. One month post-operatively, the average PTA was 112 dB in the unmonitored cohort but only 98 dB in the monitored cohort (p<0.05).

Conclusions: ASSR is a viable tool that can provide real-time feedback to the surgeon during cochlear implant surgery. These data suggest that this may permit an improved rate of long-term hearing preservation. Specific surgical techniques that we have found to facilitate hearing preservation will be discussed.

IRB: H-18374

7.

Cochlear Implantation in Children with Congenital X-linked Deafness

Konstantina M. Stankovic, MD, PhD
Annmarie Hennessey; Leila A. Mankarious, MD

Objective: To report the technique used and results of 4 patients with congenital X-linked deafness, all of whom underwent cochlear implantation for severe to profound sensorineural hearing loss.

Methods: Retrospective chart review at tertiary care institution.

Results: Four children, 3 of whom are siblings, were all successfully implanted using a standard transmastoid, transfacial recess technique. A large cerebrospinal fluid leak through the cochleostomy was encountered with each patient. Techniques to minimize CSF leak included occlusion of the cochleostomy with fascia and fibrin sealant, and concurrent lumbar drain for a minimum of 72 hours. An intraoperative skull film was obtained to insure proper placement of the electrode array. Patients were followed for a mean of 2.5 years (range 1-5 years). Postoperative results revealed proper functioning of the implant, no recurrent CSF leak, and limited progress with expressive and receptive oral language. Three of the 4 patients show signs of other learning disorders, while the remaining patient is too young for a complete assessment. Other patients with this congenital X-linked deafness have been found to have other associated chromosome X mutations that may be responsible for various degrees of developmental delay.

Conclusions: Preoperative gene mutation analysis is warranted in patients with congenital X-linked deafness scheduled to undergo cochlear implantation to help in long-term counseling.

8.

The "G-Flap" Incision for Cochlear Implantation

Ryan McCool, MD; Frank M. Warren, MD
Clough Shelton, MD

Objective: To describe a novel incision for cochlear implantation and assess the surgical results of this approach.

Study design: Retrospective chart review.

Setting: Tertiary referral center.

Patients: Cochlear implant recipients from June 1999 through September 2006 who underwent the "G-Flap" technique with at least 3 months follow-up.

Intervention(s): Rehabilitative.

Main Outcome Measure(s): Wound complications including device exposure or extrusion, wound breakdown, cellulitis, and need for re-implantation.

Results: The "G-Flap" is a unique surgical incision for cochlear implantation. It involves a curvilinear post-auricular incision beginning at 12 o'clock extending down to the linea temporalis, and two "back cuts" one directed superiorly at 12 o'clock and a second posteriorly along the linea temporalis. A skin flap is then elevated posteriorly, and an offset incision is made posteriorly in the periosteum, which is elevated forward to expose the mastoid. There were 117 patients that underwent cochlear implantation using the "G-Flap" technique and had greater than three months of follow-up. Two of these procedures were re-implantations. Three patients who underwent the G-Flap procedure had to undergo revision, all for device failures. There were two patients who developed cellulitis in the immediate post-operative period, which resolved with antibiotic therapy. There were no incidents of wound dehiscence, skin breakdown, implant exposure or extrusion.

Conclusions: The "G-Flap" technique allows excellent exposure of the mastoid and adjacent skull for cochlear implantation. This technique has a remarkably low incidence of wound complications, and provides a viable alternative to traditional post-auricular approaches.

IRB: 12867

9.

Treatment of Idiopathic Sudden Sensorineural Hearing Loss (ISSNHL) with Intratympanic Dexamethasone and/or Prednisone Taper

Alex Battaglia, MD, PhD; Roberto Cueva, MD

Objective: This study seeks to compare hearing results in patients with Idiopathic Sudden Sensorineural Hearing Loss (ISSNHL) who have received high dose prednisone taper (HDPT), intratympanic dexamethasone (IT-Dex) alone, or IT-Dex and HDPT.

Study design: Multi-centered, double-blinded, placebo-controlled, randomized clinical trial.

Setting: Tertiary referral centers.

Patients: Patients must have been diagnosed with idiopathic sudden sensorineural hearing loss within 6 weeks to be eligible to enter the trial.

Intervention(s): Fifty-one patients with less than a 6-week history of ISSNHL were randomized to one of three arms and followed prospectively. Group A (17 patients) received IT-Dex therapy with placebo taper while Group B (18 patients) were given HDPT and placebo intratympanic injections. Patients in Group C (16 patients) were administered IT-Dex and HDPT. Injections (IT-Dex/placebo) and audiograms were performed weekly for three weeks, and a final audiogram was obtained 4 weeks after the final injection.

Main outcome measure(s): Hearing improvement.

Results: Group C patients had significant improvements in speech discrimination (p=.0089) and in overall hearing improvement (p=.0005) compared to Group B patients. Group C patients recovered their hearing more quickly than Group B patients (p=.0005). Logistic regression analysis indicates that Group C patients demonstrated better overall hearing results than Group A and B (p<.05), when all three groups were adjusted for age, vertigo, initial hearing levels and time delay between onset of hearing loss and treatment.

Conclusions: ISSNHL patients treated with IT-Dex and HDPT experience statistically significantly improved hearing recovery compared to treatment with HDPT or IT-Dex alone.

IRB: 3837

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10.

Safety of High-dose Corticosteroids for the Treatment of Autoimmune Inner Ear Disease

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Michael H. Weisman, MD; AIED Study Group

Objective: To report the adverse effects associated with prolonged high-dose prednisone for the treatment of autoimmune inner ear disease (AIED).

Study Design: Prospective data collected as part of a multi-center, randomized, controlled trial for the treatment of corticosteroid-responsive AIED with methotrexate.

Setting: Tertiary referral centers.

Patients: 116 patients with rapidly progressive, bilateral sensorineural hearing loss.

Intervention: All patients completed a 1-month course of prednisone 60 mg/d. 67 patients with improvement in hearing underwent a monitored 18-week prednisone taper (average dose 23 mg/d during taper). 33 patients were randomized to receive methotrexate during the prednisone taper. 34 received prednisone and placebo. Patients were followed for 52 weeks.

Main outcome measure: Adverse events (AE) in patients treated with prednisone only.

Results: No patient had to stop therapy during the 1-month prednisone challenge. Five of 34 patients were unable to complete the 18-week taper due to AE. The most common AE were elevations in blood glucose and weight gain. Only one patient experienced a serious AE—the diagnosis of lung cancer at the start of the taper.

Conclusions: Although high-dose corticosteroids are associated with known serious side effects, prospective data in the literature is limited. The present study suggests that with appropriate monitoring and patient education, high-dose corticosteroids are a safe and effective treatment of AIED.

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Acknowledgements:

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11.

Clinical and Diagnostic Characterization of Canal Dehiscence Syndrome: A Great Otologic Mimicker

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Dennis S. Poe, MD

Objective: To identify otologic and audiologic characteristics of superior (and posterior) semicircular canal dehiscence (SCD).

Study design: retrospective case review

Setting: tertiary referral center

Patients: Sixty adult patients evaluated for SCD; 25/60 (33 ears) had dehiscence.

Intervention(s): Otologic examination, high-resolution computerized tomography (CT), air and bone audiometry, tympanometry, acoustic reflex and vestibular evoked myogenic potential (VEMP).

Main outcome measure(s): Imaging demonstrating canal dehiscence, preferentially including Poschel and Stenvers reconstructions. Audiologic findings of pseudo-conductive hearing loss, intact ipsilateral stapedial reflex, and abnormally low VEMP thresholds.

Results: The most common presenting complaints were autophony of voice and a "blocked ear" (94%), mimicking patulous Eustachian tube (pET), including relief with Valsalva or supine position (50%), but without autophony of nasal breathing. Pseudo-conductive loss was found in all dehiscence cases, and 55% of these ears had better than 0 dB HL bone conduction thresholds at 250 and/or 500 Hz. Acoustic reflex was present in 92%. Assuming CT as the "gold standard," VEMP resulted in 90% sensitivity and 94% specificity. One false positive CT, with abnormal VEMP, resulted in surgical explorations negative for Superior SCD but positive for Posterior SCD dehiscence.

Conclusions: SCD may present with various symptoms such as autophony, ear blockage and dizziness/vertigo. A combination of high-resolution CT and audiologic testing is recommended for diagnosis. Low-frequency conductive hearing loss with better than 0 dB HL bone conduction threshold and normal tympanometry, with intact acoustic reflexes, are audiologic signs of SCD. VEMP is highly sensitive and specific for SCD, possibly better than CT.

Acknowledgments:

IRB: M06-09-0426 Children's Hospital Boston

12.

Persistent Dizziness after Surgical Treatment of Vertigo: Prognostic Factors

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Antonio De la Cruz, MD

Objective: Determine factors affecting outcome in surgeries for vertigo.

Study Design: Patient survey and chart review.

Setting: Tertiary referral neurotologic private practice.

Patients/Intervention: Of 113 patients in a questionnaire study (57.5% F, mean age at surgery = 52.3 years), 61 underwent vestibular nerve section, including middle fossa (MFVNS), retrolabyrinthine (RLVNS) and translabyrinthine vestibular nerve section (TLVNS), 25 underwent transmastoid labyrinthectomy, and 27 underwent endolymphatic sac shunt (ES). 80% had Meniere's disease. Mean follow-up was 4.3 years.

Main Outcome Measures: Primary outcomes included AAO-HNS vertigo treatment class, change in AAO-HNS disability rating, current vertigo and imbalance severity ratings, current number of vertigo spells/month and current frequency of imbalance.

Results: Patients in every surgical group indicated currently having 'spinning dizziness', approximately 25% for most of the approaches and 62.5% for MFVNS. 15% had Class C or poorer AAO-HNS vertigo result. Multiple regression analyses using sex, age at surgery, diagnosis, time to follow-up, and pre-surgery vertigo characteristics as independent variables found that for all primary outcome measures, the one factor that significantly predicted outcome was pre-surgery disability rating (higher disability ratings poorer outcomes) (all $p < .02$). For change in disability and current vertigo severity, diagnosis group was also a significant predictor (Meniere's having better outcomes) followed by pre-surgery disability rating. Both procedure type and diagnosis group were significantly related to improvements in imbalance and disability (labyrinthectomy and non-Meniere's patients having poorest outcomes). Additional surgical factors are being evaluated as possible predictors.

Conclusions: Persistent spinning dizziness and imbalance after surgical treatment for vertigo can occur regardless of surgical approach. Those who rate themselves as highly disabled before surgery are less likely to achieve the best outcomes, while frequency and severity of preoperative vertigo are not predictive.

IRB:04-036

**13.
Meniett Pump for Meniere's Disease:
Use and Compliance at Two Years**

Douglas E. Mattox, MD; Mary Reichert, RN

Objective: To review the use of the Meniett pump and control of Meniere's symptoms two years after the device's initial prescription.

Study design: Retrospective case series

Patients: Patients fitting AAO-HNS criteria for Meniere's disease who had failed conventional medical therapy (salt restriction, diuretics) who chose the Meniett pump as a non-surgical alternative in Meniere's management.

Outcome Measures: Continued use or non-use of the device and vestibular symptom control.

Results: Twenty-three patients were prescribed and obtained the Meniett pump between 2/2002 and 4/2004. Two patients were lost to follow-up. Of the 21 evaluable patients, 11 (52%) patients continued to use the device and have good control of vertiginous symptoms at 2+ years. Four patients (19%) were asymptomatic at one year and discontinued the use of the device. Six patients (29%) had no impact on their Meniere's symptoms and stopped using the device within the first 3 months. No complications were attributable to the device; one pump had a mechanical failure and was replaced. Three patients developed otitis media from the myringotomy tube, all of which responded to topical and oral antibiotics without long term complications.

Conclusions: We conclude that the Meniett pump is a useful minimally invasive alternative in the management of Meniere's disease. Among these patients who had failed previous medical management, 71% required no additional intervention beyond the Meniett pump at a minimum of 2 years follow-up. Patients who failed to gain benefit did so from the start of therapy and were able to take advantage of the return policy.

Acknowledgments: Financial Disclosure: This study was not supported financially or otherwise by Medtronic, Inc or its subsidiaries.

IRB: 950-2005

**14.
Use of Stacked ABR and CHAMP Analysis in the
Evaluation of the Dizzy Patient**

Andrea H. Yeung, MD; Wileen Chang, MS, CCC-A
Robert W. Sweetow, PhD; Lawrence R. Lustig, MD

Stacked ABR and CHAMP have been useful in the detection of small acoustic tumors and patients with endolymphatic hydrops. However, the usefulness of these two modalities in standard clinical practice has been largely unstudied. We provide a prospective study to assess the utility of stacked ABR and CHAMP in the clinical evaluation of patients with vestibular complaints.

In a tertiary referral center, 100 patients with a chief complaint of dizziness were prospectively evaluated with stacked ABR and CHAMP. The tests were reliably completed 91% of patients.

43 patients had abnormal stacked ABRs including increased intraaural difference in 49%, decreased amplitude in 37%, and abnormal absolutes in 9% of cases. Clinical diagnoses varied in those with abnormal stacked ABR including BBPV 7%, acoustic neuroma 3%, atypical migraine 17%, vestibular migraine 2%, central etiology 5% and labyrinthitis 2% of cases. For acoustic neuromas, abnormal stacked ABR had a sensitivity of 60% and a specificity of 57%.

Abnormal CHAMP was identified in 11 patients, with clinical diagnoses including vestibular migraine, acoustic neuroma, atypical migraine, Meniere's disease, central origin, and cardiogenic causes. For Meniere's disease, CHAMP had a sensitivity of 40% and a specificity of 90%.

Although stacked ABR and CHAMP are useful in the evaluation of specific vestibular disorders, the role of these two modalities in the clinical evaluation of vestibular patients remains unclear. Future studies should be aimed at determining the function of these studies in clinical decision making.

15.

ErbB and Nrg: Potential Molecular Targets for Vestibular Schwannoma Pharmacotherapy

Joni K. Doherty, MD, PhD

Objective: Identify molecular targets for tumor-specific pharmacotherapeutic development aimed at treating vestibular schwannomas (VS).

Background: VS are associated with loss of functional merlin. Merlin, a putative tumor suppressor, down-regulates ErbB2 receptors in rodent Schwann cells. ErbB2 receptors and neuregulin (Nrg) stimulation are essential for Schwann cell differentiation, survival, and proliferation, and activated ErbB2 and ErbB3 are expressed in VS. Unregulated ErbB pathway activity may contribute to VS tumorigenesis.

Study design: Molecular analyses with retrospective clinical correlation

Setting: Tertiary referral center

Patients: 27 tumor bank specimens from patients operated for sporadic (N= 16) and NF2-related (N = 11) VS.

Intervention(s): VS cell line and tumor bank tissue molecular analyses via cell culture, quantitative PCR, Western, and ELISA techniques; correlation with patient clinical data.

Main outcome measure(s): ErbB receptor family and ligand expression levels, tumor size, NF2 status, and patient age.

Results: VS demonstrated upregulation of EGFR in 77% (63% of sporadic and 91% of NF2-related) and 85% ErbB2 upregulation (69% of sporadic and 100% of NF2-related). ErbB3 was upregulated in 37% of VS and ErbB4 is downregulated in NF2-related. Nrg 1 (69%) and Nrg 4 (75% sporadic, 18% NF2 VS), are upregulated in VS, while Nrg 2 and Nrg 3 are not. Moreover, EGFR expression levels correlate directly with VS tumor size, and EGFR, ErbB3, and Nrg expression levels correlate positively with patient age.

Conclusions: These findings implicate the ErbB pathway in VS growth and as potential molecular targets for VS pharmacotherapy. VS sensitivity to ErbB inhibition, however, requires further investigation.

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16.

Pharmacologic Prevention of Noise Induced Hearing Loss

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Brenda Lonsbury-Martin, PhD; Martin Slade, PhD
Laura Dreisbach, PhD; Peter Torre III, PhD
Ronald Jackson, PhD; Alicia R. Sanderson, MD
Peter Rabinowitz, MD

Objective: To study the effect of oral N-acetylcysteine (NAC) given during weapons training to reduce the rate of noise-induced threshold shifts as well as to determine the safety and tolerance of this antioxidant compound.

Study Design: A prospective, randomized, double-blind, placebo-controlled study.

Setting: Marine Corps training depot field study.

Patients: 566 healthy subjects (289 placebo and 277 NAC)

Intervention: Subjects received three 900mg tablets/day for 16 days of NAC or placebo.

Main outcome measures: Hearing status was assessed prior to and ten days following the 16-day weapons training using pure tone audiometry and distortion product otoacoustic emissions and Navy STS criteria. Questionnaires were completed to monitor tinnitus, side effects and adverse events.

Results: Among right-handed shooters, 21.4% of NAC versus 28% of placebo showed a significant threshold shift (STS) in their right ear ($p=0.044$). The rate of STS trended lower in the trigger-hand ear for NAC compared to placebo (21.6 vs. 27.6% respectively), and NAC significantly reduced STS rate in right ear overall (Navy Stds) as the right ear was exposed to significantly greater sound levels. Side effects of NAC were primarily limited to GI complaints. The number of people experiencing side effects was not significantly different between NAC and placebo. There were no differences in tinnitus between groups.

Conclusion: The results suggest a significant biological effect of NAC in reducing STS rates in ears exposed to more intense rifle fire at the dose used. This study supports the safety of oral NAC. Dose ranging studies for NAC seem warranted.

17.
**Effectiveness of Combinations of Antioxidant Drugs
in the Treatment of Acute Acoustic Trauma**

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Angelica Vasquez-Weldon, BS; Ronald L. Jackson, PhD
Robert A. Floyd, PhD; Richard D. Kopke, MD

Background: Acute acoustic trauma results in oxidative stress to the cochlea leading to overproduction of cellular reactive oxygen, nitrogen, and free radical species. Antioxidants such as N-acetyl-L-cysteine (NAC), a glutathione prodrug, acetyl-L-carnitine (ALCAR), a mitochondrial biogenesis agent, and hydroxylated alpha-phenyl-tert-butyl nitron (4-OH-PBN), a nitron-based free radical trap, have been shown to reduce this damage.

Objective: This study tested the effectiveness of combinations of these three agents in treating acoustic trauma since each agent addresses a different injury mechanism.

Methods: Three groups of chinchillas (n=6 per group) were exposed to a 105 dB narrow-band noise centered at 4 kHz for 6 hours and administered different drug combinations with different doses: 1) administered carrier solution only; 2) administered 4-OH-PBN (50mg/kg) + NAC (100mg/kg); 3) administered 4-OH-PBN (20mg/kg) + NAC (50mg/kg) + ALCAR (20mg/kg). Carrier solutions or drugs were intraperitoneally injected beginning four hours after noise exposure with injections repeated twice daily for the next two days. Auditory brainstem responses (ABR) were measured at 0.5, 1, 2, 4, 6, and 8 kHz before, immediately after, and 3 weeks after noise exposure. Mean ABR threshold shifts were obtained and statistically analyzed using two-way ANOVA.

Results: Both drug combinations completely eliminated permanent threshold shifts. The effective dose of each agent in the three drug combination was approximately half that of the two drug combination which was about half the effective dose for either NAC or 4-OH-PBN alone.

Conclusion: These results demonstrate that combinations of antioxidants can effectively treat acute acoustic trauma. Drug combinations may increase the effectiveness of treatment and decrease the required medication dose.

Acknowledgments:
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18.
**Treatment of Inner Ear Diseases Using New Drug
Delivery System**

Juichi Ito MD, PhD; Takayuki Nakagawa MD, PhD
Tsuyoshi Endo MD, PhD

The experimental and clinical studies were performed to examine the efficacy of the biodegradable gel for application of neurotrophic factors or other drugs into the inner ear.

For the experimental study the concentration of brain-derived neurotrophic factor (BDNF), insulin-like growth factor-1 (IGF-1) and other drugs in the perilymph harvested from guinea pig cochleae after application using a biodegradable gel was measured. The efficacy of application of drugs by a biodegradable gel was evaluated by histologically and functional analysis for protection of spiral ganglion neurons and inner ear hair cells from ototoxic drugs was also evaluated.

An application of BDNF or IGF-1 by a biodegradable gel significantly increased the number of surviving spiral ganglion neurons and inner ear hair cells following deletion of those cells by ototoxic treatment.

Functional assessment by auditory brain stem responses or electrical stimulated auditory brain stem responses demonstrated that an application of BDNF or IGF-1 by a biodegradable gel significantly decreased elevation of thresholds.

These results indicated that biodegradable gel is useful for application of neurotrophic factors and other drugs into the inner ear.

Together with the experimental results, result of preliminary clinical trial of using IGF-1 with biodegradable gel for sudden deafness patients will be presented.

19.

Patient Perceived Benefit Using the Bone Anchored Hearing Aid in Unilateral Deafness

John W. House, MD; J. Walter Kutz, Jr., MD

Objectives: Determine the benefit of the bone anchored hearing aid (BAHA) in patients with unilateral deafness.

Study design: Retrospective case review and questionnaire study.

Setting: Tertiary referral center.

Patients: 127 consecutive patients with unilateral deafness over a four year period were implanted with a BAHA. 51 patients responded. 34 patients (66.7%) had unilateral deafness after translabyrinthine removal of an acoustic neuroma. 8 patients (15.7%) had persistent unilateral severe to profound hearing loss as a result of a sudden sensorineural hearing loss.

Interventions: Administration of the Abbreviated Profile of Hearing Aid Benefit (APHAB) and the Speech, Spatial, and Qualities of Hearing Scale (SSQ).

Main Outcome Measures: Benefit achieved with a BAHA as measured by the APHAB and SSQ scales in patients with unilateral deafness.

Results: Patients with unilateral deafness demonstrated a benefit with BAHA use as measured with the APHAB. Most improvement with the BAHA was seen in the Background Noise (BN) subscale, with a 16.9% improvement. Ease of Communication (EC) and Reverberation (RV) subscales also demonstrated a 14.4% and 6.8% benefit, respectively. The SSQ scale demonstrated better scores in the quality of sound subscale. Most hearing disability as measured by the SSQ scale was related to questions concerning spatial awareness.

Conclusions: The BAHA offers an alternative for patients with unilateral deafness to obtain better hearing in background noise and ease of communication. Localization of sound continues to be difficult for patients with unilateral deafness even with a BAHA.

H01006-1190

20.

Single-stage BAHA Implantation: Is It Safe?

Darius Kohan, MD

Objective: To assess safety and efficacy of one-stage implantation of the titanium retained cochlear stimulator (BAHA) in the adult and pediatric population.

Study Design: Retrospective review of all patients undergoing single-stage BAHA surgery between 2002 and 2006, with minimum 6 month followup. Processors were provided 3 months postoperatively. Data were compared to published outcome studies for two-stage BAHA implantation.

Setting: Ambulatory surgery by a single otologist.

Patients: 30 operated ears in 27 patients. 16 children aged 5-13 with microtia-atresia and maximum conductive hearing loss underwent 18 single-stage BAHA and spare fixture implantation operations under general anesthesia. Monitored anesthesia care was utilized in 10 of 12 adults, 10 of whom received a spare fixture, for various etiologies of hearing loss.

Results: In the pediatric group, there were 2 (11.1%) complications – skin overgrowth and cellulitis – both requiring operative revision. In the adult group, there were 6 patients (46.1%) with complications – flap infection, overgrowth, or failure of osseointegration – of whom 3 required operative revision. Two patients required reimplantation; one patient had the spare fixture exteriorized in the office. Three patients experienced skin overgrowth over the abutment, treated successfully with local wound care and flap revision in the office.

Conclusions: In both adults and children, the single-stage technique for BAHA implantation is a safe and efficient method for aural rehabilitation. Safety profiles for one and two-stage surgery are similar, although the single-stage procedure is more cost effective, avoids a second procedure, and provides for earlier aural rehabilitation.

IRB exempt 10-12-06/212-434-2521

21.

Accelerational Stability of a Bone Anchored Electromechanical Transducer

Travis J. Pfannenstiel, MD; Drew M. Horlbeck, MD
Jim Easter, MS, ME; David Basinger, BSEE

Hypothesis: Under high accelerational load a bone anchored electromechanical transducer will retain its functional relation to the stimulated ossicles without lasting change to conductive auditory physiology.

Background: Incus head displacements of 100 microns have been recorded with yawning, chewing, and atmospheric pressure changes. In some Implantable Middle Ear Hearing Devices (IMEHDs), an electromechanical transducer is anchored to cortical bone while the vibrating tip maintains a stable relationship less than 100 to 200 microns to the stimulated ossicle. This study investigated the effect of high gravitational load on ossicular displacement, IMEHD transducer stability, and resultant function of the transducer and middle ear transfer mechanism.

Methods: Four human cadaveric temporal bones were fitted with an IMEHD transducer (MET; Otologics LLC, Denver, CO) loaded onto the body of the incus. Device and middle ear transfer function were assessed preceding and following acceleration via Laser Doppler Vibrometry (LDV) measurements of incudostapedial joint response to tone burst and mechanical stimulation. Displacement of the transducer reed tip was estimated using real-time inductance measurements as 9G accelerational load was applied six times for each specimen (3 axes, 2 directions).

Results: Small deflections of the transducer reed were measured under high accelerations, with the largest deflection (15 microns) measured in the medial-lateral axis. Following acceleration testing the IMEHD's function was unchanged, and no significant alterations in acoustic or mechanical transfer function were noted.

Conclusions: Conductive auditory physiology was unaffected by high acceleration loading with the IMEHD in place.

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The device tested in this project was the Middle Ear Transducer (MET) developed by Otologics LLC, Boulder, CO. Co-investigators Jim Easter and David Basinger are employees of Otologics, LLC. LtCol Drew Horlbeck, MD, USAF and CPT Travis Pfannenstiel, MD, USA, are presently serving within the Department of Defense and have no financial or other binding affiliation with Otologics LLC.

22.

Phase I Otologics Fully Implantable Hearing System: One Year Results

Herman A. Jenkins, MD; James S. Atkins, MD
Drew Horlbeck, MD; Michael E. Hoffer, MD, CDR MC USN
Ben Balough, MD, CDR MC USN; Joseph V. Arigo, MD
George Alexiades, MD; William Garvis, MD

Objective: A clinical study to assess the safety of the Otologics Fully-Implantable Hearing system.

Study design: Phase I clinical trial with repeated-measures, within-subjects design

Setting: Ambulatory facilities in tertiary hospitals and private practice offices.

Patients: Adult patients with bilateral moderate to severe sensorineural hearing loss.

Intervention(s): Surgical insertion of this prosthesis included securing the transducer to the mastoid bone through an atticotomy, attachment of the transducer tip to the incus via insertion into a laser drilled hole and postauricular subcutaneous implantation of the microphone/battery/electronics capsule.

Main outcome measure(s): Safety of the implantation and subjective patient benefit, aided sound field thresholds and speech discrimination with the subject's own, appropriately fit, walk-in hearing aid(s) and the prosthesis were assessed.

Results: No pre-post implant differences were noted for bone conduction ($p > 0.03$), but slight differences occurred in the pre-post implant air conduction results ($p < 0.05$). These differences were attributed to the healing process and reversed to almost pre-implant assessment levels by the third month evaluation. Results demonstrated 10 to 20 dB of functional gain initially across audiometric frequencies; this increased by 5 to 10 dB with improved fitting algorithms. Pure tone averages and monaural word recognition scores were slightly better for the walk-in-aided condition ($p < 0.05$), while the patient benefit scales favored the postoperative implant-aided conditions.

Conclusions: This prosthesis was well tolerated by the patient without significant surgical complications. Results of this Phase I trial provide evidence that this fully implantable device may be a desirable alternative to currently available hearing aids in patients with sensorineural hearing loss.

IRB Approval Number: IDE G 040052/COMIRB 04-0579

23.

Anatomy of the Round Window and Hook Region of the Cochlea with Implications for Cochlear Implantation and Other Surgical Procedures

Peter M.M.C. Li, MA MBBS; Haobing Wang
Clarinthra Northrop; Saamil Merchant, MD
Joseph B. Nadol, Jr., MD

The anatomy of the hook region is complex and spatial relationships can be difficult to evaluate using two-dimensional histologic slides or cadaveric temporal bones. The goal of this study was to create a three-dimensional model of the anatomy of the hook region to identify the optimal site for cochleostomy in cochlear implant surgery. The model also has implications for other surgical procedures of the inner ear.

The right temporal bone of a 14-year old male was used to create a three-dimensional model. Sections containing the round window membrane (RWM) and surrounding cochlear structures were stained, digitized and imported into a general purpose 3-D rendering and analysis software program (Amira, version 4.1). 3-D models of the RWM, basilar membrane, osseous spiral lamina, spiral ligament, cochlear aqueduct, inferior cochlea vein, scala media, scala vestibuli, scala tympani and surrounding bone were generated. The relationship between these structures and the RWM was evaluated.

The antero-inferior margin of the RWM or adjacent otic capsule was identified as the site for a cochleostomy that will avoid damage to critical cochlear structures and allow implantation directly into the scala tympani.

This model can be downloaded from the Eaton-Peabody Laboratory website: <https://research.meei.harvard.edu/otopathology/3dmodels>.

24.

Hearing Restoration in Old Radical Cavities with the Round Window Implant

Vittorio Colletti, MD; Marco Carner, MD
Liliana Colletti, PhD

Objective: Over the last two years we utilized the Medel-Vibrant Soundbridge (MVSb) onto the round window (RW) in 20 patients who failed to benefit from repeated ossiculoplasties (Colletti et al, in press). In this study we describe patients previously operated on radical cavity.

Study design: Retrospective case review.

Setting: Primary care vs. tertiary referral center.

Patients: Nine adult subjects. Preoperatively, unaided threshold ranged 70-85 dB and speech reception threshold (SRT) at 50% intelligibility averaged 90 dBHL. The patients were assessed at activation, at 6 and 12 months after surgery. **Intervention:** All patients had a radical cavity revision surgery with tympanic membrane reconstruction. No attico-antral obliteration was performed. The floating mass transducer was positioned onto the RW. A groove was created along the remnant of the inferior wall of the ear canal to receive the wire, and the internal processor of the VSB was positioned into the bone of the squama temporalis.

Results: The activation of the RW implant was performed in all patients the day after surgery with immediate hearing recovery. At 12 months aided threshold achieved 30 dBHL or less, aided SRT at 50% intelligibility averaged 40 dBHL with 7/9 patients reaching 100% intelligibility. No complication was observed.

Conclusions: This study indicates that the RWVSB implantation is a viable treatment for hearing rehabilitation of subjects operated on repeated radical cavity surgeries.

Colletti et al: Treatment of Mixed Hearing Losses via Implantation of a Vibratory Transducer on the Round Window. *Int J Audiol.* 45(10):600-8, 2006.

25.

Transient and Distortion Product Evoked Oto-Acoustic Emissions in Normal Hearing Patients with and without Tinnitus

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Vanessa F. Almeida, MD, MSc; André L. L. Sampaio, MD

Subjective tinnitus is generally related to hearing loss but it may be present in 10 to 15% of normal hearing patients. About 35% of temporal bones from patients who had significant tinnitus during their life have normal histology. It is a consensus that tinnitus is abnormal neural activity that may be present at any level of the auditory pathway. However some authors believe that tinnitus begins with a dysfunction of outer hair cells.

In order to test this hypothesis we studied by means of transient (TEOAE) and distortion product evoked oto-acoustic emissions (DPEOAE) 32 patients with tinnitus and pure tone thresholds below 25 db in the 500 to 8000 hz interval and 37 patients with normal hearing and no tinnitus.

The two groups were homogeneous regarding age and gender and did not differ significantly one from another. The distortion product evoked oto-acoustic emissions were abnormal in 68.4% of the patients in the study group and most abnormalities were in the 3000 to 4000 hz interval. The amplitude of the signal and the amplitude/noise index were significantly smaller in the study group in all frequencies when compared with the control group. Transient evoked oto-acoustic emissions were abnormal in 70.2% of the patients in the study group.

Again most abnormalities were found in the 3000 to 4000 hz. Reproducibility and signal/noise index were significantly smaller in all frequencies tested except 1500 hz.

We discuss the meaning of these findings in relation to pathophysiology of tinnitus.

Key words: Tinnitus, oto-acoustic emissions, normal hearing.

094/04

26.

Comparing Distortion Product Otoacoustic Emissions, Auditory Brainstem Response, and Electrocochleography for Intraoperative Monitoring of Auditory Function During Cerebello-pontine Angle Tumor Surgery

Krzysztof F. Morawski, MD, PhD
Kazimierz Niemczyk, MD, PhD
Jorge Bohorquez, PhD; Fred F Telischi, MEE, MD

Problem Addressed: To investigate and compare three strategies of intraoperative monitoring (IM) of auditory function during cerebello-pontine angle tumor (CPAT) surgery: transtympanal electrocochleography (TT-ECochG), auditory brainstem responses (ABR), and distortion product otoacoustic emissions (DPOAEs).

Methods and Measures: Patients with CPAT (n=31) were operated using middle fossa approach. Auditory function was monitored intraoperatively using TT-ECochG, ABR, and DPOAEs. ABR and TT-ECochG were elicited acoustically by clicks (75-85 dB nHL) and DPOAEs were obtained using two primary tones (L1,L2 - 60 to 70 dB SPL; F1,F2 - 2.0 to 5.0 kHz). In all TT-ECochG monitored patients the following components of compound action potential (CAP) were analyzed: N1-Amplitude, N1-Latency, summation potential (SP). In ABR subjects waves III and V were analyzed. Amplitude and phase of DPOAE were monitored as a measure of cochlear status intraoperatively.

Results: In all cases, clear and repeatable CAPs in TT-ECochG strategy were obtained after 64 – 128 samples averaged. TT-ECochG morphology, including N1-Amplitude, N1-Latency and SP, were displayed and sufficiently analyzed on-line every 3-6 sec. Interpretable ABR waveforms required at least 256 (and frequently more) samples during critical moments of tumor removal. DPOAE phase fluctuations were quicker to change at the onset of changes in cochlear function while amplitude measures were better in evaluation of recovery of cochlear function. DPOAE strategy reflecting cochlear activity also needed ABR as a supporting tool for effective IM of hearing.

Conclusions: TT-ECochG and DPOAE effectively recorded even minimal changes in peripheral part of auditory function in real time but needed to be supported by ABR when dissection involved the more distal parts of cochlear nerve and brainstem.

Clinical Significance of Study: TT-ECochG/ABR or DPOAE/ABR strategy may serve as the most effective tool for intraoperative monitoring of auditory function during CPAT surgery.

Acknowledgments: KBN - Poland, Grant No 4 P05C 056 17
IRB: AM - 172/01

27.

Molecular Pathogenesis of Otitis Media in a Mouse Model

Jiang Ping Zhang, MD, PhD; Christopher M. McCarty
Heping Yu; Jill M Giggey; Leah Rae B; Qing Yin Zheng

Although otitis media (OM) is still a common disease in children and adults, the pathogenesis and the underlying genetic pathways are not yet fully understood. We have discovered that mice with the hypophosphatemia-Duke mutation (PhexHyp-Duk) present with a high incidence of otitis media. PhexHyp-Duk/Y hemizygous males are mildly growth retarded in overall body size, show elevated hearing thresholds, and some exhibit circling behavior.

The incidence of OM in PhexHyp-Duk/Y mice was 64.7%. The goblet cells presented metaplasia and hyperplasia in the middle ear epithelia of PhexHyp-Duk/Y males. Increased proliferating nuclear cell antigen (PCNA) expression indicated proliferation of some ciliated cells, nonciliated cells, basilar cells and fibroblasts in PhexHyp-Duk/Y adult males. In addition, increased expression in the ear of Muc5ac, Muc5b and Fgf23 was found in PhexHyp-Duk/Y mutant ears compared to X+/Y wildtype littermate control ears.

The PhexHyp-Duk mutation was previously shown to cause elevated levels of fibroblast growth factor 23 (Fgf23), which in turn is known to increase mouse prostaglandin E2 (PGE2) production. PGE2 is considered to be a mediator of inflammation because of its potent vascular permeability increasing activity. High PGE2 expression may be responsible for the increased Muc5ac and Muc5b gene expression observed in our study, and be a contributor to OM.

We hypothesize that upregulation of PGE2 and Mucin genes represent a new signal transduction pathway for OM.

Acknowledgments:

This project was supported by NIH grant DC005846.

28.

Complications with Hydroxyapatite Cement for Mastoid Cavity Obliteration

Janell S. Ridenour, PA-C; David W. Roberson, MD
Dennis S Poe, MD

Objective: To determine whether hydroxyapatite (HA) bone cement is a suitable material for mastoid cavity obliteration.

Study design: Retrospective case review

Setting: Tertiary care pediatric hospital

Patients: 3 patients, aged 11 – 16, underwent canal wall down mastoidectomy for removal of extensive middle ear and mastoid cholesteatomas.

Intervention: Mastoid cavity obliteration was performed using hydroxyapatite bone cement. Obliteration was done in two patients during the primary operation and in one patient during a planned “second-look” procedure. Cement was covered with vascularized tissue flaps in each case.

Main outcome measures: Failure was defined as the necessity for revision surgery to remove the HA implant.

Results: All three patients required revision surgery to remove the HA cement. Two patients (one primary and one “second-look” obliteration) presented with persistent granulations in the mastoid cavity and the cement was surrounded by granulations. One patient developed a draining post-auricular fistula, vertigo, and mild sensori-neural hearing loss 2 months post-op. Intraoperative findings included extensive skull base osteitis with erosion of the posterior and middle fossa dural plates, and fistulae of the lateral and superior semicircular canals. All patients recovered fully after removal of the HA cement.

Conclusion: This study raises concerns over the use of HA cement for mastoid cavity obliteration. 3/3 implanted patients required revision surgery, two with delayed failure of integration and infection, and one with severe osteitis and significant complications. HA cement may be used for repair of middle ear and small mastoid defects but may not be suitable for obliterating large mastoid cavities.

IRB: pending

29.

Titanium Clip Piston Versus Platinum-Ribbon Teflon Piston: Piston and Fenestra Size Affect Air-Bone Gap

Charles A Mangham, Jr., MD, MS

Objective: To determine if titanium material and a clip attachment to the incus offer a hearing result advantage over the traditional Teflon piston.

Study design: Patient information was gathered retrospectively from medical records. Sixty consecutive patients with Teflon pistons were compared with 30 consecutive patients with titanium pistons.

Setting: Subspecialty private practice.

Patients: Patients with a clinical diagnosis of stapes fixation and a greater than 10 dB air-bone gap on their pre-operative audiogram were eligible for surgery.

Intervention: After informed consent, patients in 2003-2004 received either a Teflon 0.6mm piston or Teflon 0.5 mm piston, and in 2005 received a titanium 0.6 mm piston. Stapes footplate fenestra diameter varied from 0.55 to 0.80 mm.

Main outcome measures: Air-bone gap was evaluated using AAO-HNS guidelines and by ANOVA.

Results: There was a significant advantage in mean air-bone gap for the Teflon 0.6 mm piston (4.9 dB) when the fenestra was 0.7 to 0.75 mm in diameter compared to the titanium 0.6 mm piston (9.1 dB), and compared to the Teflon 0.5 mm piston (8.5 db). Although labeled as 0.6 mm pistons by their respective manufacturers, the Teflon piston had a diameter that was 10% greater than the titanium piston.

Conclusions: Titanium material and clip attachment did not improve hearing outcome compared with a conventional platinum-ribbon Teflon piston. Most of the difference among prostheses could be explained by the observed monotonic decrease in air-bone gap with increasing piston diameter.

IRB: I was contacted by the chairman of the Swedish Medical Center IRB. He told me that my study was exempt and did not need formal review by the IRB. His name is Richard Bensinger MD, 1221 Madison Ste 1200, Seattle WA 98104, phone 206-292-6427.

30.

High Frequency Sensorineural Hearing Loss Following Stapedectomy

Michele B. St. Martin, MD, MBA; Barry E Hirsch, MD

Objective: To describe the pattern and duration of high frequency sensorineural hearing loss following stapedectomy in patients over and under 40 years of age.

Study design: Retrospective case series

Setting: Tertiary referral center.

Patients: All patients who underwent stapedectomy by the senior author during the period between January 1, 1998 and October 1, 2005, with preoperative, four-to-six week postoperative, and at least nine month postoperative audiograms were included. Fifty-nine patients met inclusion criteria, with surgeries performed on sixty-seven ears.

Intervention(s): Stapedectomy was performed using a CO2 laser.

Main outcome measure(s): Change in high frequency (1000, 2000, and 4000 Hz) bone conduction pure tone average (BC PTA) and frequency-specific change in bone conduction.

Results: The mean change in high frequency BC PTA was 2 dB overclosure. While overclosure of 4 dB occurred at 1000 Hz (p<.01) and 6 dB at 2000 Hz (p<.01), a worsening in bone conduction of 6 dB was noted at 4000 Hz at four to six weeks (p<.01). Bone conduction at 4000 Hz improved by nine months, but remained 3 dB lower than preoperatively (p<.05). This effect was more pronounced for patients over 40 years of age. In patients under 40, the difference was not statistically significant.

Conclusions: While overclosure occurs at 1000 and 2000 Hz, a small decrease in bone conduction thresholds occurs at 4000 Hz following stapedectomy. This loss is statistically significant in patients over 40 years of age. Increasing age may be a risk factor for postoperative sensorineural loss in stapedectomy.

Acknowledgments: The authors have no conflicts of interest to disclose.

IRB: 0606040

31.

Investigation of the Mechanics of Type III Stapes Columella Tympanoplasty Using Laser Doppler Vibrometry

Wade Chien, MD; John Rosowski, PhD
Saumil N. Merchant, MD

Background: Type III stapes columella tympanoplasty consists of placing a fascia graft directly onto the stapes head, and is performed for chronic otitis media in conjunction with canal-wall down mastoidectomy. Postoperative hearing results vary widely – from 10 to 60 dB.

Objective: To investigate the mechanics of type III tympanoplasty.

Study Design: Prospective

Methods: Laser Doppler vibrometry was used to measure velocity of the tympanic membrane (TM) graft in 22 patients (23 ears). Measurements were made at three locations: over the stapes, round window and protympanum. These velocity measurements were correlated with stapes mobility (judged at surgery), post-operative aeration status (assessed by autoinflation or postoperative CT scan), and the postoperative audiogram.

Results: The 23 ears were divided into three groups: 1) Non-aerated ears, n=2. The air-bone gaps were 40-60 dB. TM velocities over all three locations were 20-40 dB lower than umbo velocity in normal hearing subjects. 2) Fixed stapes with an aerated middle ear, n=2. The air-bone gaps were 40-60 dB, and TM velocities were equivalent to normal umbo velocity in one case, and lower by 15-20 dB in another case. 3) Mobile stapes and aerated middle ear, n=19. There were two subgroups: smaller air-bone gaps < 30 dB (n=7) and larger gaps > 30 dB (n=12). There were significant differences in TM graft velocities over the stapes between these two subgroups: In the subgroup with smaller gaps, velocities were 3-5 dB lower at frequencies below 350 Hz and 5-10 dB higher at frequencies above 1000 Hz (p < 0.05). This pattern is suggestive of inadequate coupling between the graft and the stapes in the larger gap group. The higher frequency differences could also be explained by a mass effect related to too-thick grafts in the larger gap group.

Conclusions: In addition to stapes mobility and middle-ear aeration, other important determinants of hearing may include how well the TM graft moves with sound and how well it couples to the stapes. Also, laser Doppler vibrometry has utility in post-operative diagnosis of non-aeration of the middle ear.

Acknowledgments: Supported by NIDCD

32.

Phylogeny of the Stapes Prosthesis

Michael H. Fritsch, MD; Ilka C. Naumann, MD

Objective - To create the first ever phylogenetic tree for the evolution of the stapes prosthesis Study design - Retrospective literature review, personal interviews

Setting - University Medical Center

Main outcome measures - Completeness of phylogenetic branches to include all prostheses

Patients/Interventions - N. A.

Results - Many different developments and solutions for stapes prostheses design have been achieved since stapedectomy was first performed. Of the entire stapes prosthesis family tree, four main branches remain that are the sources of most currently used prostheses. Multiple examples of atavistic prostheses, single surgeon usage, and dead-end characteristics exist.

Conclusion - An overview of the complicated phylogenetic tree for stapes prostheses gives great perspective to the history of stapedectomy and insight into characteristics leading to new ways of designing prostheses.

33.

Bivalve Cartilage Inlay: A Short Simple Office Procedure for Closing Small and Medium Size Tympanic Membrane Perforations

Ashkan Monfared, MD; Christopher Bergeron, MD
Justin Ortiz, MD; Howard Lee, PhD
Todd Dray, MD; Richard Gunsalus

Objective: Whether bivalve inlay cartilage-perichondrium myringoplasty (CPM) is successful in closing small and medium perforations in an office setting.

Study design: Retrospective case review.

Setting: Community-based ambulatory

Patients: Adult patients with chronic tympanic membrane perforations.

Intervention(s): Patients underwent pre and post procedure audiograms. Office-based CPM was performed under local and topical anesthesia using cartilage and perichondrium from concha bowl.

Main outcome measure(s): Success (defined as the complete closure of the perforation at follow up of at least one month), post operative pure tone average (PTA), complication rate, causes of failure, and the operative time.

Results: 152 patients were included- 61 male and 91 female. Average age was 48.91 years. Perforations were 3.63 mm in average size (SD = 1.17, range 1-7mm in long axis) and were present for a median of 25 mo (range 1-672 mo) prior to intervention. Most common causes of perforations were chronic serous otitis media (26) followed by acute otitis media (20). Operative time average was 20.2 min (range 10-50 min). Complete closure was achieved in 93 (66.4%) with average follow up of 13.3 months (range 1-69 mo). Minor complications were seen as follows: granulation in 16, nausea and vertigo in 10, and fungal otitis externa in 6 patients. Failure was not related to age or gender of the patient, operative time, or age of the perforation.

Conclusions: Bivalve cartilage inlay technique could be used as a short, simple, and safe procedure in office for closing small and medium size tympanic membrane perforations.

Acknowledgments: None
IRB: Pending

34.

Long-Term Hearing Results after Ossiculoplasty in Comparison with Short-Term Results

Yasuo Mishiro; Masafumi Sakagami, MD, PhD
Tadashi Kitahara; Takeshi Kubo

Objectives: To evaluate the long-term hearing results after ossiculoplasty in comparison with short-term results.

Study Design: Retrospective Study.

Setting: Tertiary referral medical center.

Patients: One hundred eighty-six patients with ossiculoplasty performed by the same surgeon.

Methods: Between 1989 and 2001, 186 ears underwent ossiculoplasty by the same surgeon and were followed for more than 5 years. They comprised 122 cholesteatoma, 31 perforated chronic otitis media, 11 atelectatic ears and 22 other diseases such as middle ear anomaly and tympanosclerosis.

Results: Postoperative hearing outcomes were considered successful if one of the following criteria was achieved; 1) postoperative hearing level within 30dB, 2) postoperative hearing gain more than 15dB, 3) postoperative air-bone gap within 15dB (Otolological Society of Japan,2000). The overall rate of successful treatment was 57.0%. There was no significant difference between ears with stapes present (60.3%) and those without the superstructure of stapes (50.7%). The rate of successful outcome after 6 months was 61.3% in all ears, 65.3% in ears with stapes present and 53.8% in ears without the superstructure of stapes. There was no significant difference between outcomes after 6 months and 5 years. The rate of successful treatment of ears with cholesteatoma/atelectasis was 51.9% and of ears with other diseases were 69.8%. There was a significant difference between cholesteatoma/atelectasis and other diseases ($p<0.05$).

Conclusions: The overall long-term hearing results of ossiculoplasty were not satisfactory. However, the outcomes in ears without cholesteatoma/atelectasis were satisfactory. A breakthrough in the management of cholesteatoma/atelectasis is necessary to improve long-term hearing results.

IRB: not required in Japan

35.

Hyperventilation-Induced Nystagmus and Evaluation of the Dizzy Patient

Angela G. Shoup, PhD; Peter S. Roland, MD

Objective: Nystagmus provoked by hyperventilation may indicate perilymph fistula, cerebellar dysfunction, space occupying lesion or vascular compression. Space occupying lesions and vascular compression may also cause prolongation of the ABR I-III interval. The purpose of this study is to evaluate the prevalence of hyperventilation-induced nystagmus and delineate diagnosis categories and findings from other procedures associated with a positive hyperventilation response.

Study design: Retrospective case review

Setting: Outpatient clinic

Patients: Patients with vertigo and balance dysfunction referred for auditory and vestibular testing, including electronystagmography

Intervention: Addition of hyperventilation testing to the ENG test battery

Main outcome measures: Presence of hyperventilation-induced nystagmus and other associated ENG abnormalities. When available, information about interwave intervals on auditory brainstem response testing, electrocochleography, MRI, rotary chair, platform posturography, and other findings will be included. Finally, the diagnosis provided by the managing physician will be noted.

Results: To date, 649 charts have been reviewed of patients that underwent ENG testing. Of these, 585 (90%) were assessed with hyperventilation. 14.87% (87) had hyperventilation-induced nystagmus. 6 of these (6.9%) were diagnosed with neoplastic growths. 41% were diagnosed with inner ear disease (18 unspecified; 18 Meniere's). 11.5% (10) had cerebrovascular or microvascular disease, 8% had general nervous system disease and 3.4% had migraines. ABR test results were available on 61 (70%) of the 87 patients with hyperventilation-induced nystagmus, and 16 (26%) evidenced prolonged I-III interwave intervals.

Conclusions: Addition of hyperventilation testing to the ENG battery may aid in diagnosis of the patient with vertigo.

IRB: 0402-190

36.

Vestibular-Evoked Potentials in Bilateral Vestibulopathy

Brandon Isaacson, MD

Emily Klerekoper Murphy BA; Helen S. Cohen EdD, OTR

Objective: To determine if patients with bilateral vestibulopathy have measurable vestibular evoked myogenic potentials (VEMPs). To determine if the presence or absence of VEMPs has any correlation with dynamic visual acuity measures.

Study design: Retrospective case review.

Setting: Tertiary referral center.

Patients: Six patients with bilateral vestibulopathy as measured by ENG bithermal calorics and rotary chair testing. Intervention(s): VEMP and dynamic visual acuity (DVA) measures were recorded in all six patients.

Main outcome measure(s): The presence or absence of measurable VEMPs in patients with bilateral vestibulopathy.

Results: In six patients, 9 of 12 ears had intact VEMPs. One subject had bilaterally absent VEMPs and had the worst walking DVA score. Normalized amplitude and threshold measures did not differ significantly between normal subjects and patients. Walking and standing DVA scores were significantly decreased in bilateral vestibulopathy patients compared to normals.

Conclusions: Patients with bilateral vestibulopathy often have residual otolith function as was found in five of the six subjects in this study. Those patients with bilateral vestibulopathy with intact VEMPs may have less risk of falling and decreased oscillopsia compared to patients with absent VEMPs. VEMPs may be used to stratify patients with bilateral vestibulopathy. Bilateral vestibulopathy patients with absent VEMPs may warrant more extensive counseling for fall prevention.

Center for Balance Disorders

Bobby R. Alford Department of Otolaryngology - Head and Neck Surgery

Interim Progress Report for the American Otological Society Research Grants

Effects of Low-Dose Gentamicin on Labyrinthine Structure - Progress Report PI: John Carey, MD

This project has focused on the effects on the labyrinth of intratympanic gentamicin as it is used in the treatment of vertigo in Ménière's disease. Specifically, we have been interested in the structural effects of single intratympanic injections of the drug. Using a chinchilla model, we have previously found that after intratympanic gentamicin treatment vestibular nerve afferents continue to fire spontaneously but lose most of their sensitivity to head accelerations. We correlated these physiologic findings with a number of structural changes: loss of hair cells that appeared to be type I cells, loss of calyceal afferent endings, and loss of stereocilia on many remaining hair cells.

Work during this grant period has focused on explaining the remarkable toxicity of intratympanic gentamicin for type I hair cells. We hypothesized that type I hair cells take up gentamicin more avidly than other cells in the vestibular neuroepithelia. To test this hypothesis, gentamicin was localized within the vestibular epithelium by both direct and indirect methods. Gentamicin conjugated to Texas Red® was used as a direct tracer, and anti-gentamicin antibody provided an indirect means of localization. Conjugated or unconjugated gentamicin was injected into the left tympanic space of chinchillas. The right labyrinth served as control, either untreated or treated with unconjugated Texas Red®. Animals were sacrificed and fixed one or three weeks post-treatment. Confocal fluorescence microscopy was used to determine the localization of gentamicin in semicircular canal cristae.

Results from animals sacrificed within one week of administration showed that numerous type I hair cells still remained throughout the epithelium. The mean intensity in grayscale units of anti-gentamicin labeling for type I hair cells was 28.14 (95% CI 24.60-31.69), for type II hair cells was 17.09 (14.99-19.20), and for support cells was 5.35 (5.34-5.46) ($p < 0.001$, ANOVA). In order to control for the effects of inter-animal variation as well as inter-specimen variation, the ratio of intensity of fluorescence of anti-GT antibody in type I hair cells to that in type II hair cells was determined for each optical slice in order to control for differences in antibody labeling efficacy. The mean ratio was 2.08 (95% CI 1.91-2.24) in treated specimens, but 1.08 (95% CI 1.00-1.15) in controls. Anti-gentamicin antibody labeling appeared in the majority of type I hair cells throughout their cytoplasm, but with greater intensity at the apex ($p < 0.001$). Intensity of fluorescence with Texas-Red conjugated gentamicin was

25.38 (22.83-27.94) in type I hair cells, 15.60 (14.73-16.48) in type II cells and 12.62 (12.06-13.173) in support cells ($p < 0.001$, ANOVA).

In order to again control for the effects of variation between animals and specimens, the intensity of fluorescence of type I hair cells was also expressed as a ratio to the intensity of fluorescence of type II hair cells in the same optical section. The mean ratio of type I to type II fluorescence with GTTR was 1.66 (95% CI 1.36-1.95), again demonstrating greater affinity of type I cells for gentamicin labeled with TR. The ratio within control specimens was 1.02 (95% CI 1.00-1.05).

These results suggest that type I hair cells are more susceptible to gentamicin because they more avidly take up or retain the drug in the early period after administration.

I would like to gratefully acknowledge the assistance of Sofia Lyford-Pike, a Johns Hopkins medical student who devoted a year of research to this project; Dr. Eugene Chu, who worked to bring these techniques to success in our laboratory during his research rotation; Dr. Charles Della Santina, who has been a co-investigator on many of the aspects of gentamicin research; Casey Vogelheim and Mohamed Lehar, our laboratory technicians; and the generous support of the Research Fund of the American Otological Society.

ErbB Regulation of Vestibular Schwannoma Tumorigenesis—Progress Report
PI: Joni K. Doherty, MD, PhD

The objective of this research is to identify molecular targets for tumor-specific pharmacotherapeutic development aimed at treating vestibular schwannomas (VS). VS are associated with loss of functional merlin. Merlin, a putative tumor suppressor, down-regulates ErbB2 receptors in rodent Schwann cells. ErbB2 receptors and neuregulin (Nrg) stimulation are essential for Schwann cell differentiation, survival, and proliferation, and activated ErbB2 and ErbB3 are expressed in VS. Unregulated ErbB pathway activity may contribute to VS tumorigenesis. Molecular analyses with retrospective clinical correlation has been performed on 27 tumor bank specimens from patients operated for sporadic (N= 16) and NF2-related (N = 11) VS via cell culture, real-time PCR, Western blot, and ELISA techniques to quantitate ErbB receptor family and ligand expression levels and their role in tumor cell survival. Expression levels were correlation with patient clinical data, including tumor size, NF2 status, and patient age.

VS demonstrated upregulation of EGFR in 77% (63% of sporadic and 91% of NF2-related) and 85% ErbB2 upregulation (69% of sporadic and 100% of NF2-related). ErbB3 was upregulated in 37% of VS and ErbB4 is downregulated in NF2-related. Nrg 1 (69%) and Nrg 4 (75% sporadic, 18% NF2 VS), are upregulated in VS, while Nrg 2 and Nrg 3 are not. Moreover, EGFR expression levels correlate directly with VS tumor size, and EGFR, ErbB3, and Nrg expression levels correlate positively with patient age.

Western blot analysis of VS confirmed findings of qPCR and protein expression levels correlated well with mRNA expression, indicating that qPCR is a valid measure of ErbB family expression in VS. ELISA is currently being performed to quantitate protein expression in VS and control samples for EGFR, ErbB2, EGF, amphiregulin, and TGF α , based on Q-PCR findings. Because such abundant overexpression of EGFR was evident from Q-PCR results in the majority of VS, EGFR protein expression was confirmed via immunohistochemistry in primary VS. Additionally, the effect of EGFR inhibition using gefitinib (Iressa®) on EGFR expression and phosphorylation was assessed. While EGFR protein expression levels were unaffected by gefitinib expression, as expected, phosphorylation was inhibited.

To explore the clinical relevance of ErbB expression, mRNA expression levels were correlated with clinical parameters, including patient age at presentation, tumor size, and NF2 status. Data were analyzed statistically using the Fisher's Exact test (for age and size data), the Mann-Whitney test (for NF2 vs. sporadic data), and the Spearman's R for correlations. The average age at presentation differed

($p=0.0002$) between NF2 patients (25.83 years ($n=17$); SD 16.34) and sporadic VS patients (avg. 48.19 yrs. ($n=21$); SD 13.07), but VS did not differ significantly in size between NF2 patients (avg. 2.58 cm; SD 1.3) and sporadic VS (2.23 cm; SD 1.13). Nrg expression correlates directly with age ($p=0.0005$) and is an independent predictor of non-NF2 status ($p<0.01$). ErbB4 is downregulated in NF2-related VS and thus predicts non-NF2 patient status ($p<0.01$) if upregulated. The association between NF2 status and ErbB2 upregulation approached significance ($p=0.06$). There was a trend between ErbB3 expression level and patient age ($p=0.06$), and the relationship between Hst expression and tumor size also showed a positive trend ($p=0.09$).

Several trends were observed between expression of ErbB signaling molecules and clinical parameters. A positive correlation was found between EGFR expression levels and tumor size, an inverse relationship between EGFR expression with patient age was identified, and a direct relationship was observed between Nrg expression and patient age ($p<0.05$), indicating that EGFR may be a predictive factor for VS growth. A positive correlation was found between ErbB3 expression and VS in NF2-related VS, but not in sporadic VS; however, due to the small sample numbers in each category, this result did not attain statistical significance. Additionally, a negative correlation was found between NF2 status and ErbB4 expression, which may suggest a less-differentiated state of NF2-related VS, since ErbB4 signals for differentiation. These data are preliminary, and need to be replicated with larger numbers of VS patients and nontumor vestibular nerve samples. Additional genes, especially EGF, as well as proteins levels and activation states should be evaluated. However, the results are very suggestive, and indicate that ErbB signaling state is altered in tumors and correlated with clinical characteristics.

These findings implicate the ErbB pathway in VS growth and as potential molecular targets for VS pharmacotherapy. VS sensitivity to ErbB inhibition, however, requires further investigation.

The Role of Direct Transdifferentiation in Hearing Recovery after Drug Damage in an Avian Model Progress Report

PI: Vincent Y.W. Lin, AOS Research Training Fellow

The specific goal of this grant is to characterize *in vivo* the extent to which direct transdifferentiation as the sole mechanism for hair cell regeneration leads to functional recovery of hearing after drug-induced hair cell loss. Initially, our laboratory had developed an *in vitro* model to study direct transdifferentiation by blocking all mitotic hair cell regeneration in the chicken basilar papillae using aphidicolin. Aphidicolin is a DNA polymerase inhibitor that blocks cell division during S phase. I spent the first 3 months of my grant period attempting to translate the application of aphidicolin to an *in vivo* model, using modified Alzet osmotic pumps to deliver the drug directly into the chicken inner ear. However, I encountered difficulties with compatibility of the solvent used to deliver aphidicolin with the osmotic pump, which led to inconsistent outcomes in translating our *in vitro* results, including animal mortality.

During the past 3 months, I have developed novel *in vitro* and *in vivo* models to study direct transdifferentiation using cytarabine (Ara-C). Ara-C is a DNA chelator and inhibitor of DNA polymerase that also causes mitotic cells to undergo apoptosis. Preliminary *in vitro* cultures using Ara-C confirmed that mitosis of hair cell progenitors after streptomycin damage is completely halted. Further, I have determined a minimum Ara-C dose required to induce full attenuation of mitotic activity *in vitro*. Our most recent experiments confirmed that hair cell regeneration via direct transdifferentiation continues in these cultures.

Additionally, I successfully translated our *in vitro* Ara-C model into an *in vivo* model using the same Alzet osmotic pumps. Ara-C is freely soluble in water and thus did not present any solvent compatibility issues. My first series of experiments focused on the confirmation of full attenuation of mitotic activity. My second series of experiments determined that an ideal dose of 0.5% Ara-C delivered at a rate of 0.5 uL/hr effectively significantly halted mitotic division in lesioned avian basilar papillae while keeping systemic toxicity minimal. I have also confirmed the presence of hair cell regeneration via direct transdifferentiation in birds that were allowed to survive 14 days after a single subcutaneous gentamicin injection (Fig. 1 top panel). Cells that are labeled red (myosin 6, a hair cell marker) are regenerated hair cells. Green labeled cells are positive for bromodeoxyuridine (BrdU), which marks all post-mitotic cells. Therefore, regenerated hair cells that were mitotically derived would label both red and green. As expected, most regenerated hair cells in the experimental birds did not demonstrate any BrdU uptake suggesting they were derived through direct transdifferentiation.

The small number of cells that were derived mitotically (double-labelled or BrdU labelled) appeared on further examination to be in various stages of apoptosis – consistent with the mechanism of Ara-C.

When this is compared to birds in which typical regeneration is allowed to occur (Fig 2 lower panel), there are a significant number of double-labeled cells present.

Future experiments will initially involve quantitative spatial and temporal analyses of hair cell regeneration in experimental and control birds using this new *in vivo* model. Then, using auditory brainstem response testing, I will compare the level of hearing recovery that occurs in experimental birds, which regenerate hair cells entirely through direct transdifferentiation, with recovery in control birds, which employ both mitotic and non-mitotic modes of regeneration.

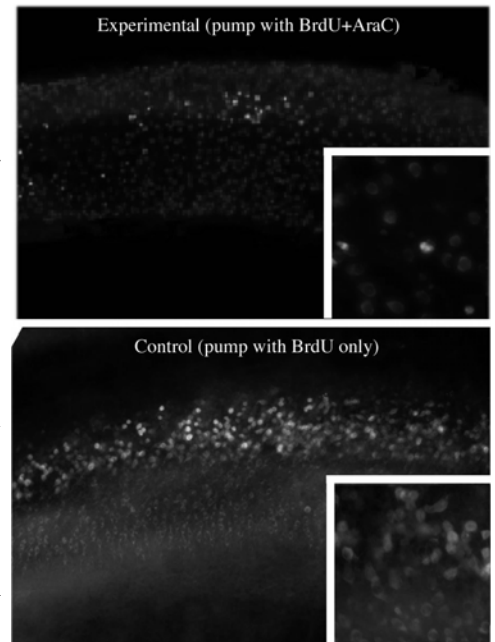


Fig 1: Top panel (experimental) is 14 days post gentamicin injection to allow ample time for regeneration. Bottom (control) panel is 6 days post gentamicin injection.

**Optimization of Local Drug Delivery to the Cochlea –
Progress Report**
PI: Anthony Mikulec, MD

The goal of this study is to develop procedures to optimize drug entry into the cochlea following local application to the round window membrane. We hypothesize that round window membrane (RWM) permeability can be manipulated to allow drugs to more easily and reliably enter the fluid spaces of the inner ear. Currently used local treatment methods for inner ear disorders use medication concentrations and delivery protocols dictated mostly by convenience and anecdotal experience. Agents delivered to the human cochlea through the round window include gentamicin for the treatment of Meniere's syndrome and steroids for the treatment of sudden sensorineural hearing loss, Meniere's syndrome, and tinnitus. A variety of compounds delivered to the round window of animals have shown efficacy in prevention of ototoxicity and age related sensorineural hearing loss. In the future, cochlear gene therapy and support of stem cell transplants will likely require controlled delivery of drugs and growth factors to the fluid spaces of the inner ear.

Round window membrane permeability was evaluated in the guinea pig using the ionic marker TMPA (trimethylphenylammonium). The rate of entry of TMPA into scala tympani was quantified using TMPA-selective microelectrodes sealed into the scala. Marker entry was quantified before and after experimental treatments, permitting the effect of treatments to be assessed in individual animals and minimizing the influence of interanimal variations in RWM permeability. Marker was applied by RW irrigation using a syringe pump at a continuous rate of 5 $\mu\text{L}/\text{min}$. Maintaining a constant middle ear concentration by irrigation allowed changes of TMPA entry rate to be interpreted in terms of RWM permeability alterations. Round window treatments were chosen based on deviations from physiologic values of current clinically utilized drugs. Osmolarity variations and benzyl alcohol concentration (a preservative in some drug preparations) were recreated in TMPA-containing solutions irrigated across the RWM and permeability changes were assessed. The effect of applying suction near the RWM (#3 French) was also similarly evaluated. Results show that suction applied near the RWM results in an approximate doubling of round window permeability, while the presence of benzyl alcohol increases permeability by a factor of about 1.5. Osmolarity changes increased RWM permeability to a small extent. The increased RWM permeability seen with benzyl alcohol and suction have immediate applicability for clinical protocols.

We will now quantify the modulation of entry into the cochlea of clinically relevant drugs using the apical sampling method, in which ten individual 1 μL samples are taken from an apical cochleostomy following drug application to the RWM. Specifically, the entry of clinically relevant concentrations of methylprednisolone, dexamethasone, and gentamicin, with and without benzyl alcohol and with suction of the RWM will be evaluated. In addition, different delivery protocols (round window irrigation, bolus injection, wick systems) will be evaluated using a combination of apical sampling and two-electrode TMPA experiments, where one electrode is sealed into the basal turn of scala tympani and the other is located in the round window niche, allowing direct assessment of concentration on the middle ear aspect of the RWM.

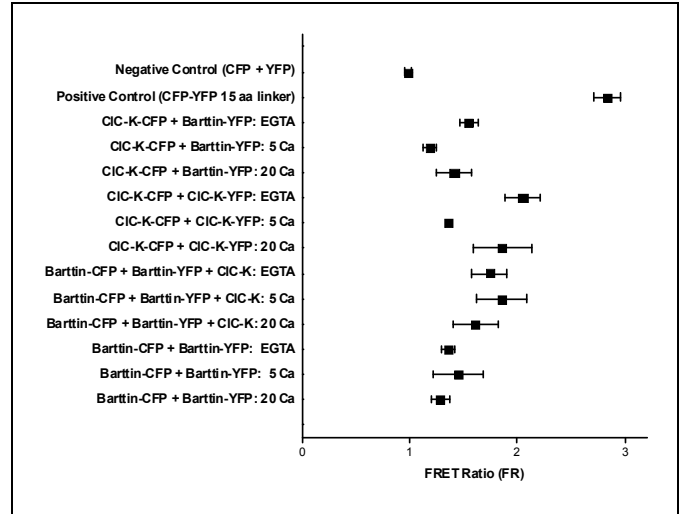
The Role of Chloride Channels in Inner Ear Fluid Homeostasis—Progress Report
PI: Karen J. Mu, AOS Medical Student Training Fellow

The specific aim of this grant is to understand the role of the inner ear lateral wall-specific Cl⁻ channel, CIC-K. We hypothesize that the properties of Cl⁻ currents in the cells of the *stria vascularis* have distinct features that allow them to maintain high Cl⁻ outflow across marginal cells to generate the endocochlear potential. Barttin is an auxiliary subunit of the CIC-K channel and its functional importance in sound transduction is underlined by the fact that mutations in the protein result in Bartter syndrome type IV, of which deafness is a component. Barttin has been identified as crucial for the translocation and function of CIC-K. However, the stoichiometry of the assembly between Barttin and the CIC-K dimer is not known.

We employed Fluorescence Resonance Energy Transfer (FRET) technology in order to determine the composition of CIC-K channels on the surface membrane of human embryonic kidney (HEK) cells. CIC-K1-CFP, CIC-K1-YFP, Barttin-CFP and Barttin-YFP fusion protein constructs were generated using a modified pEGFP-N3 vector. A FRET Ratio (FR) > 1 is defined as a positive FRET signal, indicating a donor-acceptor separation over the range of 1-10 nm, while a FR ≤ 1 indicates an absence of FRET between the two proteins. Co-expression of CIC-K1-CFP and Barttin-YFP fusion proteins displayed a positive FRET signal, demonstrating that these subunits do indeed form an intimate physical interaction. Interestingly, cells co-expressing Barttin-CFP, Barttin-YFP and CIC-K1 (with no fluorescence signal) also displayed a positive FRET signal, implicating the assembly of more than one Barttin subunit with the CIC-K1 dimer in the assembly of the functional channel.

A unique property of CIC-K1 channels within the CIC family is the potentiation of current upon increased extracellular calcium, and we have observed this phenomenon in macroscopic recordings from *Xenopus laevis* oocytes co-expressing CIC-K and Barttin. Upon examination of this effect on HEK cells co-expressing the fusion protein constructs using 1 mM EGTA and 5 and 20 mM of extracellular calcium, we observed that the increase of extracellular calcium does not have an effect on FRET efficiency, reflecting that the observed potentiation of current upon increasing extracellular calcium is most likely not due to modifiable physical interactions between the CIC-K and Barttin subunits. These findings provide a starting-point in developing a working model that will help us better understand the structure and function of CIC-K channels.

See graph on page 68.



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Deceased since 2006 Meeting

Merle Lawrence, PhD (Associate 1959)
Date of Death: 1/29/2007

