during ossiculoplasty. A new strategy of IM of hearing threshold (HT) evaluation was developed by a team of engineers and surgeons on the basis of previously performed researches.

Subjects and Methods: Patients (n = 25) underwent two-stage canal wall-up tympanoplasty due to chronic otitis media with cholestaetoma. During the second look surgery performed 12 months later ossiculoplasty was monitored intraoperatively by LDV and round window electrocochleography (RW-ECochG). Both measures were performed via an enlarged posterior tympanotomy. LDV and RW-ECochG intraoperative tests recorded simultaneously for the same stimulation set. Intraoperative HT was defined automaticaly in auditory steady state response (ASSR) option as well as prosthesis vibration by LDV. Using both intraoperative techniques various configurations of prosthesis placement were tested. On the basis of the preoperative tonal audiometry and post-ossiculoplasty RW-ECochG & LDV thresholds a mini-software calculated an optimal ABGC. Prosthesis moveability tested simultaneously by LDV was showed and correlated with RW-ECochG thresholds.

Results: Postop ABG closure ranged between 15 to 45 dB. HT improvement evaluated intraoperatively correlated with postop ABGC ($r > 0.5$; $p < 0.05$). Various prosthesis configurations and placements resulted in measurable changes in the RW-ECochG thresholds. LDV appeared sensitive mostly to prosthesis position changes manifesting by moveability improvement at 0.5- and 1.0kHz.

Conclusions: RW-ECochG measured in ASSR option was found to be an objective and sensitive technique for IM of HT improvement significantly corresponding with postop ABG-C. LDV showed their usefulness to control prosthesis position changes by confirming better acoustic energy transfer through the reconstructed ossicular chain.

doi:10.1017/S0022215116001663

Basic and translational research in cholesteatoma and ear surgery (N633)

ID: 633.4

Preliminary Analysis of Genetic Alterations in Cholesteatoma

Presenting Author: **Krzysztof Szyfter**

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Learning Objectives:

The Clinic is operating annually over 100 choleasteatomas (655 operations in the years 2010 -2015). Because of a common bacterial infection a bacteriologic analysis indicates for Pseudomonas aeruginosa, Proteus mirabilis and Staphylococcus aureus as the most commonly detected in middle ear infection.

Having in mind a literature suggestion of a partial analogy between oncogenesis and cholesteatoma formation and own experience in identification of oncogenes and tumor suppressor genes modulating progression of laryngeal cancer we have undertaken a molecular analysis targeting for an identification of genetic backgroung of cholesteatoma. Array-CGH scanning of a genome indicated for frequent gains and losses of gene copy number in the genome. The results will be further analyzed to identify amplified regions potentially indicating location of oncogenes and homozygous deletions covering loci oftumor suppressor genes involved in cholesteatoma.

Independently a molecular cytogenetic technique was applied to analyze 8q24 chromosome region to estimate an amplification and potential rearrangement(s) of c-Myc oncogene. Fluorescent in situ Hybridization (FISH) with the use of specific DNA probes (regular fluorescent, break a part) is being applied.

The results will be presented during the meeting.

doi:10.1017/S0022215116001675

Basic and translational research in cholesteatoma and ear surgery (N633)

ID: 633.5

Inflammatory pathways in middle ear cholesteatoma

Presenting Author: **Ewa Olszewska**

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Learning Objectives:

Introduction: Middle ear cholesteatoma (MEC), accompanied by chronic inflammatory response is characterized by invasive growth and osteolytic activity.

Aim: Present the cellular and inflammatory pathways in the pathogenesis of cholesteatoma and adjacent tissues.

Material and methods: Congenital, acquired MEC (study groups) and retroauricular skin specimens (control group, CS) were investigated for markers of inflammation using various immunohistochemistry, Western Blot, cell culture and flow cytometry techniques. Studied markers included proliferation and apoptosis of keratinocytes (PCNA, Ki67, p53, p21, APO2.7), angiogenesis and inflammation (TGF-α), proteasomal degradation pathway (low-molecular mass polypeptide-7 subunit of the immunoproteasome (LMP7), and selected molecular signalling (the DNA-binding high-mobility box 1 (HMGB1) in the protein advanced glycation endproducts (RAGE) axis.

Results: The significantly more intense expression of LMP7 and p21-positive cells was seen in MEC. The LMP7(+) cells

were observed in MEC matrix and perimatrix. There was no meaningful difference between congenital and acquired MEC with respect to p21 contrary to p53. A statistical significance was obtained for APO2.7-positive cells in MEC epithelium (43.23 ± 4.8%) as compared to CS (29.89 ± 6.2%).

More extensive positive immunohistochemical reaction with anti-TGF-alpha, Ki67 and PCNA was observed in MEC matrix and perimatrix compared with CS.

RAGE expression levels was present in all cholesteatoma tissues (strong in 86 %) vs skin 25% (weak) respectively ($p < 0.0001$).

Conclusion: Selected markers of apoptosis, proliferation, angiogenesis and inflammatory response are associated with cholesteatoma development. The co-expression of HMGB1 and RAGE in MEC may result in activation of the intracellular signaling pathways. This process may be responsible for faster accumulation of keratin debris, more invasive process, and affect the clinical course and the treatment outcome.

doi:10.1017/S0022215116001687

Congenital Cholesteatoma (R634)

ID: 634.1

Congenital cholesteatoma of the middle ear: a report of 62 cases

Presenting Author: **Katsumi Doi**

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Introduction: Congenital cholesteatoma (CC) of the middle ear is a rare clinical entity that classically presents as a white mass situated in the anterior-superior quadrant of the middle ear behind an intact tympanic membrane (TM). Derlacki and Clemis established the diagnostic criteria for CC: 1) A pearly white mass medial to an intact TM, 2) Normal Pars Tensa and Pars Flaccida, 3) No history of otorrhea, perforation or previous otologic procedures. CC is seen far more frequently in children, but House and Sheehy remarked adult patients with cholesteatoma behind an intact TM.

Materials and Methods: A retrospective analysis was conducted of the clinical charts of all patients with CC in both children (n = 56) and adults (n = 6) from 1992 to 2015. CCs of the petrous apex (n = 15) were excluded. 1445 cases of acquired and congenital cholesteatomas were treated, therefore, the prevalence of CC should be 4.3% (62/1445).

Results: Based on the staging system by Potsic 54 patients were classified into stage1–4 according to the surgical findings: 11 cases in stage1, 7 in stage 2, 24 in stage3, and 20 in stage4. It was suggested that most CCs could be derived from the epidermoid formation (EF) in 53 cases. A planned two-staged surgery was conducted in 54 cases (87%), while one-stage surgery was adopted in 8 cases. The residual cholesteatoma at the time of second stage surgery was detected in 19 out of 48 cases (40%). The most common residual sites were at oval window (n = 7). Hearing assessment was done in 55 cases: success in 46 cases (84%), moderate in 8 cases, and failure in one.

Discussion: As the stage of CC advanced, the area of its invasion could be enlarged, which should result in a higher risk of CC residual. Considering that CC is usually discovered in its advanced stages (stage 3–4), the establishment of a screening program including otoscopic and CT examinations and hearing tests for early CC diagnosis should be required.

doi:10.1017/S0022215116001699

Back to the future: the evolution of cholesteatoma diagnosis and management (N635)

ID: 635.1

Back to the Future: The Evolution of Cholesteatoma Diagnosis and Management

Presenting Author: **John McElveen**

John McElveen

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Confucius once said, “Study the past if you would define the future.” As an introduction to the 10th International Conference on Cholesteatoma and Ear Surgery, the American Neurotology Society has assembled panelists (Mr. David Moffat (Addenbrooks Hospital), Dr. Jack Lane (Mayo Clinic), Dr. Clough Shelton (U. of Utah), Dr. Moises Arriaga (LSU) and Dr. Dennis Poe (Harvard) to discuss the evolution of cholesteatoma diagnosis and management. Dr. John McElveen (Carolina Ear Research Institute) will moderate the panel.

Mr. Moffat will trace the history of the diagnosis of cholesteatoma from ancient times to the present. Based on the research in 1967 by McKenzie and Brothwell, the existence of chronic suppurative otitis media in prehistoric times has been clearly documented. It was the French anatomist Joseph-Guichard Du Verney who in 1683 first described a temporal bone tumour which was probably a cholesteatoma. However, the term, “cholesteatoma”, was first used by Johannes Peter Muller in 1838. Although a misnomer, it has continued to be used to describe “keratomas” involving the temporal bone and skull base. Abramson *et al* in 1977 provided a more detailed definition of cholesteatomas at the First International Conference on Cholesteatoma.

The classification of cholesteatoma into congenital and acquired and the latter’s subdivision into primary and secondary acquired was the natural sequel of refinements in diagnostic capability which accompanied the use of the microscope both in histopathology and in the clinical examination of the ear (Nylen, 1921).

Since the dawn of medical imaging, radiographic examination of the temporal bone has been used in the evaluation and management of cholesteatoma. X-ray modalities have evolved from plain radiographs (1900–1940s) to polytomography (1950–60s) to single slice Computed Tomography (CT) acquired separately in the axial and coronal planes (1970–1980s) to multislice CT with multiplanar