

losses. However surgery should be individually tailored in majority of the cases.

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Middle ear implants in chronic ears (R774)

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Middle ear implants in chronic ears (R774)

Presenting Author: **Joachim Mueller**

Joachim Mueller¹, Stefan Dazert², Robert Mlynski³, Javier Gavilan⁴, Katsumi Doi⁵, Levent Olgun⁶

¹Section Otolaryngology and Cochlear Implants, ²Ruhr Universität Bochum, ³Klinik und Poliklinik für Hals-, Nasen-, Ohrenheilkunde, Kopf- und Halschirurgie „Otto Körner“

⁴Universitätsmedizin Rostock, ⁵Hospital Universitario La Paz Madrid, ⁶Department of Otolaryngology and Sensory Organ Surgery Osaka University Graduate School of Medicine,

⁶ENT Clinic of Izmir Bozyaka Teaching & Research Hospital

Learning Objectives: To learn how active middle ear implants can contribute to hearing restoration in reconstructive middle ear surgery, especially in chronic ears and mastoid cavities. The RT discusses the coupling strategies to deliver vibrations to the cochlea, compares different coupling methods and reports on the experience in different countries. Also experience with Revision Surgeries, and strategies how to avoid complications are discussed.

During the round table the panelists comment and discuss in a structured way with the audience, how active middle ear implants can contribute to hearing restoration in reconstructive middle ear surgery, especially in chronic ears and mastoid cavities. The RT discusses the coupling strategies to deliver vibrations to the cochlea, compares different coupling methods and reports on the experience in different countries. Also experience with Revision Surgeries, and strategies how to avoid complications are discussed.

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Basic research on the otological fields (N775)

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Regulation of osteoclasts is required to maintain morphology and function of ossicles in middle ear

Presenting Author: **Sho Kanzaki**

Sho Kanzaki¹, Kaoru Ogawa², Koichi Matsuo³
¹School of Medicine, Keio University, ²Scholl of Medicine, Keio University, ³Laboratory of Cell and Tissue Biology, Scholl of Medicine, Keio University

Little is known about how bone-resorbing osteoclasts play a role in the vibration of auditory ossicles. Osteoclasts are specialized multinuclear macrophages that resorb bone. Once bones develop through endochondral and intramembranous ossification (bone modeling), osteoclastic bone resorption in adults is usually followed and balanced by osteoblastic bone formation through “coupling” mechanisms, which maintain bone integrity (bone remodeling). Turnover of temporal bones including the otic capsule and ossicles is much slower than that of the long bones because the former contain high levels of osteoprotegerin (Opg), which inhibits osteoclast formation. We analyzed hearing function and morphology of ossicles in both osteoporotic and osteopetrotic mice. Ossicles in Opg deficient (*Opg*^{-/-}) mice are massively resorbed by abundant osteoclasts, resulting in impaired hearing function. In *Opg*^{-/-} mice, the ligament at the junction of the stapes and the otic capsule is lost by bony ankylosis. In addition, administration of the anti-resorptive drug bisphosphonate prevents not only erosion of auditory ossicles but also progression of hearing loss, suggesting that excessive bone resorption underlies impaired hearing in *Opg*^{-/-} mice. Conversely, osteopetrotic mice, which lack osteoclasts due to either c-Fos or RANKL deficiency, show a smaller volume of the tympanic cavity but larger ossicles compared to controls. The malleal processus brevis thus touches the medial wall of the tympanic in osteopetrotic mice. These data demonstrate that regulation of osteoclastic bone resorption is required to maintain morphology of ossicles and normal hearing function.

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Basic research on the otological fields (N775)

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N775 (Basic Research on the Otological Fields), Middle Ear Mucosal Regeneration by Nasal Mucosal Epithelial Cell Sheets Transplantation

Presenting Author: **Hiromi Kojima**

Hiromi Kojima, Kazuhisa Yamamoto
Jikei University

Learning Objectives: Postoperative regeneration of the middle ear mucosa and pneumatization of the middle ear cavity are of great importance after middle ear surgery. This study developed a new method to transplant autologous nasal mucosal epithelial cell-sheets into the damaged middle ear cavity. The aim of this study was to evaluate postoperative healing after the transplantation of the cell sheets in rabbits. Rabbit nasal mucosal epithelial cell-sheets were fabricated from a temperature-responsive culture dish and transplanted into the damaged middle ear of rabbit, which was surgically created. The healing of middle ears was evaluated with histological methods and computed tomography findings at 8 weeks after transplantation. Functional evaluation was performed by measuring the maximum middle ear total pressure reflecting a trans-mucosal gas exchange function. Two control groups were used: the normal control group and the mucosa-eliminated control group. Transplantation of nasal mucosal epithelial cell-sheets

suppressed the bone hyperplasia and the narrowing of pneumatic space in the middle ear cavity more clearly than the mucosa-eliminated control group. The mucosal gas exchange function was also found to be good in the cell sheet-transplanted group. These results suggested that post-transplanted middle ear cavity was not only morphologically but also functionally similar to the normal middle ear cavity. Nasal mucosal epithelial cell-sheet was confirmed to be useful as an effective graft material after middle ear surgery and hopefully become a novel therapy in the future.

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Basic research on the otological fields (N775)

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Novel biomarker to detect perilymph leakage, CTP (Cochlin tomo-protein, an isoform of Cochlin)

Presenting Author: **Tetsuo Ikezono**

Tetsuo Ikezono¹, Han Matsuda², Tomohiro Matsumura³, Shinnichi Usami⁴, Mamoru Suzuki⁵, Kaoru Ogawa⁶, Yasuhiro Kase⁷

¹Saitama Medical University Faculty Of Medicine, The PLF Study Group, Japan, ²Department of Otorhinolaryngology, Saitama Medical University Faculty Of Medicine, The PLF Study Group, Japan, ³Department of Biochemistry & Molecular Biology, Nippon Medical School, ⁴Department of Otorhinolaryngology, Shinshu University, the Genetic And Anomalous Ear Diseases Study Group, Japan, ⁵Department of

Otorhinolaryngology, Tokyo Medical University, the Peripheral Vestibular Disorder Research Committee, Japan, ⁶22. Department of Otorhinolaryngology, Keio University, the Acute Severe Hearing Loss Study Group, Japan, ⁷Department of Otorhinolaryngology, Saitama Medical University Faculty Of Medicine

Learning Objectives: Perilymphatic fistula (PLF) is an abnormal connection between the inner and middle ear. A procedure for obtaining definite proof of a PLF remains elusive, and methods of diagnosis remain controversial. CTP is a novel biochemical marker that allows a definitive diagnosis of the etiology of PLF-related hearing loss and vestibular disorders. The science of PLF will be discussed in this talk.

Introduction: Numerous biomarkers for dizziness and hearing-loss has been suggested including autoantibodies, inflammatory cytokines, CRP. Among these, CTP (Cochlin tomo-protein, an isoform of Cochlin), perilymph specific protein, is a novel and unique biomarker. We have reported a biochemical test for perilymph leakage detecting CTP in middle ear lavage (MEL, lavaging the middle ear cavity using 0.3 ml saline).

Methods: Recently we could establish a highly reliable ELISA-kit to detect CTP. The Japanese PLF diagnosis criterion is now based on the visual identification of the fistula (not a leakage) and/or detecting CTP. With a help of private clinical test enterprise (SRL inc.) in Japan, CTP test is widely available nationwide, in 170 hospitals.

Diagnostic Accuracy of the test is very high. If there is 2ul of leaked perilymph in the MEL, the test is positive. The diagnostic performance of the test has a high reliability, and the AUC in ROC analysis was greater than 0.90.

Results: The pattern of hearing loss of CTP positive PLF cases varies, including sudden onset, progressive, fluctuating or recurrent. In some patients with positive CTP test, dizziness is their chief complaint not hearing loss.

Conclusions: What We Could Learn from the CTP Test in hearing loss and/or dizzy patients. We believe CTP test will give the answer to the long-standing debate about the existence of PLF.

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Basic research on the otological fields (N775)

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Molecular mechanisms and fundamental therapies for a mouse model of Gjb2-related deafness

Presenting Author: **Katsuhisa Ikeda**

Katsuhisa Ikeda
Juntendo University Faculty of Medicine